A Prospective Study of Mean Birth Weights of Neonates according to Gestational Age at the time of Preterm Premature Rupture of Membranes

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Abstract
Preterm premature rupture of membranes (pPROM) is an important cause of premature delivery. It complicates only 2% pregnancies but is associated with 40% of preterm deliveries. In this prospective study in PGIMER, Chandigarh we recruited 100 women with preterm premature rupture of membranes (pPROM) between 26 to 34 weeks period of gestation. The decision for termination of expectant management was taken by the treating obstetricians according to their clinical judgment and some laboratory parameters. Because of possibility of acquiring chorioamnionitis following pPROM which can adversely affect maternal and foetal well being, pregnancies are terminated, if foetal survival is reasonably certain and birth weights noted according to gestational age at leakage.

Introduction
Preterm premature rupture of membranes (pPROM) is an important cause of premature delivery. In PGIMER, the incidence of pPROM is about 9-10%, which is higher than the reported rate of 3-4%, attributed to it being a referral hospital. In 2011, of the total live born babies, 7% were in the gestational group of 31-32 weeks and 24% in between 33-34 weeks. The survival rate was 63.3% at 28-30 weeks, 86.4% at 31-32 weeks and 92.2% at 33-34 weeks (adjusted) (Annual Statistics of the Departments of Obstetrics and Neonatology). The exact aetiology of pPROM is unknown. Black patients, patients with lower socioeconomic status, smokers, history of sexually transmitted infections, have had a previous preterm delivery, have vaginal bleeding, or have uterine distension (e.g., polyhydramnios, multifetal pregnancy) are at increased risk. Procedures that may result in preterm PROM include circlage and amniocentesis. Multiple factors which cause membrane stretching or degradation, inflammation or increased susceptibility to ascending infection may predispose to it.

Preterm premature rupture of membranes (pPROM) is one of the significant contributor for prematurity. It complicates only 2% pregnancies but is associated with 40% of preterm deliveries1. pPROM is strongly associated with maternal infectious morbidity like chorioamnionitis, endometritis and bacteraemia. The diagnosis of pPROM requires a thorough history, physical examination, and selected laboratory studies.
Evidence of fluid pooling in the vagina, or leaking from the cervical os when the patient coughs or when fundal pressure is applied, will help determine pPROM. Current management remains focussed on interventions to optimize outcomes once pPROM is diagnosed. Treatment varies depending on gestational age and includes consideration of delivery when rupture of membranes occurs at or after 34 weeks gestation. Management of women with pPROM requires an accurate diagnosis in addition to an individual assessment of benefits and risks of continuing pregnancy vs. immediate delivery. Because of possibility of acquiring chorioamnionitis following pPROM which can adversely affect maternal and foetal well being, pregnancies are terminated, if foetal survival is reasonably certain. Preterm delivery occurs within 48 hours in 60-70% of women with pPROM, between 24-32 weeks of gestation and in rest within 2 weeks. When membranes rupture between 28-34 weeks, 50%women go into labour within 24 hours and 80-90%within one week.2 Events leading to preterm birth are thought to be multifactorial and include medical conditions of mother or fetus, genetic influences, environmental exposure, infertility treatments, behavioral and socioeconomic factors and iatrogenic prematurity. Approximately 40-50% of preterm births are idiopathic, 30% are related to preterm premature rupture of membranes (pPROM) and other 15-20% are attributed to medically indicated or elective preterm deliveries.3,4

Materials & Methods
This randomized study was conducted in Clean Labor Room & Antenatal OPD of Department of obstetrics and gynecology of Postgraduate Institute of Medical Education and Research, Chandigarh. A total of 100 women with preterm premature rupture of membranes (pPROM) between 26 to 34 weeks period of gestation were recruited for this study after assessing their eligibility criteria. Pregnant women with period of gestation less than 26 weeks or more than 34 weeks, congenital malformations in fetus, intrauterine fetal death and women having features of chorioamnionitis were excluded from study.

After inclusion criteria were fulfilled, an informed consent was taken from all women prior to recruitment. Detailed history which was followed by general physical and obstetric examination. Obstetric sonography was done to assess fetal biometry, amniotic fluid along with fetal biophysical profile. Non stress test was also performed for complete assessment of fetal well-being. Screening for major congenital anomalies was done in case it had not been done during routine sonography between 16 to 20 weeks. A speculum examination was performed under all aseptic conditions pooling of fluid and swabs were taken from the cervix for bacterial culture and antibiotic susceptibility testing. Hematological tests including hemoglobin, TLC, DLC, and urine analysis (routine and culture) were done at admission. Intravenous Ampicillin 2 gm every 6 hrs for 48 hours followed by oral amoxicillin 500mg every 8 hours for 5 days and after the diagnosis of pPROM was confirmed based on history, clinical examination or on ultrasonography then oral Erythromycin 250mg were given every 6 hourly for 7 days starting from the time of admission. If patient was on conservative management and shifted toward details of cervical swabs sent for culture were noted and monitoring was done till the women goes into labor either spontaneously or after induction. They were monitored for signs and symptoms of infection daily. The decision for termination of expectant management was taken by the treating obstetricians according to their clinical judgment and laboratory parameters. Indications for termination included clinical and/or laboratory evidence of chorioamnionitis, non-reassuring fetal surveillance test results, suspicion of placental abruption, spontaneous onset of labor, induction of labor when patients on conservative management reach 34 weeks if they did not go into labor or were not terminated for
any other indication. If the patient was in labor, mode of delivery and details of delivery and baby details were noted.

