



Original Research Article

Outcome of neonates born to mothers with premature rupture of membranes

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ABSTRACT

Introduction: Premature rupture of membranes (PROM) is a syndrome characterized by rupture of the fetal membranes before labour. Acute chorioamnionitis complicates 0.5% - 10% of all pregnancies but the incidence may be as high as 3-25% in pregnancies complicated by PROM of more than 24 hours duration. Intrauterine infection specially chorioamnionitis is one of the most serious problems found by the practicing Obstetrician and subsequently by the Pediatrician. The incidence of neonatal infection for infants born to women with PROM range from 1 – 2.6%.

Aims & Objectives: To know the incidence, clinical course, outcome of early onset sepsis following PROM more than 18 hours. **Materials & Methods:** This is a prospective study conducted from December 2018 to September 2020 in SCB Medical College and Hospital and SVPPGIP Cuttack. All neonates born to healthy mothers with PROM more than 18 hours during their hospital stay were studied.

Results: 53.3% of the cases had Premature rupture of membranes of 18-24 hours duration, 38.3% cases had Premature rupture of membranes of 24 to 72 hour and 8.4 % cases had Premature rupture of membranes of more than 72 hr. RDS was the most common clinical manifestation (37.5%) followed by septicemia (10%), meningitis (1.7%) and pneumonia 1.7%. Most common organisms isolated in blood culture were Staphylococcus followed by Klebsiella, E. coli, Pseudomonas. The incidence of neonatal infection in neonates born to mothers with PROM was 10%.

Conclusion: Premature rupture of membranes is responsible for increased perinatal morbidity among preterm neonates & directly proportional to duration of PROM.

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1. Introduction

Premature rupture of membranes (PROM) is one of the most common problems in Obstetrics complicating approximately 5-10% of term pregnancies. Preterm premature rupture of membranes (PPROM) occurs approximately in 1% of all pregnancies.¹ The fetal and neonatal morbidity and mortality are significantly affected by duration of latency and gestation at PROM. The primary complication for the mother is risk of infection,

complications for the newborn consists of prematurity, fetal distress, perinatal asphyxia, cord compression, deformation and altered pulmonary development.² The most significant maternal risk of term PROM is intrauterine infection the risks of which increases with the duration of membrane rupture.³ For patients with PPRM the most likely outcome is preterm delivery within one week with its associated morbidity and mortality risks such as respiratory distress, necrotizing enterocolitis, intraventricular haemorrhage and sepsis.⁴ Neonatal sepsis can be divided into two main sub types depending on whether the onset is during the first

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72 hours of life or later. Early onset septicemia is caused by organism prevalent in the genital tract or in the labour room. Early onset bacterial infections occur either due to ascending infection following rupture of membranes or during the passage of baby through infected birth canal.⁵ PROM of duration more than 18 hours is the appropriate cut off for increased risk of neonatal infection.⁶ There are recommendations of antenatal antibiotic administration in pregnant women who had PROM \geq 18 hours the regimen to prevent neonatal infection postnatally still varies among institutions.⁷ The key to the management is an accurate assessment of gestational age, pulmonary maturity and presence or absence of sepsis. However the management is special in preterm patient in whom the risk of fetal and maternal infection that can accompany expectant treatment has to be weighed against potential improvement in neonatal outcome that comes with greater maturity of fetal lungs. Currently most authorities accept a plan of active management which includes prevention of infection, delay of delivery until fetal maturity is achieved and active intervention by induction if labour is no longer preventable or if early infection is suspected. The knowledge of incidence of early onset sepsis in relation to PROM and its effect on neonatal outcome is essential in order to prevent the neonatal morbidity and mortality. Diagnosis of early onset sepsis close observation for early signs of sepsis, aggressive evaluation and early treatment has decreased the incidence of early onset sepsis associated with PROM. The present study was undertaken to evaluate newborns born to mothers with PROM for early onset sepsis. Neonatal outcome has also been evaluated in the prospective study.

2. Aims & Objectives

To know the incidence, clinical course, outcome of early onset sepsis following PROM more than 18 hours and compare risks of individual outcomes among neonates according to the latency periods from membrane rupture until the time of delivery.

