Original Research Paper

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CLINICO-MICROBIOLOGICAL PROFILE AND FETO-MATERNAL OUTCOME IN PRETERM PREMATURE RUPTURE OF MEMBRANES: A 1YEAR PROSPECTIVE, TERTIARY CARE SINGLE-CENTRE STUDY.

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ABSTRACT

Background- The global burden of premature babies is mostly contributed by preterm births. Preterm premature rupture of membranes (PPROM) account for nearly 40% of all preterm deliveries.

Objective-The study was done to evaluate the clinic-bacteriological profile and the obstetric outcome in pregnancies complicated by preterm premature rupture of membranes.

Material and methods-This was a prospective cohort study of cases of PPROM admitted in the teaching hospital which is a major referral tertiary care centre. A total of 64 women were enrolled. We studied the patient demographics, bacterial profile and obstetric outcome in these women.

Results-Most of the cases of PPROM were seen in low risk primigravidae. Infections were the commonest cause for PPROM. Enterococcus Faecalis was the most commonly isolated organism. The mean latent period was 3-7 days. Most women delivered vaginally. Respiratory distress and low birth weight with Apgar <6 were the common indications for NICU admission. Co-relation between TLC and hs-CRP levels was not statistically significant across different groups.

Conclusion- Effective screening for cervico-vaginal infections in pregnancy and appropriate antibiotic therapy will help reduce infection related feto-maternal morbidity and mortality. Lesser gestational ages are associated with poorer outcome.

KEYWORDS : Preterm premature rupture of membrane, RDS, LBW, neonatal sepsis.

INTRODUCTION-

Preterm premature rupture of membranes (PPROM) complicates close to 3% of all pregnancies and 40% of all preterm births[3]. PPROM is defined as the rupture of membranes less than 37 weeks of gestation. Its incidence in singleton pregnancies is around 2-4% and in multiple gestation around 7-10%[1]. It has multifactorial etiology. Cervico-vaginal infections, incompetent cervix, multiple gestation, polyhydramnios, amniocentesis, placenta previa, maternal trauma, smoking etc are causes of PPROM[2,14]. In low-and middle-income countries, vaginal infections are the leading cause.

In the pathogenesis of PPROM, ascending infection play an important role to weaken th amniotic membranes.Vaginal infections and mechanical stretching of amniotic membranes cause release of inflammatory mediators resulting in collagenolysis- mediated membrane disruption leading to PPROM[14,15].

Pregnancies complicated by PPROM encompass need for multi-modality approach with appropriate antibiotics, corticosteroids, timely delivery and prolonged neonatal intensive care[1,2,3]. Most patients of PPROM need an in-utero transfer to tertiary healthcare level. Preterm births are complicated by prematurity, low birth weight, cord compression, respiratory distress, primary pulmonary hypertension, perinatal death, hyperbilirubinemia etc. In-addition to these, PPROM increases the risk of maternal and neonatal sepsis[12,13,14]. Appropriate antibiotic therapy and timely delivery will help prevent both maternal and neonatal mortality. We do not have many studies on the microflora and its association with feto-maternal outcome in our population.

MATERIALAND METHODS-

This was a prospective cohort study done between January 2019 to December 2019 in the teaching hospital attached to KAHER's Jawaharlal Nehru Medical College, Belagavi. We followed universal sampling to collect from study participants.

Women who presented to labour room with complaints of per vaginal leak between gestational age of 24 weeks to <37 weeks who were willing to participate in the study were included. Depending on the gestational age, the participants were divided into 3 groups. Group 1 was 24-28 weeks, Group 2 was 29-33 weeks and Group 3 was 34- 36 completed weeks.

Diagnosis of PPROM was made by demonstrating gush of amniotic fluid on sterile per-speculum examination. All participants were managed as per the hospital protocol for PPROM which included estimation of TLC (total leucocyte count) & hs-CRP (highly sensitive C-reactive protein), Culture and antibiotic sensitivity of vaginal swabs, administration of intravenous antibiotics and Betamethasone, estimation of expected fetal weight and amniotic fluid by ultrasound. The high vaginal swabs were cultured on blood, chocolate and Mac Conkey agar. Gram staining was done after 24 hrs of culture.

