Study on the Management of Pregnancies Complicated by Late Preterm Prelabour Rupture of Membranes between 34 and 37 Weeks of Gestation in Woman's Health Centre-Assiut University: A Prospective Study

HAZEM S. MOHAMAD, M.D.
The Department of Obstetrics & Gynecology, Woman's Health, University Centre, Assiut University, Assiut, Egypt

Abstract

Background: Preterm prelabour rupture of membranes (PPROM) is the rupture of membranes during pregnancy before the end of 37 weeks gestation. It occurs in approximately 2-20% of pregnancies and is the cause of about one third of preterm deliveries. PPROM is associated with 18-20% of perinatal deaths. It can lead to significant perinatal morbidity. Treatment varies depending on gestational age, and includes consideration of delivery when rupture of membranes occurs at or after 34 weeks gestation.

Objectives: The aim of this study was to determine the scope of problem of (PPROM) in Woman's Health Center-Assiut University and to address a question about which is better, the expectant management or the decision of labour induction.

Design and Setting: A randomised prospective controlled study was carried out in Woman's Health Centre-Assiut University during the period from first of July 2012 to 31 of December 2012-Assiut-Egypt. Participants were randomly allocated in a 1:1 ratio to induction of labour or expectant management using block randomisation.

Patients and Methods: One hundred, non-laboring, pregnant women with more than 24-hours of PPROM between 34 (+0) and 37 (+0) weeks of gestation were scheduled for this study. Half of them (50 women) were managed by labour induction (group A), while the other half (50 women) were treated expectantly (group B).

Every patient eligible for admission to this study was allotted serially a number from the table of random numbers, so all patients with even numbers induced labour (group A), and those with odd numbers received expectant management (group B).

The primary outcome was the presence or absence of neonatal respiratory distress syndrome as well as the mode of delivery, while the secondary outcome included neonatal sepsis, neonatal hypoglycaemia or neonatal hyperbilirubinaemia.

Results: In the expectant group (B), neonatal sepsis was found in 9 cases (18%), neonatal respiratory distress syndrome was found in 8 cases (16%), neonatal hyperbilirubinaemia was found in 5 cases (10%) and no reported cases of neonatal hypoglycaemia. In the induction of labour group (A), no reported cases of neonatal sepsis, neonatal respiratory distress syndrome was found in 29 cases (58%), neonatal hyperbilirubinaemia was found in 20 cases (40%) and neonatal hypoglycaemia was found in 18 cases (36%).

Conclusion: This current study showed that the expectant management in cases of premature prelabour rupture of membranes between 34 and the start of 37 weeks gestation remains the reasonable choice according to our local social and financial circumstances as regards the availability and cost of neonatal pediatric care units and medications needed for those preterm neonates.

Key Words: Preterm prelabour rupture of membranes – Preterm birth – Antenatal corticosteroids – Antibiotics.

Introduction

PREMATURE prelabour rupture of membranes (PPROM) refers to rupture of the foetal membranes prior to the onset of labour [1], and can occur at any gestational age even at 42 weeks, gestation. For this reason it is also referred to as prelabour ROM. PPROM can occur either at term or preterm (before 37 completed weeks gestation). Prolonged PPROM refers to that longer than 24 hours and is associated with an increased risk of ascending infection [2]. Approximately 8-10% of term pregnancies will experience spontaneous rupture of membranes prior to the onset of uterine activity [3-6]. Intra-amniotic infection and decidual haemorrhage (placental abruption) occurring remote from term, for example, may release proteases into the chorioamnion and amniotic fluid,
leading to rupture of membranes [5]. Also, invasive procedures performed during pregnancy as amniocentesis, chorionic villus sampling, foetoscopy or cervical cerclage, can damage the membranes causing them to leak [7,8].

Preterm PROM is associated with a 4-fold increase in perinatal mortality and a 3-fold increase in neonatal morbidity including respiratory distress syndrome (RDS), polymicrobial intra-amniotic infection, and intraventricular haemorrhage (IVH) [9-11]. The risk of caesarean delivery with its attendant surgical risks to the parturient is higher in preterm PROM as compared with term deliveries [12].

Preterm PROM is largely a clinical diagnosis. Diminished amniotic fluid volume by ultrasound alone cannot confirm the diagnosis but may help to suggest it in the appropriate clinical setting [2].

