

Maternal and Neonatal Outcomes and the Associated Risk Factors for Premature Rupture of Membranes

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ABSTRACT

Premature rupture of membrane (PROM) has significant adverse events in the prenatal, peripartum, and neonatal period. Understanding the maternal and neonatal outcomes of PROM is very important to reduce maternal and child mortality by prevention of complications and better management of the condition. The present study is undertaken to determine the maternal and fetal outcomes in patients with PROM and factors influencing the maternal and neonatal outcomes following PROM. We retrospectively evaluated the maternal and neonatal outcomes and the associated risk factors for 200 consecutive singleton pregnancy outcomes by PROM. Our results suggest that the mean age of the study participants was 22.90 ± 3.45 years ranging from 18–40 years. The estimated occurrences of unfavorable maternal and neonatal outcomes were 24.5 and 28.0%, respectively. Fever (67.3%) followed by puerperal sepsis (12.3%), wound infection (6.1%), and postpartum hemorrhage (6.1%) were common maternal outcomes and birth asphyxia (55.4%) followed by neonatal septicemia (25.0%) and convulsion (5.4%) were common neonatal outcomes. C-reactive protein (CRP) was positive among 44.0% of the mothers, and *Escherichia coli* was the commonest organism isolated in the cervical swab. The positive serum maternal CRP levels with an adjusted odds ratio (AOR) of 3.3 and 4.8 and latency in conducting delivery with an AOR of 1.1 each were the significant independent predictors of the maternal and neonatal morbidities ($p < 0.05$).

Keywords: C-reactive protein, Maternal, Neonatal morbidities, Premature rupture of membrane.

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INTRODUCTION

Amniotic fluid is the fluid that is encased by the amniotic membranes which provides a protective environment for developing fetus. An important parameter for the fetal well-being is to have an adequate volume of amniotic fluid. Premature rupture of membranes (PROM) can decrease its volume, leading to adverse maternal and fetal outcomes.¹ Rupture of membranes (amniotic sac) before the onset of labor and beyond the viable age is termed as PROM.² Being the most common problem in obstetrics, it complicates approximately 5–10% of term pregnancies.³

The etiology is multifactorial. The exact cause of spontaneous PROM is not known but it has been speculated that infection or degeneration may weaken the membranes and spontaneously rupture. The membranes respond to various stimuli like membrane stretching, infections of the reproductive tract by producing mediators like prostaglandins, cytokines, and other enzymes.⁴ Evidence also suggests that PROM is related to membrane dysfunction at a molecular level, collagen dysfunction, and programmed cell death in fetal membranes.^{5,6}

Risk factors associated with PROM are black race, lower socioeconomic status, smoking, past history of sexually transmitted infection (STI), previous preterm delivery or abortion, polyhydramnios, multiple pregnancies, and procedures, such as cerclage or amniocentesis.² The frequency and severity of complications following PROM are inversely proportional to the gestational age at the time of membrane rupture and its duration.⁴ The fetal and maternal outcome are dependent on many factors, such as gestational age, interventions (antibiotics, steroids) done, duration of labor, development of intrapartum chorioamnionitis. Among these, the key factor for determining the maternal and fetal outcome is the latent period of leaking which refers to the interval between the rupture of membranes and the onset of labor.²

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Some of the serious maternal and neonatal complications associated with PROM include chorioamnionitis, cord prolapse, placental abruption, and preterm labor leading to various fetal complications like fetal death, neonatal pulmonary hypoplasia and respiratory distress syndrome (RDS), neonatal sepsis, and intraventricular hemorrhage.⁴ Further morbidities can increase the need for obstetric interventions in terms of instrumental deliveries or cesarean section due to fetal distress or an incoordinated uterine action.²

The management of PROM advocates aggressive termination of pregnancy which is found to have a major role in the potentially severe maternal and fetal infections. However, some promote conservative management in patients with the absence of labor or signs of infection to allow for a favorable gestational age.⁴

PROM continues to be an obstetric paradox in terms of cause and management despite advanced perinatal care. Hence

to understand the maternal and neonatal outcomes of PROM to reduce the maternal and child mortality by prevention of complications and better management of the condition, the present study was undertaken to determine the maternal and fetal outcomes in patients with PROM and factors influencing the maternal and neonatal outcomes following PROM.

