

Incidence and Pattern of Morbidity among Neonates with Premature Rupture of Membranes: A Prospective Cohort Study

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ABSTRACT

Introduction: Conventionally, Premature Rupture of Membranes (PROM) lasting more than 18 hours is considered to be associated with neonatal morbidities. However, recent research has shown that PROM of shorter duration is also associated with neonatal morbidity.

Aim: The present study was conducted to estimate the incidence and pattern of morbidity in neonates born following PROM of more than 12 hours.

Materials and Methods: The present prospective cohort study was conducted in the Neonatal Intensive Care Unit (NICU) of Kilpauk Medical College, Chennai, Tamil Nadu, India. from September 2019 to September 2020. One hundred neonates born following PROM of more than 12 hours were recruited and followed until recovery. Their clinical morbidities, including sepsis and duration of hospital stay, were recorded. The primary outcome was expressed as proportion. Secondary outcomes were analysed using the Chi-square test, and a p-value less than 0.05 was considered statistically significant.

Results: The mean {Standard Deviation (SD)} birth weight of the cohort was 2.84 (0.47) kg. Fourteen percent of the neonates were preterm, and 52% were male. The incidence of morbidity among the study population was 40%. The morbidities encountered in neonates born following PROM of more than 12 hours included respiratory distress, birth asphyxia, Small for Gestational Age (SGA), and sepsis. Morbidities were almost equal (41% vs 39%) in neonates born following PROM of 12-18 hours and more than 18 hours. Culture-positive sepsis and duration of hospital stay were higher in neonates born following PROM of more than 18 hours ($p=0.017$). The rate of culture-positive sepsis increased with longer duration of PROM ($p=0.009$).

Conclusion: According to the present study findings, a significant number of neonates born following PROM of more than 12 hours experienced morbidities. Hence the conventional PROM cut-off of 18 hours should be reconsidered.

Keywords: Birth asphyxia, Culture positive, Neonatal morbidity, Neonatal sepsis, Respiratory distress

INTRODUCTION

Spontaneous rupture of membranes occurring at any time beyond 28 weeks of pregnancy but before the onset of labour is known as PROM. When it occurs before 37 completed weeks, it is referred to as Preterm Premature Rupture of Membranes (PPROM) [1]. PROM is one of the most common problems in obstetrics, complicating approximately 5-10% of term pregnancies, while PPRM occurs in about 1% of all pregnancies [2]. The duration of latency and gestational age at the time of PROM have a major impact on foetal and neonatal morbidity and mortality risks [3]. Complications in the newborn include impaired foetal growth, neonatal sepsis, neonatal respiratory distress, and perinatal asphyxia [4]. Many studies have linked PROM to neonatal sepsis [5-7]. In contrast, Drassinower D et al., in their study, dismissed the association between PROM and neonatal sepsis [8].

PROM lasting more than 18 hours is usually considered an appropriate cut-off for increased risk of neonatal infection [9]. However, a study reported a higher rate of newborns with either clinical or culture-positive sepsis in mothers with ruptured membranes lasting more than six hours [10]. The present study was undertaken to evaluate the incidence and pattern of morbidities among neonates born to mothers with PROM lasting more than 12 hours. The primary objective was to estimate the incidence of morbidities in these neonates. The secondary objectives were to describe the pattern of morbidity and to compare the duration of hospitalisation in neonates born following PROM of 12-18 hours and more than 18 hours.

MATERIALS AND METHODS

The present prospective cohort study was conducted in the NICU of Kilpauk Medical College Hospital, Chennai, Tamil Nadu, India from September 2019 to September 2020. The study was initiated after obtaining approval the Institutional Ethics Committee (IEC approval number 250/2019 of Kilpauk Medical College, dated 05/09/2019). Written informed consent was obtained from a parent before enrolment.

Inclusion criteria: All neonates, irrespective of gestational age and birth weight, born to mothers with PROM lasting more than 12 hours were included.

Exclusion criteria: Neonates born to mothers with antepartum haemorrhage, toxemia of pregnancy, or co-morbidities including infection, and neonates with major congenital malformations were excluded.

Sample size calculation: The sample size was calculated based on a previous study that reported a morbidity prevalence of 50% in neonates born following PROM, with an α error of 5% and an allowable error of 10%. Using N Master software, the required sample size was determined to be 100 [11].