The initial management of a woman presenting with suspected PPROM should focus on confirming the diagnosis, validating gestational age, documenting foetal wellbeing, and deciding on the mode of delivery [13,14].

Absolute contraindications to expectant management include, intra amniotic infection (chorio-amnionitis), non-reassuring foetal testing, active labour, intraterine foetal death or multifoetal anomalies [14,15].

A favorable gestational age (defined as >34 weeks) can also be regarded as a relative contraindications to continued expectant management in the setting of preterm PROM [2].

Several areas of controversy in the management of preterm PROM still exist. However, preterm PROM is a relative contraindication to the use of tocolytic agents [16]. There is now substantial evidence to suggest that adjunctive prophylactic (empiric) broad-spectrum antibiotics and administration of antental corticosteroids, can significantly prolong latency in the setting of preterm PROM remote from term [17,18].

This study was designed trying to settle the answer about which is better to the mother and her foetus in cases with preterm PROM, the expectant management trying to reach term or the descision of inducing labour.

Patients and Methods

This randomized prospective-controlled study was conducted between the first of July 2012 to 31 of December 2012 at Woman's Health Centre, Assiut University, Assiut, Egypt, and comprised one hundred pregnant women with premature PROM between 34th and the beginning of 37th week of gestation scheduled for this study. 50 Women were managed by labour induction (group A) and the other 50 were managed expectantly (group B).

All patients gave a clear written consent to participate in this study. Every patient eligible for admission to this study was allotted serially a number from the table of random numbers, so all patients with even numbers induced labour (group B) and those with odd numbers received expectant management (group B). The primary outcome was the presence or absence of neonatal respiratory distress syndrome as well as the mode of delivery, while the secondary outcome included neonatal sepsis, neonatal hypoglycaemia or neonatal hyperbilirubinaemia.

This study was approved by the Institutional Review Board of the Faculty of Medicine.

Every effort was taken to exclude contraindications to expectant management. Absolute contraindications included:
- Intra-amniotic infection (chorio-amnionitis) whose diagnosis remains primarily a clinical one with evidence of foetal tachycardia, maternal tachycardia, maternal fever (>37.8 °C) and/or uterine tenderness. Evidence of pus leaking from the cervix on sterile speculum examination can also confirm the diagnosis.
- Non-reassuring foetal testing.
- Patients actively in labour (true labour pain and cervical dilatation and/or ripening).
- Patients with multi foetal anomalies.
- Patients with previous uterine scar (CS, myomectomy or metroplasty).
- Diabetics and immunosupressed ladies.
- Intraterine foetal death.
- Multifoetal pregnancies.

The key recommendations for conservative regimen of treatment included [19]:
- Antibiotics had to be administered to patients with PPROM because this prolongs the latent period and improves the outcomes.
- Corticosteroids had to be given to those patients to decrease the risk of intra ventricular haemorrhage, neonatal respiratory distress syndrome and necrotizing enterocolitis.
- Digital vaginal or cervical examination had not to be performed and sterile speculum usage was preferred.
- Long-term tocolysis was not indicated, although short-term regimen might be considered to facilitate maternal transport and the use of corticosteroids as well as antibiotics.
- Multiple (repeated) courses of corticosteroids were not recommended.

Termination of pregnancy was done to patients of (group A) (induction group), once the diagnosis of PPROM was established. For patients of (group B), there was no place for outpatient management, and the expectant regimen had to be undertaken in Woman’s Health University Hospital because it was not possible to accurately predict which patient would develop complications as infection or placental abruption.

Modified bed rest was notified to all participants of group (B) in this study, in an attempt to enhance reaccumulation of amniotic fluid and to improve uteroplacental perfusion and thereby foetal growth.

Neonatal sepsis was defined as follows [20]:

- Blood culture taken at birth found positive for bacteria excluding staphylococcus epidermidis.
- Two or more symptoms of infection within 72 hours after birth (aponea, temperature instability, lethargy, feeding intolerance, respiratory distress, or haemodynamic instability).
- C-reactive protein >20nmol/L.

Data were collected and analyzed with SPSS version 11 (statistical package for social science, Chicago IL, USA). Statistical methods were applied including descriptive statistics (frequency, percentage, mean and SD) and tests of significance (by $X^2$ statistics or Fisher’s exact test as appropriate). A $p$-value <0.05 was considered statistically significant.