3. Materials and Methods

This is a prospective study conducted from December 2018 to September 2020 in SCB Medical College and Hospital and SVPPGIP Cuttack. This has been approved by institutional ethical committee clearance vide letter no-452/14-10-2020. All neonates born to healthy mothers with PROM more than 18 hours during their hospital stay were studied. Total neonates included in the study were 120, who have qualified for the study as per criteria described. A detailed history of mother was taken including age, parity, socioeconomic history, occupation, history of previous pregnancy loss, history of antepartum haemorrhage, Obstetric history with emphasis on exact time of rupture of membranes, duration history and antibiotics

before labour were evaluated. Detailed birth history including resuscitation details, Apgar score and gestational age assessment were evaluated. In examination of the neonate the pulse, respiratory rate, CRT and temperature were noted followed by systemic examination. Required investigations are done for the neonate and followed during their hospital stay.

3.1. Inclusion criteria

All neonates born to healthy mothers with PROM more than 18 hours.

3.2. Exclusion criteria

1. Antepartum haemorrhage.
2. Medical disease in mother other than infection.
3. Neonates with major congenital malformation.
4. Neonates born with meconium stained liquor.

3.3. Methods

Following investigations were carried out:

1. Hb%, TLC was estimated by automated analyzer.
2. Differential leucocytes count (DLC), Band cell count, toxic granules was done by peripheral smear.
3. CRP semi quantitative estimation by latex agglutination technique.
4. Blood culture and sensitivity.
5. Chest x-ray (if required).
6. CSF analysis and head ultrasound (if required).

3.4. Statistical analysis

All observational data was tabulated and analyzed by appropriate statistical method to draw final inference and conclusion.

Statistical methods like descriptive methods (graphs, numerical summaries), inferential methods (confidence interval, significance tests) are used.

P-Value In statistics: The P-value is the probability of obtaining results at least as extreme as the observed results of a statistical hypothesis test, assuming that the null hypothesis is correct. The p-value is used as an alternative to rejection points to provide the smallest significance at which null hypothesis is rejected.

Smaller P-value means that there is stronger evidence in favor of alternate hypothesis.

4. Observation

The analysis of the present study shows that out of 120 neonates 64(53.3%) were males and 56(46.7%) were females, 9(7.5%) cases weighing <1500gms, 32(26.6%) cases were weighing between 1500 and 2500gms and 79(65.9%) cases weighing >2500 gms, 25(37.5%)

Table 1: Distribution of cases according to different parameter (n=120)

Parameters		Number	Percentage
Sex	Male	64	53.3
	Female	56	46.7
Birth weight In grams	<1500	9	7.5
	1500-2500	32	26.6
	>2500	79	65.9
Gestational age	<37 Weeks	45	37.5
	>37 Weeks	75	62.5
Mode of delivery	Normal	84	70
	Caesarean section	36	30
Prom in hours	18-24 Hours	64	53.3
	24-72 Hours	46	38.3
	>72 Hours	10	8.4
Cry history	Immediately after birth	114	95
	Delayed cry	6	5
	R.D.S	45	37.5
	Septicemia	12	10
	Meningitis	2	1.7
Type of morbidity	Pneumonia	2	1.7
	NEC	0	0
	IVH	0	0
	Asymptomatic	59	49.1
	<22,>18	42	35
Maternal age in years	>22-<27	61	52.2
	>28	17	14.8
Parity	PRIMI	78	64.8
	MULTI	42	35.2
Socio-economic status	Lower	62	51.6
	Middle	50	41.6
	Higher	8	6.8

were of <37 weeks and 75 cases (62.5%) were of gestational age more than 37 weeks, 84 (70%) neonates are delivered by normal vaginal delivery and 36 (30%) were delivered by caesarean section, 64 (53.3%) had PROM of 18-24 hrs duration, 46 (38.3%) had 24-72 hrs and 10 (8.4%) had >72 hrs of duration. 114 (95%) neonates cried immediately after birth and 6 (5%) babies have history of delayed cry. Morbidity was seen in 61 (50.9%) out of which RDS being most common 37.5%. PROM is more in primipara cases (64.8%) and more common in lower socioeconomic status (51.6%). Table 1

Out of 120 cases 61 cases (50.8%) had morbidity. In that 61 cases (50.8%) 45 cases were born before 37 weeks. So neonatal morbidity was common in preterm babies. Out of 45 cases of RDS (37.5%), 31 cases (25.8%) were of preterm gestation. There was highly significant difference in morbidity among preterm (<37 weeks) and term (>37 weeks). Table 2

Chi-Square Tests shows p-value < 0.001 which is statistically significant. Neonatal morbidity like RDS, Septicemia are more common in preterm premature rupture of membrane cases. Table 3

As duration of PROM increases incidence of Septicemia also increases. Thus if duration of PROM is more than 24 hours, the incidence of septicemia was 10% in comparison to zero incidence when it is less than 24 hours. R.D.S was more common when duration of PROM was less than 24 hours. Morbidity is more in the neonates with longer duration of PROM. Table 4

