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The maternal and perinatal outcome in preterm premature rupture of membrane (pPROM): A prospective observational study

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Abstract
Introduction: Preterm premature rupture of the membrane is one of the obstetric enigmas, which occurs in 3- 8% of pregnancies. It has got multiple etiologies and is associated with significant maternal and neonatal morbidity and mortality. It is also responsible for one-third of the preterm births. Prematurity is the leading cause of neonatal morbidity and mortality; pPROM is an adding factor to this. Timely diagnosis, close monitoring, active management, and protocol-based termination of pregnancy has got a pivotal role in managing the condition.
Aims: To identify the risk factors for pPROM and to study the maternal and fetal outcomes of such patients in a tertiary care center in southern India.
Methods: This prospective observational study was conducted on 123 antenatal patients between the gestational age of 28-36 +6 days admitted with a diagnosis of pPROM. Patients were monitored, and they were treated with iv antibiotics, tocolytics, steroids, and magnesium sulfate, depending on the gestational age. The outcome was studied in terms of maternal and perinatal morbidity and mortality.
Results: The study showed that pPROM is more prevalent in young patients (20-25 years), low-socio-economic status, primigravida and around 34-36 weeks of gestation. Among the patients, 66.7% had a vaginal delivery, and the cesarean section rate was 31.7%. Among maternal morbidities, UTI was on the higher side (13%). Among the babies born, 55 % had NICU admission of which 50.7% had RDS and 20.9 % had septicemia.
Conclusion: There is an overall increased chance of maternal and neonatal morbidity in pPROM. As the most leading cause of neonatal morbidity among these patients is prematurity, conservative management to prolong the pregnancy is recommended unless there is evidence of chorioamnionitis or fetal distress. Prompt identification of complications, and treatment of infection is important in preventing maternal and neonatal morbidity. The management should be based on the gestational age, the fetal well-being and the presence or absence of complications.

Keywords: pPROM, maternal and perinatal morbidity, chorioamnionitis, sepsis

Introduction
The preterm premature rupture of membrane (PPROM) is referred to as the rupture of the amniotic membrane before 37 completed weeks of gestation [1]. PPROM complicates 1-4% of all pregnancies, and it is associated with 30-40% of all preterm births [2, 3]. Preterm birth is the second largest direct cause of death in children younger than 5yrs [3]. PPROM is multifactorial in origin. Multiple etiological risk factors for PPROM have been proposed, including ethnicity, socioeconomic status, and nutrition [4]. The increased neonatal morbidity associated with PPROM is found to be inversely related to gestational age [5]. Certain risk components identified are pPROM in a previous pregnancy, smoking, socioeconomic status, poor nutrition, prior cervical conization, cervical cerclage, second- and third- trimester bleeding, acute pulmonary disease, prior episodes of preterm contractions, infection (bacterial vaginosis), amniocentesis, polyhydramnios, and multiple gestations, but in most cases, the cause remains unknown and is not apparent at the time of membrane rupture [6]. pPROM is associated with increased maternal morbidities like chorioamnionitis, sepsis, abruption, dysfunctional labour, increased incidence of operative delivery, postpartum endometritis and third stage complications like PPH and retained placenta. Prematurity is associated with nearly 70% of perinatal mortality in India [7]. There is an increased incidence of perinatal mortality in pPROM, which may be due to RDS, infection, asphyxia and congenital anomalies.

Other causes of death are cord accidents, intracranial hemorrhage, trauma and necrotizing enterocolitis. The inefficient blood-brain barrier makes them more prone to brain damage.

Management of PROM requires an accurate diagnosis as well as evaluation of the risks and benefits of continuing pregnancy or expeditious delivery. An understanding of gestational age-dependent neonatal morbidity and mortality is important in determining the potential benefits of conservative management of preterm PROM at any gestation [6]. An active management plan is now accepted by all regulatory and control or governing bodies that includes prevention of infection, delay of delivery until fetal maturity is achieved and active intervention by induction, if labor is no longer preventable or if early infection is suspected [8].

This study aims at evaluating the perinatal outcomes associated with pPROM, in terms of maternal and neonatal morbidity and identifying associated risk factors, if any.

Methodology

The study was conducted on antenatal patients, who were admitted with a diagnosis of pPROM in the department of obstetrics and gynecology, MES medical college Perinthalmanna during the period from January 2018 to December 2018. Approval for the study was taken from the institutional ethics committee. Patients with pregnancy complicated by pPROM between 28 to 36weeks, confirmed by sterile speculum examination were included while those before 28 weeks of gestation or pregnancy complicated by other medical conditions were excluded from the study.