**Statistical Analysis**

Quantitative data was presented as mean ± SD or median and inter quartile range, as appropriate. Normality of data was be checked by measures of Kolmogorov- Smirnov tests of normality. For normally distributed data means were compared using unpaired t-test. For skewed data or ordinal data Mann-Whitney test was applied. For categorical variables; number & percentages was calculated .Chi-sq test or Fisher’s exact test was applied for comparison of categorical data. All calculations were two sided & was performed using SPSS version 15 (Statistical Packages for the Social Sciences, Chicago, IL). A P value of <0.05 was considered to indicate statistical significance.

**Results**

Nearly 88% of the women were between 20 -30 years. The mean age in the group A was 26.32 ± 4.79 years, while that in the group B was 26.14 ± 3.82 years (table1). More than half (59%) were nulliparous and the difference in the two groups was not significant, hence the groups were matched for age.

The mean gestational age was 31\textsuperscript{3/7} weeks in group A and 30\textsuperscript{2/7} weeks in group B respectively at the time of recruitment and at the time of pPROM. The women in the group A had higher mean gestational age at the time of recruitment (p=0.140) and at the time of pPROM than in group B (p=0.067)

The mean gestational age at delivery in the group A was 32\textsuperscript{3/7} weeks, while that in the group B was 31\textsuperscript{3/7} weeks. The women in the group A had a significantly higher mean gestational age at delivery than in group B (p= 0.151).

The criteria for diagnosis of pPROM in the present study were: suggestive history plus any of the following, demonstrable leakage on speculum examination and/or AFI <5 cm.

Antibiotics coverage consisting of ampicillin IV for 48 hours followed by oral amoxicillin for 5 days and oral erythromycin for 7 days was given to all patients. Seventeen (34%) out of fifty women in group A and eighteen (36%) out of fifty women in group B completed the antibiotic course.

There were 7 women diagnosed with clinical chorioamnionitis in the group A and 6 in group B.

**Table:** Antibiotics course in both groups

| Antibiotics Course | Group A (n=50) | Group B (n=50) |
|--------------------|----------------|----------------|
| Completed          | 17 (34%)       | 18 (36%)       |
| Not completed      | 33 (66%)       | 32 (64%)       |
| p value            | 0.883          |                |

Out of 50 patients in group A, one patient had follow up outside PGIMER. Out of 49 patients, 36 (73.5%) patients went into spontaneous labor and delivered. In group B 41 (82%) out of 50 patients went into spontaneous labor and delivered. The difference was not statistically significant.

The expectant management had to be terminated in 22 patients: 13(26.5%) in group A and 9(18%) in group B for various reasons. The indications for termination are shown in table. Two patients in group A presented with bleeding per vaginum and diagnosed to have abruption placenta and terminated. At delivery retro placental clots were present in both. One woman in group B had abruption. Seven women (14.3%) in group A and 6 (12%) in group B presented with signs of clinical chorioamnionitis and terminated. One woman from each group was induced for labor before 34 weeks due to poor biophysical profile (decreased fetal movements).One woman in group A had placenta previa and presented with bleeding per vagina and underwent emergency caesarean section.

**Table:** Indications of termination of conservative management

| Indication                  | Group A (n=49) | Group B (n=50) |
|-----------------------------|----------------|----------------|
| Spontaneous onset of labor  | 36 (73.5%)     | 41 (82%)       |
| Clinical Chorioamnionitis   | 7 (14.3%)      | 6 (12%)        |
| Abruptio                     | 2 (4.1%)       | 1 (2%)         |
| Completion of 34 weeks       | 2 (4.1%)       | 1 (2%)         |
| Poor Biophysical Profile    | 1 (2%)         | 1 (2%)         |
| Placenta Previa             | 1 (2%)         | 0 (0%)         |
| p value                     | 0.877          |                |
Of the women in the group A, 36(73.5%) out of 49 had vaginal delivery. One woman delivered outside PGIMER. Two (4.1%) out of 36 needed forceps delivery in view of fetal bradycardia. Thirteen underwent caesarean section. Emergency caesarean was done in 12(24.5%) out of 13 and 1(2.2%) patient had undergone elective caesarean. In the group B, 41(82%) out of 50 had vaginal delivery and 9(18%) out of 50 had undergone emergency caesarean section. One patient of the 41 in group B who had a vaginal delivery had a forceps delivery.

| Mode of delivery | Group A (n=49) | Group B (n=50) | p value |
|------------------|----------------|----------------|---------|
| Vaginal          | 34(69.4%)      | 40(80%)        |         |
| Emergency LSCS   | 12(24.5%)      | 9(18%)         |         |
| Elective LSCS    | 1(2.2%)        | 0              |         |
| Instrumentation  | 2(4.1%)        | 1(2%)          |         |

Post-partum complications
No woman had postpartum hemorrhage. Post-partum fever was recorded in 3 (6%) patients in group A and 1 (2%) in group B. Details of the cases that developed post-partum fever are given in table 15. There was no case of maternal mortality in woman included in either of the groups. Three out of 4 patients had chorioamnionitis which was clinically significant (p=0.01).

