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Original Research Article

A study to find out the association between duration of preterm premature rupture of the membrane's delivery interval and maternofetal complications

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ABSTRACT

Background: The main maternal complications of preterm premature rupture of the membranes (PPROM) are chorioamnionitis, puerperal pyrexia, abruption and the neonatal complications are neonatal sepsis, congenital pneumonia, neonatal ICU stay and neonatal death. The aim of the study is to find out the association between duration of latent period in PPROM i.e. the time period between rupture of membrane to delivery and maternofetal complications.
Methods: The present study was a Prospective observational study conducted on 240 preterm antenatal women with PPROM in the Department Obstetrics and Gynecology, SATH, GMC, Thiruvananthapuram. The gestational age at rupture of membranes, latent period from time rupture of membranes to delivery, gestational age at time of delivery and the maternal and neonatal outcome were compared and subjected to statistical analysis.
Results: Maternal chorioamnionitis in the group with PPROM delivery interval between 2-7 days (79.3%) whereas there were (13.8%) in which PPROM delivery interval was less than 24 hrs. Puerperal pyrexia in 2-7 days delivery interval was 11.3% and in <24 hrs were 2.6%. Neonatal sepsis in 2-7 days was 28.3% and 12.5% in<24 hrs. Congenital pneumonia in 2-7 days was 16.9% and in<24 hrs was 11.6%.
Conclusions: In the present study membrane rupture between 28-34 weeks gest age and latency period. 2-7 days were associated with high incidence of maternal chorioamnionitis, puerperal pyrexia congenital pneumonia, early onset neonatal sepsis and neonatal death. Undue prolongation of pregnancy may increase the risk of chorioamnionitis, neonatal sepsis and neonatal deaths.

Keywords: Preterm premature rupture of the membranes, Latent period, ICU stay

INTRODUCTION

Preterm premature rupture of membranes (PPROM) is defined as rupture of membrane before 37 completed weeks of gestation. The primary etiology of PPROM is infection where organisms have been found in one third of the samples. The time from preterm ruptured membranes to delivery is inversely proportional to the gestational age when ruptures occurs Carroll and associates, 1996.[1] The primary maternal risk with expectant management is infection. The incidence of subclinical chorioamnionitis may be as high as 60% with PPROM, but serious maternal systemic infection is rare (2%), if treatment is initiated promptly. The use of a number of therapeutic agents such as corticosteroids, antibiotics and tocolytic agents particularly with PPROM may pose additional maternal risk Kappy.[2] Chlamydia trachomatis and group B *Streptococcus* have been

implicated Gravett.[3] The risk of preterm premature rupture of membranes associated with group B streptococcal infection was independent of infection with *C. trachomatis* and *N. gonorrhoeae*, Alger.[4]

The neonatal risks of expectant management of PPROM include infection, fetal distress, fetal restriction deformities. Prematurity and associated hyaline membrane disease are the most significant factor in increased perinatal morbidity and mortality associated with PPROM, because delivery occurs within 7 days in over 80% of cases Verloove-Vanhorick.[5] Most authors report that prolonged membrane rupture is associated with increased fetal and maternal sepsis Ho and colleagues.[6]

A large randomized controlled trial, the preterm prelabour rupture of the membranes close to term (PPROMT) trial is currently under way in Australia, comparing the outcome in terms of maternal (chorioamnionitis, postpartum infection treated with antibiotics, antepartum, haemorrhage, induction of labour, mode of delivery, duration of hospitalisation, and maternal wellbeing at four months postpartum) and fetal (neonatal sepsis, respiratory distress, perinatal mortality, neonatal intensive care unit admission, assisted ventilation and early infant development) parameters of early management and expectant groups. The trial recruits 1800 cases of PPROM at between 34-36 weeks of gestation, and divides them into (a) an early planned birth group which will be delivered within 24 hours and (b) an expectant management group in which birth will occur after spontaneous labour, at term or when the attending clinician feels that birth is indicated according to usual care. Results are expected shortly.[7]

Cox and associates 19888 described pregnancy outcomes of 298 consecutive women who gave birth following spontaneously ruptured membranes between 24 and 34 weeks. Although this complication was identified in only 1.7 percent of pregnancies, it contributed to 20 percent of all perinatal deaths. By the time they presented, 75 percent of the women were already in labour, 5 percent were delivered for other complications, and another 10 percent were delivered within 48 hours. In only 7 percent was delivery delayed 48 hours or more after membrane rupture. This latter subgroup, however, appeared to benefit from delayed delivery, because there were no neonatal deaths.