Study Procedure

Details including maternal age, parity, and any maternal illness were recorded. The time of rupture of membranes was noted, and the interval between rupture of membranes and delivery was calculated

and categorised. A detailed birth history, including the nature of liquor, mode of delivery, resuscitation details, and APGAR (Appearance, Pulse, Grimace, Activity, Respiration) scores, was collected. Each baby was weighed without clothing using an electronic infant weighing scale, and the birth weight was recorded.

All neonates born following PROM were admitted to the NICU. Gestational age was assessed using the New Ballard Score. All newborns underwent a detailed clinical examination, and any signs and symptoms were documented. As per unit protocol, Complete Blood Count (CBC), C-Reactive Protein (CRP), and blood culture were performed in all neonates. A three-part differential cell counter was used to estimate the CBC, and Avitex-CRP, a rapid latex agglutination test, was used for the detection of CRP, which showed positive results at serum CRP concentrations above 6 mg/L. Additional investigations such as chest X-ray, cerebrospinal fluid analysis, and ultrasonography of the cranium and abdomen were performed when indicated.

All newborns were managed according to standard unit protocol with first-line antibiotics, namely cefotaxime and amikacin. In cases of clinical deterioration, antibiotics were escalated to second-line therapy with meropenem. If blood culture yielded microbial growth, antibiotics were modified according to the sensitivity pattern of the isolated organism. All neonates were followed daily until discharge or death, and the length of hospital stay was recorded. Outcome variables included the presence or absence of morbidity, presence or absence of sepsis, and clinical outcome of the neonate. Respiratory distress was defined as a score of one or more based on Downes' score [12]. Clinical sepsis was diagnosed in neonates with signs and symptoms consistent with sepsis, a positive sepsis screen (characterised by leukopenia or leukocytosis, thrombocytopenia, and positive CRP), and a negative blood culture. Neonates with positive blood cultures were classified as having culture-positive sepsis. Birth asphyxia was defined as a one-minute APGAR score of less than 7. SGA was defined as birth weight below the 10th percentile according to the gender-specific Intergrowth-21 growth charts [13].

STATISTICAL ANALYSIS

Data were entered into Microsoft Excel and analysed using Statistical Package for the Social Sciences (SPSS) version 23. Categorical variables were summarised as proportions, and numerical variables as means and standard deviations. Outcome variables were expressed as proportions with 95% confidence intervals. The prevalence of morbidity and sepsis was compared between neonates born following PROM of 12-18 hours and more than 18 hours using the Chi-square test. A p-value of less than 0.05 was considered statistically significant.

RESULTS

Total 100 neonates born following PROM of more than 12 hours were included. There was an almost equal gender distribution, with most mothers being primigravida. The mean (SD) maternal age was 24.31 (3.36) years. Nearly half of the babies (48%) were delivered by normal vaginal delivery, 10% by assisted vaginal delivery, and 42% by operative delivery. The mean (SD) duration of PROM was 23.52 (12.65) hours. Fourteen percent of the babies were preterm, while the remaining were term. Ninety-one percent of the babies cried at birth, while 9% required resuscitation [Table/Fig-1]. The mean (SD) birth weight was 2.84 (0.47) kg, and 28% were of low birth weight (less than 2.5 kg). Baseline parameters including birth weight, gestational age, and gender were compared between neonates born following PROM of 12-18 hours and more than 18 hours [Table/Fig-2].

Leukocytosis was observed in 59% of neonates, and CRP was positive in 21%. Blood culture positivity was noted in 13%. Chest radiography

was performed in 35 neonates, of whom five showed abnormalities. Ultrasonography of the cranium was performed in seven neonates, of whom one had intraventricular haemorrhage [Table/Fig-3].

Parameters	Category	Frequency (n)	Percentage (%)
Sex of neonate	Male	52	52
	Female	48	48
Gravida	Primigravida	74	74
	Multigravida	26	26
Duration of PROM	12-18 h	34	34
	18-24 h	33	33
	>24 h	33	33
Mode of delivery	Normal vaginal delivery	48	48
	Assistant vaginal delivery	10	10
	LSCS	42	42
Amniotic fluid	Clear	87	87
	Blood stained	2	2
	Meconium stained	11	11
Cry at birth	Did not cry	9	9
	Required tactile simulation	6	6
	Required bag valve-mask ventilation	3	3
Gestational age	<37 weeks	14	14
	37-40 weeks	79	79
	>40 weeks	7	7

[Table/Fig-1]: Baseline parameters.