METHODOLOGY

Design and Setting

A retrospective audit was conducted on all pregnancies managed in the Department of Obstetrics and Gynecology and the Special Care Baby Unit of the Department of Paediatrics of a tertiary care hospital, Chamarajanagar Institute of Medical Sciences and Hospital, Chamarajanagar, for a period of 3 months from July to September 2020 with the American College of Obstetricians and Gynecologists guidelines. Based on previous literature,⁷ an estimate of occurrence of PROM was considered to be 12%, with 95% confidence interval (CI) and absolute precision of 5%. A sample size of 162 was calculated using the formula $n = z^2(pq/L^2)$, where $z = 1.96$ at 95% CI, $p =$ estimated occurrence (30%), $q = 100 - p$ and $L =$ absolute precision (5%). Considering additional 20% accounting for incomplete records (33), the total sample size of $195 \approx 200$ was considered for the study.

A total of 200 pregnant women with a history of PROM and delivered at our labor ward along with their newborns were included in the study and the patients who did not have available laboratory data were excluded. Maternal details like maternal age, obstetric score, socioeconomic status, type of registration, PROM to the onset of labor, mode of delivery, presence of CRP (C-reactive protein), presence of growth in the cervical swab, and maternal morbidities/outcomes and neonatal details like Apgar score, birth weight, and neonatal morbidities/outcomes were extracted from the records. The records with incomplete data were excluded.

Ethics

The ethical clearance was obtained from the institutional ethical committee bearing reference number CIMS/IEC-2/40/2020. Along with the sociodemographic details, the status of antenatal care, duration of PROM to admission, duration of PROM to delivery, and the maternal and newborn outcomes were collected from the records.

Statistical Analysis

Data were entered in Microsoft Excel and analyzed using SPSS version 18.0. Results were presented as proportion, mean \pm standard deviation. Logistic regression was undertaken to assess the various factors associated with maternal and neonatal outcomes. Odds ratios and corresponding 95% CIs were reported. A p -value <0.05 was considered statistically significant.

RESULTS

There were a total of 200 study participants. The mean age was 22.90 ± 3.45 years and it ranged from a minimum of 18–40 years. Those under the age of 25 years formed the majority (166/200, 83.0%). Unbooked cases were the commonest, i.e., 152 (76.0%) and most of them belonged to lower socioeconomic status (73.0%). One hundred thirty-two (66.0%) were primigravida and 68 (34.0%) were multigravida. The normal vaginal delivery was the commonest type of delivery (69.5%) and among them, 0.7% (1/139) had to undergo ventouse delivery and 5.0% (7/139) underwent

forceps delivery. Sixty-one (30.5%) underwent a lower segment cesarean section with the commoner indications being a failure to progress (20/61, 32.8%), fetal distress (18/61, 29.5%), and previous history of PROM (17/61, 27.8%). The median hours of PROM were 6 hours and it ranged from a minimum of 1–72 hours and the mean Bishop score was 4.17 ± 1.16 . The mean durations from induction to delivery and from PROM to delivery were 12.98 ± 4.76 hours and 20.75 ± 8.6 hours, respectively. Also, 76.5% had the duration of PROM before admission for less than 12 hours, and 73.0% had a duration of delivery from PROM for less than 24 hours (Table 1).

The commonest maternal outcome was fever (67.3%) followed by puerperal sepsis (12.3%), wound infection (6.1%), postpartum hemorrhage (PPH) (6.1%), urinary tract infection (UTI) (4.1%), and lower respiratory tract infection (LRTI) (4.1%). The majority of the neonates had birth asphyxia (55.4%) followed by neonatal septicemia (25.0%), convulsion (5.4%), congenital hydrocele (3.5%), umbilical cord sepsis (3.5%), and meconium aspiration syndrome (MAS), conjunctivitis, stillbirth with cord prolapse, and LRTI 1.8% each. Most of the neonates had good Apgar scores (85.0%), indicating no neonatal respiratory depression and 15.0% of the neonates had moderate–severe neonatal respiratory depression with Apgar <7 at 5th minute. Low birth weight was reported in 16.5% of the neonates (Table 2). The mean Apgar score at 5th minute among the neonates was 7.69 ± 1.50 and the mean birth weight of the neonates was 2.65 ± 0.60 kg.