Birth weight
The overall mean birth weights in the group A ranged from 1735.60±392.67 grams, and in the group B from 1588.34±409.34 grams. The difference in the two groups was not statistically significant. The mean birth weights in the two groups are detailed in table 17.

Table: Mode of delivery in both groups

| Mode of delivery | Group A (n=49) | Group B (n=50) | p value |
|------------------|----------------|----------------|---------|
| Vaginal          | 34(69.4%)      | 40(80%)        |         |
| Emergency LSCS   | 12(24.5%)      | 9(18%)         |         |
| Elective LSCS    | 1(2.2%)        | 0              |         |
| Instrumentation  | 2(4.1%)        | 1(2%)          |         |

Table: Mean birth weights according to gestational age at leakage

| Gestation at leakage(weeks) | Mean birth weight (grams) | p value |
|-----------------------------|----------------------------|---------|
| Group A (n=49)              | Group B (n=50)             |         |
| Overall                     | 1735.60±392.67             | 1588.34±409.34 | 0.069 |
| 26-27<sup>W</sup>           | 1491±387.72                | 1211±489.35  | 0.345 |
| 28-30<sup>W</sup>           | 1543.75±406.41             | 1448.73±462.48 | 0.548 |
| 31-33<sup>W</sup>           | 1870.53±334.88             | 1777.70±209.39 | 0.221 |

Discussion
This present study was planned to look for neonatal weights after patient went into preterm premature rupture of membranes. The women recruited for the two groups had comparable demographic profile. The mean age of women in group A was 26.32±4.79 years while that in group B was 26.14±3.82 years. The difference was not statistically significant. The mean gestational age was 31<sup>3/7</sup> weeks and 30<sup>2/7</sup> weeks in group A and group B respectively at the time of recruitment. More than half (59%) were nulliparous and the difference in the two groups was not significant.

In the present study, the criterion used for the diagnosis of pPROM was a suggestive history along with leakage demonstrable on speculum examination or sonographic evidence of reduced amniotic fluid. Demonstrable leakage on speculum examination was present in 85% women and overall 78% women had an evidence of oligohydramnios defined by AFI<5. In the present study 36(73.5%) women from group A and 41(82%) from group B went into spontaneous labor. In the group A 2(4.1%) women were terminated for completion of 34 weeks as compared to 1(2%) in group B. The difference was not statistically significant probably due to the small sample size. Clinical chorioamnionitis was the indication of termination in 13 women in both the groups. Amongst the women who underwent induction of labor, misoprostol was used as the cervical ripening agent in 7 out of 11 (63.6%) and 7 out of 9 (77.8%) women in group A and group B respectively. In group A 73.5% had a vaginal delivery including two patients delivered by forceps in view of fetal bradycardia. This was comparable to that in the group B (82%). In the present study, expectant management was terminated at 34 weeks if no other indication of termination developed (as recommended by the RCOG and ACOG guidelines)<sup>2,5</sup>. The mean gestational age at delivery in the group A was 32<sup>3/7</sup> weeks, while that in the group B was 31<sup>3/7</sup> weeks. The women in the group A had a higher
mean gestational age at delivery than in group B (p= 0.151) which was not statistically significant. The overall mean birth weights in the group A ranged from 1735.60±392.67 grams, and in the group B from 1588.34±409.34 grams. The difference in the two groups was not statistically significant (p=0.069). Khandelwal et al⁶ was reported 1804.5+/−882.2 grams and 1720.9+/−847.6 grams as the mean birth weights in group A and group B groups respectively. David⁷ in his study was reported mean birth weight as 1717.4 ±631 grams and 1637.7 ±630 grams respectively in both groups. The higher birth weights can be explained probably by the ethnic differences.

Conclusion
The data suggests that the two groups had comparable demographic profile. The mean gestational age being 31 3/7 weeks and 30 2/7 weeks in group A and group B respectively at the time of recruitment. Demonstrable leakage on speculum examination was present in 85% women and overall 78% women had AFI<5 which were diagnostic criterion in my study. The mean gestational age at delivery in the group A was 32 3/7 weeks, while that in the group B was 31 3/7 weeks which was not significant (p=0.151). The mean birth weights in the group A ranged from 1735.60±392.67 grams, and in the group B from 1588.34±409.34 grams and the difference was not statistically significant.

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