A Prospective study of period of gestation at the time of preterm premature rupture of membranes and period of gestation at the time of delivery

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Abstract
Background: *A Prospective study of period of gestation at the time of preterm premature rupture of membranes and period of gestation at the time of delivery at PGIMER, CHD.*
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. Treatment varies depending on gestational age and includes consideration of delivery when rupture of membranes occurs at or after 34 weeks gestation. 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. 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.
Keywords: *preterm premature rupture of membranes (pPROM), period of gestation.*

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 33-34weeks. 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 deliveries[1]. 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]

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 than26 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

This study was conducted in the Department of Obstetrics and Gynecology, Nehru Hospital, attached to Post Graduate Institute of Medical Sciences, Chandigarh from July, 2012 to November, 2013.Table 1shows 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.

Table 1: Demographic profile of the women in both the groups

Age group (years)	Group A (n=50)	Group B (n=50)	Total	p value
20 – 25	20	25	45	0.547
26 – 30	23	20	18	
31 -35	6	3	6	
>=36	1	2	3	
Mean±SD	26.32±4.79	26.14±3.82		

Table 2: Period of gestation at the time of pPROM

Gestational age (weeks)	Group A (n_1=50)	Group B (n_2=50)	p value
$23 - 26^{6/7}$	1	7	
$27 - 30^{6/7}$	22	19	
$31 – 33^{6/7}$	27	24	
Mean	$31^{3/7}$ weeks	$30^{2/7}$ weeks	0.067

Table 2 shows the distribution of the women according to period of gestation at at the time of pPROM. The mean gestational age was $31^{3/7}$ weeks in group A and $30^{2/7}$ weeks in group B 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)but the difference was not clinically significant, hence the women in two groups were matched according to period of gestation at the time of Pprom.

Table 3 shows that 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. The women in the group A had a significantly higher mean gestational age at delivery than in group B (p= 0.151).

Table 3: Period of gestation at the time of delivery

Gestational age (weeks)	Group A (n=50)	Group B (n=50)	p value
$26 - 29^{6/7}$	6	12	
$30 - 32^{6/7}$	19	20	
$33 – 35^{6/7}$	25	18	
Mean	$32^{3/7}$ weeks	$31^{3/7}$ weeks	0.151

Table 4 shows the criteria for diagnosis ofpPROM in the present study suggestive history plus any of the following, demonstrable leakage on speculum examination and/or AFI <5 cm. On admission, all 100 women had presented with a history suggestive of pPROM, 85% had leakage demonstrable on speculum examination and 78% had AFI <5 on ultrasonography.

Table 4: Tests for diagnosis of pPROM at admission

Test for diagnosis	Group A (n=50)	Group B (n=50)	Total	P value
History	50 (100%)	50 (100%)	100 (100%)	1.000
Speculum test	42 (84%)	43 (86%)	85 (85%)	0.779
AFI <5 cm	41 (82%)	37 (74%)	78 (78%)	0.334

AFI: Amniotic fluid index

The mean AFI in group A was 3.654 and in group B was 2.085 with p=0.551as shown in table 5

Table 5: Mean AFI (in cms) on recruitment

	Group A (n₁=50)	Group B (n₂=50)
Mean AFI	3.654(Range:1.0-9.0)	2.085(Range:0.0-10.0)
SD	2.085	2.354
P value	0.551	

AFI: Amniotic fluid index, SD: Standard Deviation

Table 6 shows 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.

Table 6: 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	

The duration of expectant management (also called the latency period) was calculated from the time of membrane rupture till the time of delivery (following spontaneous or induced labor).
The mean latency period is shown in table 7.The mean latency period is significantly more in group B as compared to group A (1.32 days versus 3.38 days). The difference in the two groups is statistically significant in gestational age group of 26-27$^{6/7}$and31-33$^{6/7}$

Table 7: Comparison of mean latency period in the two groups

Gestation at leakage (weeks)	Mean Latency period (days)				p value
	Group A (n=50)		Group B (n=50)		
	Mean±SD	N	Mean±SD	N	
26-27$^{6/7}$	0.45±0.41	04	6.55±8.27	8	.032
28-30$^{6/7}$	1.91±3.27	16	1.47±1.73	15	.197
31-33$^{6/7}$	1.13±1.72	30	3.50±6.98	27	.025
Overall	1.32±2.29	50	3.38±6.26	50	.001

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 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 8: 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%)
Abruption	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	

Table 9: 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%)	0.513
Emergency LSCS	12(24.5%)	9(18%)	
Elective LSCS	1(2.2%)	0	
Instrumentation	2(4.1%)	1(2%)	

Discussion

Preterm premature rupture of membranes accounts for 40% preterm deliveries, resulting in significant neonatal morbidity and mortality. In the present study, women with preterm premature rupture of membranes were hospitalized and after fulfilling eligibility criterion and after randomization. All women were kept on conservative management, 77 women went into labor and 22 patients needed induction. Indication of delivery, method of termination and mode of delivery were noted. The women recruited for group A and group B had a comparable demographic profile**.** The mean age of the women in the group A was 26.32 ±4.79 years, while that in the group B was 26.14 ± 3.82 years which was not statistically significant. The mean period of gestation at pPROM in women in the group A $31^{3/7}$ weeks was comparable to that of the women with group B $30^{2/7}$weeks (p=0.067). The mean latency period in the group A was 1.32±2.29 days which was less than that in the group B 3.38±6.26   days. This difference was

statistically significant (p= .001). 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. In one large study by Schucker et al[3] of patients at term revealed that 95 percent of patients delivered within approximately one day of PROM whereas an analysis of studies evaluating patients with preterm PROM between 16 and 26 weeks' gestation determined that 57 percent of patients delivered within one week, and 22 percent had a latent period of four weeks

Clinical chorioamnionitis was the indication of termination in 13 women in both the groups. 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%). This included one instrumental

delivery. Caesarean section was done in 13 patients (26.5%) in group A and 9 (18%) patients in group B respectively. In similar study by Khandelwal[4] 120 (67.8%) women out of 120 in 12 hours group and 34 (56.4%)women out of 44 in 24 hours group underwent vaginal delivery.57 women (32.2%) out of 120 and 34(43.6%) needed caesarean section in both groups respectively.

Conclusions

This prospective randomized control study was planned to assess the period of gestation at the time of pPROM and period of gestation at the time of delivery after randomization in women with preterm premature rupture of membranes between gestation 26 weeks to 34 weeks The two groups had comparable demographic profile. The mean age of the women in the group A was 26.32 ± 4.79years, while that in the group B was 26.14± 3.82 years which was not statistically significant. 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 AFI in group A was 3.654 and in group B was 2.085 with p=0.551 which was not clinically significant. The latency period was calculated from the time of membrane rupture till the time of delivery The mean latency period in the group A was 1.32±2.29 days was less than that in the group B 3.38±6.26 days which was   statistically significant (p=0 .001). The rate of vaginal delivery (73.5% vs. (82%) and rate of Caesarean section (26.5% vs. 18%) were comparable in two groups. 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).

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