In addition, 44.0% of the study subjects had positive maternal serum C-reactive protein (CRP), and *Escherichia coli* (35.1%), *Klebsiella* (20.3%), group B *Streptococcus* (13.5%), coagulase-negative *Staphylococcus* (12.2%), and *S. aureus* (9.4%) were the commonly

Table 1: Sociodemographic and obstetric profiles of women with premature rupture of membranes (PROM)

Sociodemographic and obstetric profiles	n (%)
Age in years	
≤20	84 (42.0)
21–25	82 (41.0)
26–30	32 (16.0)
>30	02 (1.0)
Antenatal care	
Booked	48 (24.0)
Unbooked	152 (76.0)
Socioeconomic status	
Lower	146 (73.0)
Middle	54 (27.0)
Gravida	
Primi	132 (66.0)
Multi	68 (34.0)
Type of delivery	
Vaginal	139 (69.5)
LSCS	61 (30.5)
Duration of PROM in hours	
<12	153 (76.5)
≥12	47 (23.5)
Duration of PROM to delivery in hours	
<24	146 (73.0)
≥24	54 (27.0)

isolated growths accounting for at least 10.0% of the subjects (Table 3).

Among the different factors viz., type of registration, socio-economic status, obstetric score, presence of growth in the cervical

swab, presence of CRP, rupture of membranes, and latency in labor influencing the maternal outcomes, the pregnant women who were positive for CRP were having a significantly higher chance of experiencing an unfavorable outcome 3.3 times compared to those who were negative for CRP [AOR (adjusted odds ratio) -3.37, 95% CI (confidence interval): 1.31–8.66] ($p < 0.05$) and unit delay in hours in labor would have 1.1 times significantly more chances of having an unfavorable outcome [AOR-1.19, 95% CI: 1.08–1.31] ($p < 0.05$) (Table 4).

Similarly, among the different factors viz., type of registration, socioeconomic status, obstetric score, presence of growth in the cervical swab, presence of CRP, rupture of membranes, latency in labor, Apgar score at 5th minute, and birth weight influencing the neonatal outcomes, the pregnant women who were positive for CRP were having a significantly higher chance of having an unfavorable neonatal outcome 4.8 times compared to those who were negative

Table 2: Maternal and neonatal outcomes of pregnancies complicated by term PROM

Outcomes of PROM	n (%)
Maternal morbidities/outcomes (n = 49)	
Fever	33 (67.3)
Puerperal sepsis	06 (12.3)
Wound infection	03 (6.1)
PPH	03 (6.1)
UTI	02 (4.1)
LRTI	02 (4.1)
Neonatal morbidities/outcomes (n = 56)	
Birth asphyxia	31 (55.4)
Neonatal septicemia	14 (25.0)
Convulsion	03 (5.4)
Congenital hydrocele	02 (3.5)
Umbilical cord sepsis	02 (3.5)
MAS	01 (1.8)
Conjunctivitis	01 (1.8)
Stillbirth with cord prolapse	01 (1.8)
LRTI	01 (1.8)
Apgar at 5th minute	
<7	30 (15.0)
≥7	170 (85.0)
Weight of the fetus in kg	
<2.5	33 (16.5)
≥2.5	167 (83.5)

Table 3: Status of CRP and growths seen in cervical swabs among the study subjects

CRP (n = 200)	n (%)
Positive	88 (44.0)
Negative	112 (56.0)
Growth in cervical swab (n = 74)	
<i>E. coli</i>	26 (35.1)
<i>Klebsiella</i>	15 (20.3)
Group B <i>Streptococcus</i>	10 (13.5)
Coagulase-negative <i>Staphylococcus</i>	09 (12.2)
<i>S. aureus</i>	07 (9.4)
<i>E. coli</i> + coagulase-negative <i>Staphylococcus</i>	02 (2.7)
<i>Citrobacter</i>	02 (2.7)
<i>Ureaplasmaurealyticum</i>	02 (2.7)
Nonfermenting gram-negative bacilli	01 (1.35)

Table 4: Predictors of maternal outcomes among the study subjects using binary logistic regression

Particulars	Maternal outcome		Crude odds ratio	Adjusted odds ratio
	Favorable	Unfavorable		
Type of registration				
Booked	35 (72.9%)	13 (27.1%)	-0.45	0.64
Unbooked	116 (76.3%)	36 (23.7%)		
Socioeconomic status				
Low	109 (74.7%)	37 (25.3%)	0.09	1.09
Middle	42 (77.8%)	12 (22.2%)		
Obstetric score				
Primigravida	94 (71.2%)	38 (28.8%)	0.49	1.62
Multigravida	57 (83.8%)	11 (16.2%)		
Presence of growth in cervical swab				
Positive	41 (55.4%)	33 (44.6%)	0.85	2.35
Negative	110 (87.3%)	16 (12.7%)		
Presence of CRP				
Positive	51 (58.0%)	37 (42.0%)	1.22	3.37*
Negative	100 (89.3%)	12 (10.7%)		
Rupture of membranes				
			0.01	1.01
Latency in labor				
			0.17	1.19*