This contrasted with a neonatal death rate of 80 per 1000 in preterm new-borns delivered within 48 hours of membrane rupture.[8] Nelson and co-workers reported similar results.[9]

In PPROM at 24-28 weeks gestation, around 70-80% of these pregnancies deliver within one week, half within 4 days. The greatest risk to the fetus is still prematurity, and this risk currently outweighs any potential advantage in delivering a patient with occult intrauterine infection. Consequently, expectant management is the most favored option at this gestation. The use of amniocentesis to detect the possibility of occult intrauterine infection remains controversial, particularly as fetal lung maturity is unlikely Gonik.[10]

In a study conducted by Kornacki et al archives of Medical Science, the frequency of almost all neonatal complications, including infections, was found significantly higher in children delivered by mothers with PPROM before 31 weeks gestation than in babies of patients with PPROM and delivery into account, there was a significant increase of neonatal sepsis and pneumonia only in new-borns born 48 hrs or more after PPROM which occurred before 31 weeks gestation.[11]

METHODS

Design of study was Prospective observational study. Patients admitted in Obstetrics and Gynaecology Department SAT Hospital, Medical College Trivandrum, Kerala with PPROM in the period October 2010-November 2011 was included in the study group.

Inclusion criteria

Singleton pregnancies complicated by preterm premature rupture of membranes, between gestational age 24 weeks to 37 weeks that admitted in the labour room of SAT hospital during the period of study, were included in the study.

Exclusion criteria

All cases of multiple pregnancy, diabetes, severe pre-eclampsia complicating pregnancy, Fetal congenital anomaly detected by ultrasound prior to delivery, Intrauterine fetal demise prior to the onset of PPROM.

Sample size calculation

A pilot study was conducted in the labour room of SAT hospital for the purpose of estimating minimal sample size required for the prevalence study. Using the confidence limit of 31.6% for calculating the minimum sample size required for the study using the formula.

$$N = \frac{z^2 \times p \times (100 - p)}{1^2}$$

Where n is the sample size, Z is the level of significance for p value 0.05; z is 1.96

P = 31.5, 1 = p/5 = 6.3

So, n = 1.962×31.5×69.5 / 6.32 = 211.8

A sample size of 240 was chosen.

Outcome variables

Number and proportion of PPROM cases complicated by each of chorioamnionitis, placental abruption, operative delivery APGAR score at 5 minutes, early neonatal death, early onset neonatal sepsis, neonatal respiratory distress, congenital pneumonia and APGAR score at 5 minutes. The gestational age at rupture of membranes, latent period from time rupture of membranes to delivery, gestational age at time of delivery and the maternal and neonatal outcome were compared and subjected to statistical analysis.

Methodology

All consecutive cases of PPROM fulfilling the inclusion and exclusion criteria in the study period were included (240 cases). Patients were recruited as they were admitted to the labour room of SAT hospital and followed up till their discharge from the hospital

All patient details were collected on a structured proforma after getting their consent. A detailed clinical examination was done after confirming the diagnosis of PPROM by a sterile speculum examination to note the pooling of liquor in the posterior fornix. Special investigation like TC, DC, CRP and USG was done to rule out chorioamnionitis.

In labour, she was watched for progress, fetal distress, blood stained liquor and mode of delivery was noted. After delivery, a detailed neonatal examination was done by the pediatrician to determine the APGAR score, birth weight, birth asphyxia respiratory distress and evidence of sepsis. All stillbirths and neonatal deaths were noted.

Postnatally, the patients were observed for postpartum pyrexia, foul smelling lochia and antibiotics were continued. Uncomplicated patients and their babies were discharged on the third postnatal day following a vaginal delivery after pediatric clearance and fifth post-operative day following caesarean section. Babies with prolonged observation or admission in neonatal ICU stayed back.