LSCS: Lower segment cesarean section

Parameters	Categories	PROM 12-18 hours n=34 n (%)	PROM >18 hours n=66 n (%)
Gestational age	<37 weeks	5 (14.7%)	9 (13.6%)
	37-40 weeks	28 (82.3%)	51 (77.2%)
	>40 weeks	1 (2.9%)	6 (9.1%)
Birth weight (kg)	Mean	2.803	2.860
	SD	0.4203	0.4962
Gender	Male	15 (44%)	37 (56%)

[Table/Fig-2]: Comparison of baseline parameters.

Parameters	Findings	Frequency/percentage	Remarks
Total leucocyte count	Leukocytosis	59	
	Leukopenia	2	
	Normal	39	
Neutrophil count	Neutrophilia	19	
	Neutropenia	5	
	Normal	76	
CRP	Positive	21	
	Negative	79	
Blood culture	Positive	13	
	Negative	87	
*Chest X-ray (Performed in 35 Neonates)	Abnormal	5	Patchy opacities were seen
	Normal	30	
*Neuro sonogram (Performed in 7 Neonates)	Abnormal	1	Features suggestive of Intraventricular haemorrhage
	Normal	6	

[Table/Fig-3]: Laboratory investigations.

Antibiotics were escalated to second-line therapy in 15% of cases, while 85% were managed with first-line antibiotics alone. All neonates recovered and were discharged; there was no mortality. The mean (SD) duration of hospital stay was 7.37 (4.87) days. The clinical outcome of all complications are shown in [Table/Fig-4]. The incidence of neonatal morbidity among neonates born following PROM of more than 12 hours was 40% (95% confidence interval: 30%-50%), while 60% remained asymptomatic.

Parameters	Number of neonates (%)	Remarks
Culture positive sepsis	13 (13%)	All <i>klebsiella</i>
Clinical sepsis	7 (7%)	Without culture confirmation
Transient Tachypnea of Newborn (TTN)	18 (18%)	Resolved with supportive care by 48 h
Pneumonia	5 (5%)	Improved with parenteral antibiotics
Birth asphyxia	9 (9%)	4 with Respiratory distress, 2 with clinical sepsis, 1 with culture sepsis, 2 were asymptomatic
Small for Gestation Age (SGA)	9 (9%)	3 with Respiratory distress, 3 with culture sepsis, 1 with clinical sepsis, 2 were asymptomatic

[Table/Fig-4]: Clinical outcome.

A similar proportion of neonates born following PROM of 12-18 hours (41.2%) and more than 18 hours (39.4%) developed morbidities, with no statistically significant difference between the groups [Table/Fig-5]. This indicates that neonates born following PROM of 12-18 hours experience morbidity comparable to those born after PROM of more than 18 hours.

Morbidity	PROM 12-18 hours n (%)	PROM >18 hours n (%)	p-value
Present	14 (41)	26 (39)	0.99
Absent	20 (59)	40 (61)	

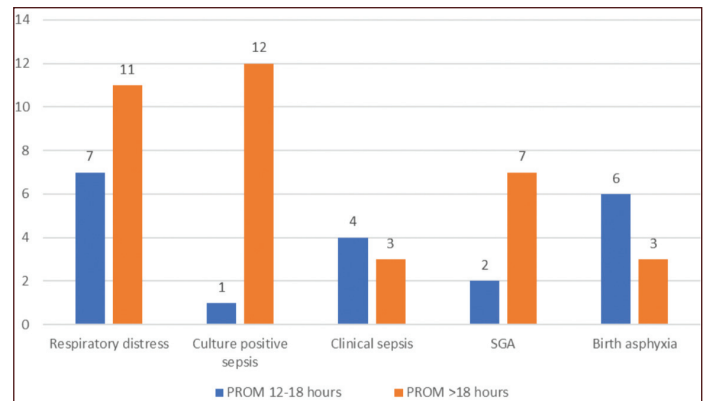
[Table/Fig-5]: Comparison of morbidity in neonates born of 12-18 hours PROM and PROM more than 18 hours.