*Indicates statistical significance at $p < 0.05$



Table 5: Predictors of neonatal outcomes among the study subjects using binary logistic regression

Particulars	Neonatal outcome		Crude odds ratio	Adjusted odds ratio
	Favorable	Unfavorable		
Type of registration				
Booked	35 (72.9%)	13 (27.1%)	-0.11	0.89
Unbooked	109 (71.7%)	43 (28.3%)		
Socioeconomic status				
Low	102 (69.9%)	44 (30.1%)	0.41	1.51
Middle	42 (77.8%)	12 (22.2%)		
Obstetric score				
Primigravida	90 (68.2%)	42 (31.8%)	0.37	1.45
Multigravida	54 (79.4%)	14 (20.6%)		
Presence of growth in cervical swab				
Positive	41 (55.4%)	33 (44.6%)	0.16	1.17
Negative	103 (81.7%)	23 (18.3%)		
Presence of CRP				
Positive	46 (52.3%)	42 (47.7%)	1.55	4.88*
Negative	98 (87.5%)	14 (12.5%)		
Apgar score at 5th minute				
<7	23 (76.7%)	07 (23.3%)	-0.26	0.77
≥7	121 (71.2%)	49 (28.8%)		
Birth weight (kg)				
<2.5	25 (75.8%)	08 (24.2%)	0.48	1.62
≥2.5	119 (71.3%)	48 (28.7%)		
Rupture of membranes in hours				
			0.01	1.01
Latency in labor in hours				
			0.16	1.17*

*Indicates statistical significance at $p < 0.05$

for CRP [AOR-4.88, 95% CI: 1.97–12.06] ($p < 0.05$) and unit delay in hours in labor would have 1.1 times significantly more chances of occurrence of an unfavorable neonatal outcome [AOR-1.17, 95% CI: 1.07–1.27] ($p < 0.05$) (Table 5).

DISCUSSION

PROM can lead to maternal and neonatal morbidities or complications. There are numerous risk factors for PROM viz., low socioeconomic status, inadequate care during pregnancy, STIs, intrauterine infection occurring at early gestational age, etc., because of which, both mother and fetus are at greater risk of infection after PROM.⁸ Among these, vaginal infection is one of the common causes and early identification and treatment would help to avoid prematurity and associated neonatal complications.⁹ The study was conducted hence to elicit the maternal and neonatal outcomes of PROM and identify the risk factors associated with those outcomes.

Pregnant women with PROM were predominantly in the age group of 20 to 25 years according to Nagaria et al., and 77.4% were belonging to less than 25 years. Similarly, in our study, majority, i.e., 83.0% belonged to those under the age group of 25 years.¹⁰ Padmaja and Swarupa found the incidence of PROM to be higher in women of lower socioeconomic group and majority, i.e., 73.3% were unbooked and 65.0% underwent normal vaginal delivery.¹¹ In line with this study, our study had most of them in a low socioeconomic status and primigravida were predominantly unbooked and 69.5% underwent normal vaginal delivery.¹¹

Surayapalem et al. recorded the average duration of induction to delivery interval as 12.9 hours and PROM to delivery as 20.2 hours and 74.5% had less than 12 hours' duration of PROM till admission. In our study, 76.5% had the duration of PROM for less than 12 hours and the mean duration from induction to delivery and from PROM to delivery was 12.9 and 20.7 hours, respectively.¹² Only 16.5% had favorable Bishop score and Padmaja and Swarupa found 57.9% had favorable score.¹¹

The estimated occurrence of unfavorable maternal outcome in our study was 24.5% and the commonest maternal outcome was fever (67.3%) followed by puerperal sepsis (12.3%), wound infection (6.1%), postpartum hemorrhage (PPH) (6.1%), urinary tract infection (UTI) (4.1%), and lower respiratory tract infection (LRTI) (4.1%). Amulya and Ashwini had reported the estimated occurrence of maternal morbidity as 16.6%, of which febrile morbidity accounted to a maximum with 9.6%, wound infection 3.3 and 1.6% PPH and puerperal sepsis each.¹³ Vishwakarma et al., in their study found nearly 15.0% to have any maternal morbidities and there were differences in the common maternal morbidities, wherein wound infection was noted among 6.3% of patients, fever and abdominal distention in around 3.5% each, and symptoms of chorioamnionitis in 2.1% of patients. The differences in the noted findings have varied and might be due to the difference in the duration of PROM before admission and different sociodemographic profile of the patients.¹⁴ The differences in the proportions are due to the differences in the denominators considered as in our study, the denominators included those with unfavorable maternal outcomes, and in the compared study, it has been calculated considering the whole study subjects.