Results

This study comprised 100 (one hundred) pregnant women with preterm prelabour rupture of membranes between the 34 (+0) and 37 (+0) weeks gestation. Sociodemographic data of these women are shown in Table (1).

Table (1): Sociodemographic data.

<table>
<thead>
<tr>
<th></th>
<th>Group (A)</th>
<th>Group (B)</th>
<th>Significance $p$-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>50 cases</td>
<td>50 cases</td>
<td></td>
</tr>
<tr>
<td>Age: (years)-range (Mean±SD)</td>
<td>28.34±2.13</td>
<td>27.63±3.19</td>
<td>N.S.</td>
</tr>
<tr>
<td>Parity (Range)</td>
<td>1-3 (1.8±2.0)</td>
<td>2-4 (2.3±1.0)</td>
<td>N.S.</td>
</tr>
<tr>
<td>Body mass index (BMI) (Kg/m$^2$) (range)</td>
<td>26.1±5.0 (17-40)</td>
<td>27.3±4.5 (18-38)</td>
<td>N.S.</td>
</tr>
<tr>
<td>Previous history of “PPROM”</td>
<td>3 cases</td>
<td>2 cases</td>
<td>N.S.</td>
</tr>
<tr>
<td>Passive % smoking (husband is smoker)</td>
<td>5 cases (10%)</td>
<td>6 cases (12%)</td>
<td>N.S.</td>
</tr>
<tr>
<td>Crowded house % (&gt;3 persons/room)</td>
<td>22 cases (44%)</td>
<td>26 cases (52%)</td>
<td>N.S.</td>
</tr>
</tbody>
</table>

Among patients had to receive expectant management 8 cases (18%) showed neonatal sepsis while no single case developed such complication among the induction group.

On other side, those offsprings who developed respiratory distress syndrome (RDS) and were incubated in the neonatal intensive care unit (NICV) for >5 days, were 29 cases (58%) among the induced group (A), while only 8 neonates (16%) among the expectant group (B) were in need for (NICV).

Neonatal hypoglycaemia (immediate postnatal blood sugar level <50mg/dl) was found in 18 cases (36%) of group (A) (induction group) while neonatal hyperbilirubinaemia occurred in 20 cases (40%) among this group. In the expectant group (B) only 1 cases of neonatal hyperbilirubinaemia accrued, while no cases of neonatal hypoglycaemia was confronted in this group (Table 2).
Study on the Management of Pregnancies Complicated

Table (2): Neonatal outcomes.

<table>
<thead>
<tr>
<th></th>
<th>Group (A) Induction group</th>
<th>Group (B) Expectant group</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neonatal sepsis</td>
<td>Zero</td>
<td>9 (18%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>(n.) (%)</td>
<td></td>
<td></td>
<td>S. significant</td>
</tr>
<tr>
<td>Respiratory distress</td>
<td>29 (58%)</td>
<td>8 (16%)</td>
<td>Statistically</td>
</tr>
<tr>
<td>syndrome RDS (n.) (%)</td>
<td></td>
<td></td>
<td>significant</td>
</tr>
<tr>
<td>Intra partum foetal</td>
<td>Zero</td>
<td>Zero</td>
<td>Not available</td>
</tr>
<tr>
<td>death (n.) (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N. hypertibirubanemia</td>
<td>20 (40%)</td>
<td>Zero</td>
<td>S.S. p&lt;0.001</td>
</tr>
<tr>
<td>Neonatal hypoglycaemia (n.) (%)</td>
<td>18 (36%)</td>
<td>Zero</td>
<td>S.S. P&lt;0.001</td>
</tr>
</tbody>
</table>

Table (3): Maternal outcomes.

<table>
<thead>
<tr>
<th></th>
<th>Group (A) Induction group</th>
<th>Group (B) Expectant group</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antepartum haemorrhage n (%)</td>
<td>1 (2%)</td>
<td>1 (4%)</td>
<td>N.S.</td>
</tr>
<tr>
<td>Cord prolapse n (%)</td>
<td>Zero</td>
<td>Zero</td>
<td>Not available</td>
</tr>
<tr>
<td>Clinical chorioamnionitis n (%)</td>
<td>Zero</td>
<td>9 cases (18%)</td>
<td>S.S.</td>
</tr>
<tr>
<td>Thromboembolic complications n (%)</td>
<td>1 (2%)</td>
<td>Zero</td>
<td>N.S.</td>
</tr>
<tr>
<td>Maternal death n (%)</td>
<td>Zero</td>
<td>Zero</td>
<td>Not available</td>
</tr>
</tbody>
</table>