A written informed consent was taken from the participants who were meeting inclusion and exclusion criteria. Data were collected using a detailed proforma, which includes antenatal history, parity, gestational age, and LMP. Also, details of the socioeconomic status was also collected. Menstrual history, past obstetric history, history of previous pPROM, onset and duration of leaking, and colour, odour and amount of fluid are noted. Associated symptoms like frequent and intermittent abdominal pain, bleeding PV, decrease in fetal movements were also observed. Detailed examination was done, including general, systemic and obstetric examination. Blood and urine investigations were done in all cases. A per-vaginal examination was done for each case to access the pelvis, and CPD and Bishop's score was also noted. All participants who were treated conservatively underwent ultrasonography to access gestational age, growth parameters and to exclude the congenital anomalies. Conservative management was done for all PPROM patients till the timing of termination, according to the guidelines or the onset of spontaneous labour or till the maternal and fetal indication for termination of pregnancy arose, whichever was the earliest. The initial treatment started with Ampicillin 1 gram IV stat, followed by 500 mg 6th hourly in all the cases. According to the Bishop's score, the labor was induced or allowed to progress spontaneously. In some patients, antibiotics had to be switched over as per the culture and sensitivity report. Two doses of steroid, injection Betamethasone 12 mg IM, 12 hours apart were administered to all patients less than 36 weeks of gestation and tocolytic coverage was provided till the completion of antenatal steroids. Injection Magnesium sulfate (MgSo4) was given at a dose of 1 gram per hour for neuro-protection according to gestational age especially in cases less than 32 weeks and if imminent delivery within 24 hours was anticipated.

Mothers were monitored for chorioamnionitis and intra-partum complications such as puerperal sepsis and abruption of the placenta. Chorioamnionitis was managed with immediate termination of pregnancy and IV antibiotics during intrapartum and postpartum periods according to sensitivity report. Clinical features of Chorioamnionitis and serum CRP were monitored regularly. Third stage complications like PPH retained placenta were noted. Neonatal outcome was studied in terms of APGAR score, admission to NICU and complications. Mothers and babies were followed up till discharge.

Results

Among the 2316 antenatal admissions during the study period, 123 patient, herein referred to as (n=123) patients, who met the eligibility criteria were included in the study with proper patient consent, and counseling. The incidence of pPROM in our study was found to be 5.3%. The baseline characteristics of the study population are described in table 1. Out of 123 patients, 67 patients (54.5%) belonged to the age group of 20 to 25 years. Descriptive analysis of socioeconomic status shows that 53.7% patients belonged to class V of modified Kupuswamy's classification. The statistics here shows a greater frequency of pPROM in primi-gravida compared to multi-gravida patients and it was more towards late gestational age (34 to 36 weeks). Here 67.5% of cases were found to have no risk factors. While breech and history of coitus were 9.8% and 8.1% respectively, reported cases of UTI were 2.4%, 3.3% had a previous history of pPROM, 4.1% appeared to have polyhydramnios, and 4.9% were twins.

As per the maternal outcomes listed in table 2, 68.2% patients had normal vaginal delivery, while 31.7% underwent LSCS. In our study, fetal distress was the most common indication for LSCS. UTI with the graphs raised to 13.0% was the first cause of maternal morbidity, while Chorioamnionitis positive results were only 2.4 %.

As per the neonatal outcomes listed in table 3, babies with a birth weight of 2 to 2.5 kg, comprised 48.8% while those with the birth weight of less than 1.5 kg was 4.9% in this study. 68 neonates (55.3%) had to be admitted in NICU, where RDS was the most common cause of neonatal morbidity. Unfortunately 4 neonatal deaths occurred.

We also tried to figure out associations existing between gestational age at which pPROM occured and various maternal outcomes (Table 4). On investigating the maternal outcome across the gestational age, it was found that the frequency of vaginal delivery and lower segment Cesarean section were higher in early and late gestational ages respectively. These results proved statistically significant. No statistically significant associations could be found out between gestational age and maternal morbidity variables like chorio-amnionitis, abruption and UTI.

When neonatal morbidities are verified across gestational age (Table 5), RDS and Jaundice were found to be the leading cause of neonatal morbidity in early gestational age, while RDS and septicemia were found to be the leading causes in late gestational age. Among the neonatal outcomes a statistically significant association could not be established between gestational age and birthweight as well as gestational age and NICU admission.