Chi-Square Test shows p-value < 0.001, which is statistically significant. The risk of septicemia increases with longer duration of PROM. Table 5

Analysis how that out of 120 neonates with history of PROM two cases (1.7%) died who had PROM duration of > 72 hours. Table 6

The analysis shows that out of 60 cases 25 (20.8%) had leucopenia and Leucocytosis was observed in 22 cases (18.4%), C-reactive protein was positive in 35 cases (29.2%) and negative in 85 cases (70.8%), 12 cases (10%) had growth in blood culture. Table 7

Staphylococcus was most common organisms causing sepsis 7 cases (58.3%) out of 12 cases. Out of 12 cases 2 cases (16.7%) died due to Staphylococcal septicemia. Table 8

Table 2: Distributions of cases according to gestational age and neonatal morbidity

Morbidity	Gestational age in weeks			Total cases
	<34	34-37	>37	
R D S	12 (10%)	19(15.8%)	14(11.7%)	45(37.5%)
Septicemia	6(5%)	4(3.3%)	2(1.7%)	12(10%)
Meningitis	0	2(1.7%)	0	2(1.7%)
Pneumonia	0	2(1.7%)	0	2(1.7%)
NEC	0	0	0	0
IVH	0	0	0	0
Total	18(15%)	27(22.5%)	16(13.3%)	61(50.8%)

Table 3: Morbidity v/s gestational age cross tabulation

Morbidity	Gestational age in weeks											Total
	32	33	34	35	36	37	38	39	40	42		
No morbidity	1	1	1	0	5	1	28	7	11	6	63	
R D S	7	3	2	4	12	2	7	1	4	2	45	
Septicemia	3	2	2	0	2	0	0	0	3	0	12	
Total	11	6	5	4	19	3	35	8	18	8	120	

Table 4: Neonatal morbidity in relation to duration of prom

Complications	P R O M		
	18-24 hours	24 -72 hours	>72 hours
R D S	25(20.8%)	17(14.2%)	3(2.5%)
Septicemia	0	5(4.2%)	7(5.8%)
Meningitis	0	0	2(1.7%)
Pneumonia	0	0	2(1.7%)
Total	25(20.8%)	22(18.4)	14(11.7%)

Table 5: Neonatal morbidity & prom duration cross tabulation

Morbidity	Prom duration in hours												
	18	20	22	23	24	26	28	30	32	36	40	48	>72
Nil	14	15	5	0	2	1	4	7	2	4	0	6	0
R D S	8	8	8	1	3	0	2	3	0	3	4	5	3
Septicemia	0	0	0	0	0	0	0	0	0	0	0	5	7
Total	22	23	13	1	5	1	6	10	2	7	4	16	10

Table 6: Distribution of neonatal death according to duration of prom

Duration in Hours	Live cases		Death cases		Total	
	No	%	No	%	No	%
18-24	64	53.3	0	0	64	53.3
24-72	46	38.3	0	0	46	38.3
>72	8	6.7	2	1.7	19	8.3
Total	118	98.3	2	1.7	120	100

Table 7: Distribution of cases in relation to different parameter (n=120)

Variable	Number of cases	Percentage
W B C (Cell/cmm)	<5000	25
	5000-20000	73
	>20000	22
C R P	Positive	35
	Negative	85
Blood culture	Positive	12
	Negative	108

Table 8: Organism isolated in blood culture

Organism isolated	Live		Death		Total	
	No	%	No	%	No	%
Staphylococcus	5	41.6	2	16.7	7	58.3
Klebsiella	2	16.7	0	0	2	14.2
E.coli	2	16.7	0	0	2	14.2
Pseudomonas	1	8.3	0	0	1	14.2
Total	10	83.3	2	16/7	12	100

5. Discussion

This was a prospective observational study conducted from December 2018 to September 2020. Total of 120 neonates were included in this study, born in SCB Medical College and Hospital, Cuttack during the study period.

Out of 120 neonates 64 (53.3%) cases were males 56 (46.7%) cases were females. In Wornart et al⁸ study out of 5182 cases 53.96% cases were males and 46.04% Cases were females which was similar to our study.

79(65.9%) babies born with birth weight more than 2500 grams and 41(34.1%) babies with birth weight less than 2500 grams. Woranart et al⁸ study shows 28.84 % babies were less than 2500 grams and 71.15% babies were more than 2500 grams.