Data were analyzed using statistical package for social sciences (SSPS) version 10. The proportion of each of the mentioned complications in PPROM cases was noted. To elucidate the associations and comparisons between different parameters, chi square test, Fisher's exact probability test and Odds ration were used as needed. Pearson's correlation coefficient was used to analyze the relationship between two selected quantitative variables. All statistical tests were two tailed. All p values less than 0.05 was considered significant.

RESULTS

Table 1 shows 218 out of 240 cases of PPROM have latency period either less than 1 day or between 1 day and 1 week. Only 22 cases are distributed across the other 4 latency period groups. PPROM to Delivery interval was less than 24 hrs in 46.7% of cases and was 2-7 days in 44.2% of cases.

Table 1: Duration of PPROM to delivery interval.

PPROM to delivery interval (days)	Frequency	Percentage
≤1	112	46.70
2-7	106	44.20
8-14	8	3.30
15-21	9	3.80
22-28	2	0.80
28	3	1.30

Table 2 shows 42.5% of cases were delivered between the gestational age 32-34 weeks, 36.7% delivered between 34-37 weeks, 15% between 30-32 weeks, 3.8% between 28-30 weeks and 1.7%≤ 28 weeks.

Table 2: Gestatational age at delivery in weeks and PPROM.

Gestational Age at delivery (weeks)	Frequency	Percentage
≤28	4	1.7
28-34	148	61.7
30-32	37	15.4
32-34	102	42.5
34-37	88	36.7

Table 3: PPROM to delivery interval and maternal Chorioamnionitis.

PPROM to delivery interval (Days)	Maternal chorioamnionitis	
	Yes	**No**
≤1	4	1
	13.80%	51.20%
2-7	23	83
	79.30%	39.30%
8-14	1	7
	3.40%	3.30%
15-21	1	8
	3.40%	3.80%
22-28	-	2
		0.09%
>28	-	3
		1.40%
Chi square: 17.559; p <0.01		

Table 3 shows there were 23 cases (79.3%) of maternal chorioamnionitis, in the group with PPROM delivery interval between 2 to 7 days where as there were only 4 cases (13.8%) in which PPROM delivery interval was less than 24 hrs. Chi square shows statistically significant difference in the proportion of chorioamnionitis between the two latency groups namely latency less than one day

and latency 2-7 days. The proportion of chorioamnionitis in the 2-7 days latency group is high enough to be statistically significant.

Table 4 shows 112 cases with latency≤1 day, one developed abruption. Among the 106 cases with latency period 2-7 days, 2 developed abruption.

Table 4: PPROM to delivery interval and abruption.

PPROM to delivery interval (days)	Abruption	
	Yes	No
≤1	1	111
	25.00%	47.00%
2-7	2	104
	50.00%	44.10%
8-14	-	8
	-	3.40%
15-21	-	9
	-	3.80%
22-28	-	2
	-	0.80%
>28	-	2
	25.00%	0.80%
Chi square: 19.119; p <0.01		

Table 5 shows among 112 cases with latency≤1 day, three developed puerperal pyrexia. Among the 106 cases with latency period 2-7 days, twelve developed puerperal pyrexia. This difference is statistically significant (p value<0.001).

Table 5: PPROM to delivery interval and puerperal pyrexia.

PPROM to delivery interval (days)	Puerperal pyrexia	
	Yes	No
≤ 1	3	109
	14.30%	49.80%
2-7	12	94
	57.10%	42.90%
8-14	-	8
	-	3.70%
15-21	3	6
	14.30%	2.70%
22-28	2	-
	9.50%	-
>28	1	2
	4.80%	0.90%
Chi square: 36.755; p <0.001		

Table 6 shows among the cases with latency≤1 day, 14 developed neonatal sepsis. Among the cases with latency period 2-7 days, 30 developed neonatal sepsis. The difference is statistically significant (p<0.001).

Table 7 shows among the cases with latency≤1 day, 13 developed congenital pneumonia. Among the cases with latency period 2-7 days. 18 developed congenital pneumonia. The difference is statistically significant (p<0.05).

Table 6: PPROM to delivery interval and neonatal sepsis.