Table 1: Descriptive analysis of baseline characteristics of the population (n=123)

Baseline variables		Frequency	Percentage
Age groups	less than 20	12	9.8%
	20 to 25	67	54.5%
	26 to 30	28	22.8%
	Greater than 30	16	13.0%
Socio-economic status	III	21	17.1%
	IV	36	29.3%
	V	66	53.7%
Parity	Primi	74	60.2%
	Multi	49	39.8%
Gestational Age	28-30+6	18	14.6%
	31-33+6	41	33.3%
	34-36+6	64	52.0%
Risk factors	Breach	12	9.8%
	History of recent coitus	10	8.1%
	Past history of PROM	4	3.3%
	Poly hydramnios	5	4.1%
	Twins	6	4.9%
	Urinary tract infection	3	2.4%
	Nil	83	67.5%

Table 2: Descriptive Analysis of maternal outcomes

Maternal outcomes		Frequency	Percentage
Mode of Delivery	Vaginal delivery	84	68.2%
	Assisted breach	11	8.9%
	Twins vaginally	5	4.1%
	LSCS	39	31.7%
Indication for LSCS	Previous LSCS	10	25.64
	Breech	01	2.56
	Fetal distress	15	38.46
	CPD	03	7.69
	Severe oligo-hydramnios	08	25.64
	Previous LSCS with severe oligohydramnios	01	2.56
	Previous LSCS with breech	01	2.56
Maternal morbidity	Chorioamnionitis	3	2.4%
	Abruption	8	6.5%
	Wound Infection	8	6.5%
	UTI	16	13.0%
	No	107	87.0%

Table 3: Descriptive analysis of neonatal outcome

Neonatal outcomes		Frequency	Percentage
NICU admission	No	55	44.7%
	Yes	68	55.3%
Neonatal morbidity	RDS	34	50.7%
	Septicemia	14	20.9%
	Jaundice	15	22.4%
	IVH	4	6.0%
Neonatal death	28-31+6	3	75.0%
	31-33+6	1	25.0%
Birth weight (kgs)	<1.5	6	4.9%
	1.5 to 2	15	12.2%
	2 to 2.5	60	48.8%
	> 2.5	42	34.1%

Table 4: Comparison of maternal outcomes across gestational age.

Maternal outcome		Gestational Age			Chi square	P value
		28-30+6 (N=18)	31-33+6 (N=41)	34-36+6 (N=64)		
Chorio-amnionitis	No	17 (94.44%)	41 (100%)	62 (96.88%)	Cannot be calculated	
	Yes	1 (5.56%)	0 (0%)	2 (3.13%)		
Abruption	No	16 (88.89%)	38 (92.68%)	61 (95.31%)	1.020	0.600
	Yes	2 (11.11%)	3 (7.32%)	3 (4.69%)		
UTI	No	16 (88.89%	37 (90.24%)	54 (84.38%	0.828	0.661
	Yes	2 (11.11%)	4 (9.76%)	10 (15.63%)		

Vaginal delivery	No	1 (5.56%)	11 (26.83%)	29 (45.31%)	11.163	0.004
	Yes	17 (94.44%)	30 (73.17%	35 (54.69%)		
LSCS	No	17 (94.44%)	31 (75.61%	36 (56.25%)	10.985	0.004
	Yes	1 (5.56%)	10 (24.39%	28 (43.75%)		

Table 5: comparison of neonatal outcome across gestational age.

Neonatal outcome		Gestational Age			Chi square	P value
		28-30+6 (N=18)	31-33+6 (N=41)	34-36+6 (N=64)		
Birth weight	<1.5kg	1 (5.56%	1 (2.44%)	4 (6.25%)	1.901	0.929
	1.5-2 kg	3 (16.67%)	4 (9.76%	8 (12.5%)		
	2-2.5kg	9 (50%)	22 (53.66%)	29 (45.31%)		
	>2.5kg	5 (27.78%)	14 (34.15%)	14 (34.15%)		
NICU	No	5 (27.78%)	18 (43.9%)	32 (50%)	2.823	0.244
	Yes	13 (72.22%)	23 (56.1%)	32 (50%)		
Neonatal morbidity	RDS	5 (38.46%)	10 (45.45%)	19 (59.38%)	Cannot be calculated	
	Septicemia	2 (15.38%)	4 (18.18%)	8 (25%)		
	Jaundice	6 (46.15%)	7 (31.82%)	2 (6.25%)		
	IVH	0 (0%)	1 (4.55%)	3 (9.38%)		

Discussion

Preterm premature rupture of membranes is one of the major complications of pregnancy. Throughout the observation, it was noted that each case had different etiologies. With the ample opportunity to witness, care, and treat 123 cases in this short time frame, methods like history, clinical examination, and ultrasonography were put to use.