Shubeck F et al study⁹ incidence of PROM was more in babies weighing less than 2500 grams (24.8%) and incidence of PROM in babies weighing more than 2500 grams was only 2%. In the present study the incidence of PROM was more in babies weighing more than 2500 grams. This is due to fact that the total number of babies weighing >2500 grams were more in the sample. Similar results were observed in Woranart et al⁸ study.

25(37.5%) cases born before 37 weeks and 75(62.5%) cases born after completion of 37 weeks. Kifah Al-Q Qa & Fatin Al-Awayshah³ study found that incidence of PROM was more in preterm gestation (62%)⁴⁵. In Woranart et al⁸ study incidence of PROM was 42.3% cases in preterm gestation and 57.7% cases occurred at term.

According to Danforth¹ 70% of cases of PROM occurred at term and 30% of PROM occurred at preterm. The present study results are consistent with Woranart et al⁸ study.

In our study out of 120 newborns 84(70%) were born by normal vaginal delivery and 36(30%) born by LSCS. Vaginal delivery found to be commonest mode. In Sanyal and Mukherjee study¹⁰ 87% cases are delivered by vaginal route and 13% are delivered by LSCS .Kodkany and Telang¹¹ study 81% are delivered by vaginal route and 19% are delivered by LSCS.

Out of 120 cases table 5 analysis shows 110(91.6%) cases had PROM of less than 72 hours duration and 10 (8.4%) case had longer duration of PROM(>72 hours). In Kifah Al-Q Qa & Fatin Al-Awayshah³ study 74% cases had PROM of <72hrs duration and 26% had PROM of >72 hrs. Woranart et al⁸ study had 92.3 % cases had PROM less

than 72 hrs duration and 7.69% cases had PROM of more than 72 hrs. Our study results are consistent with Woranart et al⁸ study in terms of duration of PROM.

In this present study 114 (95%) babies cried immediately after birth and 6 (5%) cases had history of delayed cry with APGAR score <4 at 1 minute. In Begum and Roy¹² study 91.4% of babies cried immediately after birth and 8.6% cases had history of delayed cry. Hassan and Shahin¹³ study had incidence of birth asphyxia in 4.8% cases. So with 5% cases of birth asphyxia our study is consistent with Hassan and Shahin¹³ study.

Analysing morbidity in the present study 45(37.5%) cases had RDS, Septicemia was seen in 12(10%) cases, Pneumonia in 2(1.7%) cases, meningitis in 2(1.7%) cases. AnjanaDevi and Reddy Devi et al¹⁴ found neonatal infection in 53.8% cases and RDS in 18.3%. Nili and AA shams Ansari² found RDS in 33.3% cases and septicemia in 5.5% cases and pneumonia in 2.5% cases. Anjana Devi et al¹⁴ found septicemia in 11.5%, pneumonia in 5.8% and meningitis in 2.9% cases¹²¹. The present study results are consistent with observations made by F. Nili and AA Shams Ansari.² In the present study 1.7% of cases had meningitis.

In the present study there is highly significant difference in morbidity among preterm and term babies. Out of 61 cases having morbidity 45(73.7%) cases were preterm, among 45 cases of RDS 31(68.8%) cases were premature and out of 12 cases of septicemia 10(83.3%) cases were preterm.

Analysis showed out of 120 mothers 78(64.8%) cases were primipara and 62(51.6%) mothers are of lower socioeconomic status. Sharma Sk et al¹⁵ study had also similar results with 62.5% primipara cases and 37.5% are of lower socioeconomic status.

Merenstein GB and Weisman LE¹⁶ observed that when PROM is accompanied with prematurity the incidence of proven sepsis is 4-6%. Miller HC and Jekel F¹⁷ observed that neonatal morbidity is affected mainly by prematurity itself, rather than by the occurrence of PROM. We found that morbidity was more among preterm babies which was statistically significant, p-value less than 0.001.

The complications are more as the duration of PROM Increases. All 12 cases of septicemia were of PROM duration more than 24 hours but out of 45 cases of RDS 25 (55.5%) cases had duration of PROM less than 24 hours. F Nili and AA Shams Ansari² observed that the risk of

pneumonia were much higher in group with > 24 hrs of PROM and RDS was more common if PROM duration is less than 24 hrs.

Taylor claimed that as latent period increased from 12 hours to more than 24 hours neonatal infection rate also increase from 1.3% to 13.3%¹²⁴. In our study Septicemia was seen in 10% cases with PROM more than 24 hrs which is consistent with Taylor study. RDS was more common in PROM duration less than 24 hrs consistent with F Nili and AA Shams Ansari² study.