The rate of culture-positive sepsis was higher in neonates born following longer durations of PROM, and this difference was statistically significant ($p=0.009$) [Table/Fig-6]. Comparison of morbidity patterns between PROM of 12-18 hours and more than 18 hours showed that neonates born following PROM of 12-18 hours experienced higher rates of transient respiratory distress, clinical sepsis, and birth asphyxia, whereas those born following PROM of more than 18 hours had higher rates of culture-positive sepsis and were more frequently SGA [Table/Fig-7].

Category	PROM 12-18 hours n (%)	PROM 18-24 hours n (%)	PROM >24 hours n (%)	p-value
Culture positive	1 (2.9)	3 (9.1)	9 (27.3)	0.009
Culture negative	33 (97.1)	30 (90.9)	24 (72.7)	
Total	34	33	33	

[Table/Fig-6]: Comparison of culture positive sepsis rate across PROM of varying duration.

The mean duration of hospital stay was longer in neonates born following PROM of more than 18 hours compared to those born following PROM of 12-18 hours, and this difference was statistically significant ($p=0.017$) [Table/Fig-8].



[Table/Fig-7]: Comparison of morbidity of neonates born of PROM 12-18 hours and more than 18 hours.

Category	Number	Mean	Standard deviation	p-value
PROM 12-18 hours	34	5.76	2.388	0.017
PROM >18 hours	66	8.20	3.581	

[Table/Fig-8]: Comparison of duration of hospital stay in neonates born of PROM 12-18 hours and PROM more than 18 hours.

DISCUSSION

Conventionally, neonates born following PROM of more than 18 hours are believed to have higher morbidity. The present study demonstrated that a similar proportion of neonates born following PROM of 12-18 hours were symptomatic compared with those born following PROM of more than 18 hours. However, the rate of culture-positive sepsis and the duration of hospital stay were higher in neonates born following PROM of more than 18 hours. These findings suggest that neonates born following PROM of 12-18 hours also require close observation, even when roomed in with the mother. The traditional cut-off for PROM should ideally be reconsidered and lowered to 12 hours rather than 18 hours.

PROM was more commonly observed among primigravida mothers, similar to findings in several other studies [14-16]. Gibbs RS et al., in Danforth's Textbook of Obstetrics, reported that 70% of PROM cases occur at term and 30% occur preterm [17]. In the present study, only 14% of neonates born following PROM were preterm. Furthermore, existing literature suggests that the likelihood of PROM increases with advancing gestational age [18]. Several studies have reported respiratory distress as the most common morbidity among neonates born following PROM [11,19]. Sepsis rates comparable to those observed in the present study have been reported by some researchers, while others have documented lower prevalence rates [11,19-21]. The prevalence of clinical sepsis in the present study was lower than that reported in some earlier studies, possibly due to stricter diagnostic criteria [22]. A previous study demonstrated that as the latency period of PROM increased from 12 hours to more than 24 hours, the neonatal infection rate rose from 1.3% to 13.3%, which aligns with the findings of the present study [23]. The longer hospital stay observed in neonates born following PROM of more than 18 hours can be attributed to the higher rate of culture-positive sepsis, necessitating completion of prolonged courses of parenteral antibiotics. A recent Indian study included mothers with PROM of more than eight hours and observed that neonatal morbidities occurred even with shorter durations of PROM [20]. That study reported a morbidity pattern similar to ours among neonates born following PROM of 12-18 hours, with respiratory distress being the most common (16%), followed by clinical sepsis (11%), while the remainder were asymptomatic. No cases of culture-positive sepsis were observed in that group, whereas one such case

was reported in the present study. Together, these findings highlight the need to reconsider the conventional 18-hour PROM cut-off.

Limitation(s)

A limitation of the present study is that other risk factors for early-onset neonatal sepsis, such as frequent vaginal examinations and maternal high vaginal swab culture results, were not recorded or analysed. However, as the primary focus of the study was to evaluate the morbidity pattern in neonates born following PROM of more than 12 hours rather than to identify risk factors for sepsis, these variables were not included.

CONCLUSION(S)

In the present study, nearly equal proportions of neonates born following PROM of 12-18 hours and more than 18 hours were symptomatic, indicating the need for careful observation, evaluation, and appropriate management in both groups. Although culture-positive sepsis and duration of hospital stay were significantly lower in the 12-18-hour group, morbidity was still substantial. Therefore, the conventional PROM cut-off of 18 hours should be reconsidered, and neonates born following PROM of 12 hours should also undergo observation and further evaluation. Larger multicentric studies are required to validate and reinforce these findings.

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