During our study the incidence of pPROM was found to be 5.3%, which is comparable to otherstudis [9]. When we look at the age group among the 123 cases, youngsters within the age group of 20 to 25 years outnumbered the others, giving a value of 54.5%. In a similar study by Diraviyam JMV *et al.* [10], the incidence in the age group, 20-25 years was listed to be 41%, less than 20-year-old were 11 %, 25 to 30 age group noted 31%, and above 30 years accounted to 13%. These figures are similar to our study.

When one of the important factors, the socio-economic status was observed the Vth class or the economically challenged reported a disquieting 53.7%, which is comparable with the study conducted by Swathi Pandey [11] in which the same class accounted 61% of all, while IIIrd and IVth class stood at 17.1% and 29.3% respectively. The high incidence found can be due to the relatively high prevalence of malnutrition, anemia, poor hygiene, stress, overexertion, high parity, recurrent genitourinary infections, etc. which inturn can lead to a decrease in immunity that can cause a reduction in antibacterial activity in the amniotic fluid and then PPROM. Another comparable result to Diraviyam JMV *et al.* [10] in this study was regarding the ratio of primi-gravida and multi-gravida. Primi-gravida recorded 60.2 % compared to the 39.8 % cases of multi-gravida.

This study revealed that pPROM cases were most common in the gestational age group of 34-36 weeks, which comes around 52 %. pPROM was found to be 14.6 % in 28-30 weeks and 33.3 % in 31-33 weeks. These findings were similar to the study conducted by Shweta Patil *et al.* [12], in which the percentage of pPROM in 28-31 weeks was 77%, that between 32-34 weeks was 18% and between 35-36 weeks of gestational age was 75%. Late pPROM is more common than early pPROM as stretching of the membranes is more during advanced gestational age.

This study recorded no risk factors among 67.5% of the participants, while 32.5% of cases had one or other risk factors. Cases of breech presentation showed to be 9.8 %, indications of a history of recent coitus comprised 8.1%, previous history of PROM was listed in 3.3% and polyhydramnios and twins were noted in 4.1% and 4.9% respectively. Urinary tract infection was the least occurred risk factor; the reason could be proper diagnosis and judicious use of antibiotics while anemia and UTI were the highest risk factors recorded in another study [13].

Maternal morbidity rates of reported chorioamnionitis stood at 2.4 % while abruption and wound infection accounted for 6.5% of the cases which is similar to another study which also points to less incidence of chorio-amnionitis [14] And when the situation of delivery arose, 66.7 % succeeded in vaginal delivery while 31.7 % went for LSCS, 8.9 % for assisted breech delivery, and 4.1 % for twins delivery. During our study 31.7 % of cases that went for CS, most common indication was oligohydramnios 37.4 % followed by 13.8 % breech, 9.8 % previous LSCS, 8.9 % CPD and lastly fetal distress accounting for 1.6%. But this was in contrast to other studies like Diraviyam JMV *et al.* [10] and Shwetha Anant mohokar, *et al.* [15], where malpresentation and fetal distress were the commonest indications for LSCS.

Among the babies born, the majority had a birth weight of 2-2.5 kg, while 34.1 % had more than 2.5 kg, 12.2 % had 1-5-2 kg, and lastly, 4.9 % had a birth weight less than 1.5 kg. Of the neonates, 55 % had NICU admission. This shows that the neonatal morbidity associated with pPROM is high which may be due to the factor of prematurity adding to this [10].

In the Neonatal morbidity reports in our study, 50.7% of cases had RDS, 20.9% developed septicemia, 22.4% had jaundice, and 6.0% had IVH. The commonality of RDS may be due to the incomplete dosage of cortico-steroids. There were four neonatal deaths, and 3 out of them belonged to the gestational age of 28-31 weeks and only one in 32-34 weeks.

Conclusion

It cannot be denied that pPROM is a huge hurdle in pregnancy. A right amount of controlled care and medication is required to treat the diseased. Hospitalization and due care are important factors for the betterment of both mother and baby with this condition. The socio-economic factors of the cases cannot be ignored when the challenged class showed a higher rate. Antibiotics come to a more excellent rescue from chorio-amnionitis and puerperal pyrexia when adequately diagnosed and introduced. Also any sign of urinary tract infection is to be treated as required to avoid leading infection. It is good to educate the pregnant woman in the earlier stages regarding, the care required on the road to delivery say it be regarding hygiene, stress or chances of infection which may help to be a natural cure.

The babies born after pPROM too require due care, specifically those affected with respiratory illness. The latent period is to be well noted to give the baby better care. For example, if the latent period is < 24-hours, the chances of respiratory syndromes are higher, while those born with >72 hours latent period tend to suffer from sepsis. Good neonatal care is always recommended to avoid neonatal morbidity and mortality.

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