PPROM to delivery interval (days)	Neonatal sepsis	
	Yes	No
≤ 1	14	98
	25.50%	53.00%
2-7	30	74
	54.50%	41.10%
8-14	4	4
	7.30%	2.20%
15-21	6	3
	10.90%	1.60%
22-28	1	1
	1.80%	0.50%
>28	-	3
	-	1.60%
Chi square: 23.416; p <0.001		

Table 7: PPROM to delivery interval and congenital Pneumonia.

PPROM to delivery interval (days)	Congenital Pneumonia	
	Yes	No
≤ 1	13	99
	31.70%	49.70%
2-7	18	86
	43.90%	44.20%
8-14	3	5
	7.30%	2.50%
15-21	5	4
	12.20%	2.00%
22-28	2	-
	4.90%	-
>28	-	3
	-	1.50%
Chi square: 24.456; p <0.001		

Table 8 shows 43 out of the 112 cases (30.1%) with latency≤1 day required neonatal ICU care while in the second group 82 cases (57.3%) required neonatal ICU care. Two neonatal deaths occurred in the group with latency <24 hrs whereas 8 neonatal deaths occurred in the group with latency 2-7 days.

Table 9 shows 218 out of 240 cases of PPROM have latency period either less than 1 day or between 2-7days. Only 22 cases are distributed across the other 4 latency period groups and so valid statistical analysis is limited to only the first two latency period groups. In analysing complications in the 233 PPROM cases with membrane

rupture occurring beyond 28 weeks, it was found that gestational age at PPROM and latency period till delivery were two factors strongly associated with maternal chorioamnionitis, early onset neonatal sepsis, congenital pneumonia and neonatal deaths. Analysis of correlation between continuous quantitative variables namely gestational age at membrane rupture and latency period in these 233 cases gives Pearson's correlation coefficient of -0.693 ($p<0.001$). This implies that either one of these parameters is dependent on the other or both these parameters are dependent on a third unidentified common parameter.

Table 8: PPROM to delivery interval and neonatal ICU stay, neonatal death.

PPROM to delivery interval (days)	Neonatal ICU stay		Neonatal death	
	Yes	No	Yes	No
≤1	43	69	2	110
	30.10%	71.10%	13.30	49.10%
2-7	82	22	8	96
	57.30%	24.70%	53.30%	43.30%
2	6	2	2	6
	4.20%	2.10%	13.30%	2.70%
15-21	9	-	-	9
	6.30%	-	-	4.00%
22-28	1	1	1	1
	0.70%	1.00%	6.70%	0.40
Chi square: 41.82; p <0.001			Chi square: 34.63; p <0.001	

Table 9: PPROM delivery interval and maternofetal complications.

PPROM delivery interval	Maternofetal complications						
Days	**N**	**Chorio amnionitis**	**Abruption**	**Puerperal pyrexia**	**NNS**	**NND**	**Cong. pneumonia**
≤1	112	4 (3.5%)	1 (0.89%)	3 (2.6%)	14 (12.5%)	2 1.7%)	13 (11.6%)
2-7	106	23 (21.7%)	2 (1.8%)	12 (11.3%)	30 (28.3%)	8 (7.5%)	18 (16.9%)

DISCUSSION

Of the 127 cases with PPROM who had rupture of membranes at gestational age 28-34 weeks, large majority 60.6% had a latency period 24 hrs. Of the cases with PPROM AT 34-37 weeks, 80 patients had a latency period of less than 24 hrs and the remaining 26 delivered after 24 hrs. This may be because of the fact that in our hospital, all patients with PPROM prior to 34 weeks are being conservatively managed after confirming fetal viability and ruling out anomalies. Consistent with this, 2 out of 7 patients who had rupture of membranes before 28 weeks had latency exceeding 28 days. Induction of labour is done in our hospital after 34 weeks or if the patient developed chorioamnionitis.