Mode of delivery:
A- Vaginal delivery n (%) | 32 (64%)                   | 29 (58%)                   | N.S.    |
B- Caesarean section n (%) | 18 (36%)                   | 21 (42%)                   | N.S.    |

Study population (100 cases) Enrolled and randomized

50 cases allocated to induction labour group (A)

50 cases allocated to expectant management group (B)

Labour induced once the diagnosis of PROM was established

Primary outcome:
1- Mode of delivery
2- Neonatal RDS (respiratory distress syndrome)

Secondary outcome:
1- Neonatal sepsis
2- N. hypoglycaemia
3- N. hyperbilirubinaemia

Exclude:
1- Choriammioitis
2- Foetal distress
3- Active labour
4- Mullifoetal anomalies
5- Previous uterine scar
6- JUFD
7- Mullifoetal pregnancy
8- DM or immuno-compromised women

1- Hospital admission
2- Antibiotics
3- Corticosteroids
4- Short term tocolysis
5- Modified bed rest and pelvic rest to encourage resealing and reduce infection

Fig. (1): Flowchart of the study population.
Discussion

We conducted a relatively short prospective randomized study to compare induction of labour and expectant management in women with preterm prelabour rupture of membranes (PPROM) between 34 and 37 weeks of gestational age.

We found that, in pregnancies completed by (PPROM), labour induction reduces the incidence of neonatal sepsis compared to the expectant regimen of management. The number of neonates with respiratory distress syndrome (RDS) was comparable in both arms, and induction of labour, did not increase the risk of caesarean section. However, in this current study labour induction increases the risk of neonatal hypoglycaemia as well as hyperbilirubinaemia.

Our findings are not in line with the results of Hannah et al., [20] who compared labour induction with expectant management in (5041) women with PROM at term and showed that labour induction didn’t reduce the risk of neonatal sepsis as compared to expectant management (2.5% versus 2.8%). This differences in this aspect of results may be due to some limitations in our study because of low financial sources, since our study didn’t include routine cultures from all neonates to diagnose sepsis and neonatal blood samples as well as liquor cultures were taken only for clinical indications at (NICU). In consensus, neonatologists decided whether or not a newborn had suffered neonatal sepsis (suspected or proven). Despite of the lack of blood culture from neonates in this study, we believe that no case of neonatal sepsis was missed from pediatricians in our (NICV) sector.

In our current study, labour induction reduced the risk of clinical chorioamnionitis and this was coincided with the results of Naef et al., [21] and Villar et al., [22].

Our study has also described a relationship between chorioamnionitis and increased risk of neonatal sepsis, respiratory distress and even neonatal death. This was agreeable with the results of Alexander et al., [23] Lau et al., [24] and Leviton et al., [25].

The number of caesarean sections in our study was comparable in the induction as well as expectant groups and this was coinciding with the results of Hannah et al., [20]. However, Buchanan et al., [26] reported that there was an increased risk of caesarean section among the expectant management group in their study.

The current study resulted in decreased risks of neonatal hypoglycaemia and hyperbilirubinaemia in infants of women managed expectantly. This was similar to the results of Van der Ham et al., [27] and Kayem et al., [28]. This was probably, contributed to prolongation of gestational age at the time of delivery. Hyper bilirubinaemia is potentially neurotoxic especially in infants born preterm [29]. However, total bilirubin levels below 30mg/dl, when treated appropriately are not associated with adverse neuro-developmental outcome [30].

Nevertheless, limitations of this study are many. Both strict inclusion criteria and relatively low number of participating patients weaken the collected data. Another potential limitation, is that we reported few secondary, mostly neonatal, outcomes. Although, this is uncommon in maternal-fetal medicine, it is possible that a significant difference can not be found by chance [27].

In conclusion, in pregnancies complicated by PPROM between 34 and 37 weeks of gestation, the incidence of neonatal sepsis is not low. Our study showed that induction of labour did not substantially improve pregnancy outcomes compared with the expectant management.

Acknowledgments:

We thank our colleagues, residents, house officers, high nurses, and nurses as well as all staff members of the neonatal intensive care unit in paediatric hospital-Assiut University for their great help with recruitment and data collection.

References