The rate of perinatal morbidity according to Surayapalem et al., was 26% with maximum contribution as a cause by birth asphyxia contributing to 14%, subsequently septicemia to 4%, convulsions to 3%, umbilical cord sepsis to 2%, LRTI to 1%, malformations to 1%, and meconium aspiration syndrome (MAS) to 0.5%.¹² The current study in concordance recorded 28.0% to experience unfavorable neonatal outcomes and the majority of the neonates to have birth asphyxia (55.4%) followed by neonatal septicemia (25.0%), convulsion (5.4%), congenital hydrocele (3.5%), umbilical cord sepsis (3.5%), and MAS, conjunctivitis, stillborn with cord prolapse, and LRTI contributing to 1.8% each. Similarly, Ramesh et al., also had found neonatal morbidities in 49%, of which RDS was the commonest seen in 37% of cases followed by septicemia in 8% of cases.¹⁵ The differences in the proportions are due to the differences in the denominators considered as in our study, the denominator included those with unfavorable neonatal outcomes, and in the compared study, it has been calculated considering the whole study subjects as mentioned for maternal outcomes. Apgar was <7 at 5th minute in 23.8 and 9.7% were low birth weight neonates weighing less than 2.5 kg based on the findings of Endale et al., and in this study 15.0% had Apgar <7 at 5th minute and 16.5% of the neonates had low birth weight.¹⁶

Escherichia coli was the commonest cervical growth in our study similar to other studies conducted by Ramesh et al. and Surayapalem et al.^{12,15} Surayapalem et al., isolated *E. coli* (19%), *Staphylococcus aureus* (11%), *Klebsiella pneumoniae* and coagulase-negative *Staphylococcus* contributing to 7% each, and *Citrobacter* and group B *Streptococcus* 2% each.¹² Ramesh et al., isolated *E. coli* in 22% of them, *Staphylococcus* in 20%, *Klebsiella* in 12%, and *Pseudomonas* in 8%.¹⁵ In our study, *E. coli* was isolated in 35.1%. *Klebsiella* (20.3%), group B *Streptococcus* (13.5%), coagulase-negative *Staphylococcus* (12.2%), and *S. aureus* (9.4%) were the growths commonly accounted for in at least 10.0% of the subjects.

Maternal serum CRP was positively tested among 44.0% of our study subjects. CRP is a marker for inflammation in the body and is synthesized and secreted up to 20 times high in a few hours of the onset of inflammation, indicating any type of inflammation among 44.0% of our subjects. The pregnant women who were positive for CRP were having a significantly higher chance of experiencing unfavorable maternal and neonatal outcomes 3.3 and 4.8 times, respectively, compared to those who were negative for CRP.¹⁷

Endale et al., recorded the risk of unfavorable maternal outcome to be 5.6 times and unfavorable neonatal outcome to be 12 times higher in women with a duration of PROM greater than 12 hours. The risk of unfavorable maternal outcome was 2.8 times higher in women with the duration of PROM in delivering greater than 24 hours. There were 7.8 times more chances to experience an unfavorable neonatal outcome among neonates with birth weight less than 2500 g.¹⁶ Among the different factors in our study, a unit delay in hours in labor had 1.1 times significantly more chances of having an unfavorable maternal and neonatal outcome each.

CONCLUSION

The estimated occurrences of unfavorable maternal and neonatal outcomes were 24.5 and 28.0%, respectively. The commonest maternal outcome was fever (67.3%) followed by puerperal sepsis (12.3%), wound infection (6.1%), PPH (6.1%), UTI (4.1%), and LRTI

(4.1%) and the neonatal outcomes were birth asphyxia (55.4%) followed by neonatal septicemia (25.0%), convulsion (5.4%), congenital hydrocele (3.5%), umbilical cord sepsis (3.5%), and MAS, conjunctivitis, stillborn with cord prolapse, and LRTI contributing to 1.8% each.

The mothers and the neonates with positive serum maternal CRP levels had significantly 3.3 times and 4.8 times higher chances of having unfavorable outcomes, respectively and unit delay (hours) in conducting delivery would lead to 1.1 times significantly more chances of having an unfavorable maternal and neonatal outcome each.

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