In a study by Nicaise et al among PPROM patients between 24- 34 weeks of gestation, the mean gestational age for onset of PPROM was 30.8 weeks and for delivery was 31.4 weeks. Higher values of mean gestational age for the onset of membrane rupture and delivery as well as a shorter latency in the present study may be explained by the inclusion of patients with PPROM between 34-37 weeks of gestation in the study.[12]

Maternal and fetal risks vary with the gestational age at membrane rupture. Morales et al expectantly managed 94 singleton pregnancies with ruptured membranes prior to 25 weeks. The average time gained was 11 days. Although 41 percent of infants survived to age 1 year, only 27 percent were neurologically normal.[13]

Prior to the mid-1970s, labor was usually induced in women with preterm ruptured membranes because of fears of sepsis. Two randomized trials compared labor induction with expectant management in such pregnancies. Mercer and colleagues 1993 randomly assigned 93 women with pregnancies between 32 and 36 weeks to undergo delivery or expectant management. Fetal lung maturity, as evidenced by mature surfactant profiles, was present in all cases. Intentional delivery reduced the length of maternal hospitalization and also reduced infection rates in both mothers and neonates.[14]

Expectant management may result in prolonged antenatal hospitalization with antibiotic treatment, regular monitoring and intensive care of the neonate in the event of sepsis. On the other hand, planned early delivery may necessitate intensive care of the neonate for problems associated with prematurity. Additional number of days

of admission to the hospital will increase the economic burden, particularly neonatal intensive care.

There were 23 cases (79.3%) of maternal chorioamnionitis in the group with PPROM delivery interval between 2 to 7 days whereas there were only 4 cases (13.8%) in which PPROM delivery interval was less than 24 hrs. The proportion of chorioamnionitis in the 2-7 days latency group is high enough to be statistically significant.

Similarly, the frequency of abruption, puerperal pyrexia, neonatal sepsis and congenital pneumonia were significantly higher in the 2-7 days latency group compared to the group with PPROM delivery interval<1 day.

Two neonatal deaths occurred in the group with latency<24 hrs whereas 8 neonatal deaths occurred in the group with latency 2-7 days. 43 out of 112 cases (30.1%) required IBN care while in the second group 82 cases (57.3%) required IBN care. APGAR at 5 minutes shows similar pattern with significantly higher number of newborns in the 2d-7 days latency group showing lower APGAR scores.

Though the number of patients with latencies>7 days were low, it was observed that 6 cases of neonatal sepsis and 5 cases of congenital pneumonia was observed in the group containing nine cases with PPROM delivery interval between 15-21 days. Among the three cases in which latency period was more than 28 days, two ended up in neonatal death. These findings imply that as the PPROM delivery interval is prolonged there is more chance of adverse maternal and neonatal outcome.

Limitations

Since, in the hospital setting in which this study was conducted, it is standard practice to follow expectant management as far as possible in PPROM cases with membrane rupture before 34 weeks, it can be inferred that the PPROM delivery interval is a function of gestational age at membrane rupture. It cannot be ruled out whether the influence of one of these parameters on the outcome is not due to its correlation with the other parameter.

CONCLUSION

Gestational age at PPROM and latency period till delivery were two factors strongly associated with, maternal chorioamnionitis, early onset neonatal sepsis, congenital pneumonia and neonatal deaths. Membrane rupture between 28-34 weeks gestational age and latency period 2-7 days were associated with high incidence of maternal chorioamnionitis, puerperal pyrexia, congenital pneumonia, early onset neonatal sepsis and neonatal death. The mean gestational age at PPROM in this study was 33.02 weeks. The mean PPROM delivery interval between 24 to 37 weeks of gestation was 3.5 days in this study: In the present study membrane rupture between 28-34 weeks gest age and latency period. 2-7 days were associated with high incidence of maternal chorioamnionitis, puerperal pyrexia congenital pneumonia, early onset neonatal sepsis and neonatal death. Although antibiotics are given to all patients with PPROM, the relative proportion of chorioamnionitis, neonatal sepsis and neonatal deaths were found to be significant. Undue prolongation of pregnancy may increase the rate of neonatal sepsis. Careful planning and management of pregnancy in women with history of PPROM is essential to increase the likelihood of a healthy outcome for the mother and infant. Also, strict aseptic precautions in the labour room and new born unit may go a long way in improving new born survival. A team effort by the obstetrician and neonatologist in a tertiary care setting can ensure a healthy and fruitful life for the mother and her baby. Patients should be counseled realistically regarding the outcome of pregnancies with PPROM and they should be involved in the decision-making process. It is suggested that more studies should be encouraged to find out the association between duration of PPROM delivery interval and maternofetal complications so that we can plan for effective management and reduce the complications.

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