In the present study CRP positive in 29.2% of cases. These results are consistent with observations made by Kifah AlQa Qa and Fatin Al-Awayshah³ in their study. Staphylococcus (58.3%) was the most common organism causing sepsis followed by klebsiella (14.2%) cases, E.coli in (14.2%) cases, pseudomonas in (14.2%) cases. Shubeck et al⁹ observed growth of Staphylococcus in 50% of cases followed by Klebsiella in 14% of cases and Pseudomonas in 4% of cases.

J.A. Fayaz also found that preterm with leaking has less RDS as compared to those without leaking because of PROM the fetus is exposed to stress which leads to more secretion of glucocorticoids which accelerate lung maturation.

Gluck et al¹⁸ explained the acceleration of pulmonary maturity documenting the following observations.

1. PROM of more than 24 hours duration was associated with more mature L:S ratio of amniotic fluid than normally expected for that gestation.
2. Phosphatidyl glycerol (PG) appeared in the amniotic fluid at an earlier period in gestation following PROM.
3. Trachea or pharyngeal aspirates from preterm infants born following PROM of more than 24 hours showed a mature phospholipids pattern at gestation ranging from 29 to 33 weeks.

That out of 120 cases with PROM duration more than 18 hours 2 cases (1.7%) died who had PROM duration of more than 24 hours and both deaths occurred due to septicemia.

F. Nili and A.A. Shams Ansari² observed that mortality is more with PROM more than 24 hours.

The present study analysis showed 20.8% of the neonates had leucopenia. 60.8% cases had leucocyte count between 5000 to 20000 cells/cumm. Leucocytosis was observed in 18.4% cases.

Kifah Al-Q Qa & Fatin Al-Awayshah³ observed leucopenia in 41.7% cases and 58.3% cases had leucocyte count between 5000 – 20000 cells/cumm and CRP was positive in 21.7% cases in their study.

6. Summary

The present prospective study includes 120 cases of neonates born to mothers with PROM of more than 18 hours duration delivered in SCB Medical College and Hospital,

Cuttack from December 2018 to September 2020. Out of 120 newborns 53.3% were males and 48.3% were females 70% of the total neonates were born by normal vaginal delivery and 30% were delivered by cesarean section 53.3% of the cases had Premature rupture of membranes of 18-24 hours duration, 38.3% cases had Premature rupture of membranes of 24 to 72 hour and 8.4 % cases had Premature rupture of membranes of more than 72 hr. RDS was the most common clinical manifestation (37.5%) followed by septicemia (10%), meningitis (1.7%) and pneumonia 1.7%. Out of 120 cases 49.1% neonates were asymptomatic and 50.9% were symptomatic. Neonatal morbidity was more common in preterm babies. RDS was the commonest clinical presentation in these babies. The incidence of septicemia was found to be 10 %. The incidence of septicemia was more in Premature rupture of membranes of longer duration. There is a significant increase in the incidence of early onset sepsis in preterm with Premature rupture of membranes. The incidence of neonatal deaths was 1.7% out of 120 neonates born to mothers with PROM of more than 18 hours duration. Incidence of mortality among neonates with early onset sepsis was 16.7%. CRP was positive in 29.2% of cases. Out of 120 cases 20.8% had leucopenia and 18.4% had leucocytosis. Most common organisms isolated in blood culture were Staphylococcus followed by Klebsiella, E. coli, Pseudomonas. PROM is more common in primipara and women of lower socioeconomic status.

7. Conclusion

Premature rupture of membranes is a high-risk Obstetric condition. Active management is needed to enable delivery within 18 hours of premature rupture of membranes as it offers better neonatal outcome. Premature rupture of membranes though common in term patients, is not responsible for increased maternal and fetal morbidity and mortality in them. Premature rupture of membranes is responsible for increased perinatal morbidity among preterm neonates. Morbidity increases as the duration of premature rupture of membranes increases. Advances in care of preterm babies may reduce the perinatal mortality following premature rupture of membranes, the ultimate solution lies in prevention of premature rupture of membranes before term.

7.1. What this study adds

Great attention to maternal risk factors like previous PROM, addiction, lower socioeconomic status, maternal UTI etc may decrease the incidence rate and severity of maternal and neonatal complications associated with PROM. Appropriate antibiotic coverage for PROM mother in appropriate time will reduce neonatal mortality and morbidity. Early diagnosis of neonatal sepsis using a protocol that utilizes

multiple methods and follow up for the clinical condition of these neonates are the key factors to avoid missing neonates with true sepsis and decreasing the use of antibiotics in those without infection.

8. Conflict of Interest

The authors declare that there are no conflicts of interest in this paper.

9. Source of Funding

None.

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