All patients were admitted and monitored for signs of chorioamnionitis and fetal well-being. Outcome was observed with respect to bacterial culture and antibiotic sensitivity of high vaginal swab, latent period, mode of delivery, birth weight, maternal and fetal outcome. It was approved by the institutional ethics committee.

STATISTICALANALYSIS-

Data Analysis done using R I 386 4.0.3. Categorical data represented by frequency and percentage and continuous data represented using Mean and SD. Comparison is done for continuous data using ANOVA. Multivariate analysis of data was done using Chi-square test. P value of <0.05 was considered statistically significant.

RESULTS-

The annual delivery rate at our hospital from January to December 2019 was 4816.

There were 963 preterm deliveries, of which 64 women with PPROM between 18 to 36 years with were included in the study Mean age of women was 23.6 ± 3.4yrs. Most of the cases were unregistered, they were referred to our hospital with PPROM. Majority of cases were Primigravida.

Table 1- Distribution of cases as per age, gravidity & parity.

Factor	Sub-category	Overall	PPROM (according to Gestational Age)			p-value
			Group 1 (n=8)	Group2 (n=26)	Group 3 (n=30)	
Age (in years)		23.63 ± 3.48	25.22 ± 4.71	22.94 ± 2.83	23.92 ± 3.63	0.1948[A]
Maternal Age	18-21	17 (26.56%)	2 (11.76%)	5 (29.41%)	10 (58.82%)	0.4312[CS]

	22-25	35 (54.69%)	3 (8.57%)	15 (42.86%)	17 (48.57%)	
	26-29	9 (14.06%)	3 (33.33%)	3 (33.33%)	3 (33.33%)	
	≥30	3 (4.69%)	1 (33.33%)	1 (33.33%)	1 (33.33%)	
Gravidity	Primi	37 (57.81%)	4 (10.81%)	15 (40.54%)	18 (48.65%)	0.5912[CS]
	Multi	25 (39.06%)	5 (20%)	9 (36%)	11 (44%)	
	Grand	2 (3.13%)	0 (0%)	0 (0%)	2 (100%)	
Parity	nullipara	41 (64.06%)	5 (12.2%)	15 (36.59%)	21 (51.22%)	0.6962[CS]
	Primi	17 (26.56%)	3 (17.65%)	8 (47.06%)	6 (35.29%)	
	Multi	6(9.38%)	1 (16.67%)	1 (16.67%)	4 (66.67%)	

A-anova, CS- Chi-square.

The latency period was 5.5 ± 2.2 days. This was more in the extreme preterm patients. 60% of extreme preterm had a latent period of 5-7 days where they were observed for signs of chorioamnionitis. However in very preterm and late preterm the latent period was 3-4 days. This was due to better chances of salvaging the baby.

Of the 64 cases, 4 came with established preterm labour and were delivered. Most of the pregnancies were terminated by induction of labour as per the hospital protocol. Vaginal delivery was the commonest mode of delivery. Preterm Emergency LSCS was performed in very preterm and late preterm.

Table 2. Distribution of cases according to mode of delivery and neonatal outcome.

Outcome	Sub-category	Overall	PPROM (according to GA)			P-value
			Group 1 (n=9)	Group 2 (n=24)	Group 3 (n=31)	
Mode of delivery	Vaginal delivery	35 (54.69%)	7 (77.78%)	13 (54.17%)	15 (48.39%)	0.3008[CS]
	C-Section	29 (45.31%)	2 (22.22%)	11(45.83 %)	16 (51.61%)	
Neonatal outcome	Fresh still birth	4 (6.25%)	3 (33.33%)	1(3.23%)	0(0%)	0.0070[CS]
	Neonatal death	6 (9.38%)	4 (11.11%)	4 (12.9%)	1(4.17%)	
	Live birth	54 (84.38%)	5 (55.56%)	23 (95.83%)	26 (83.87%)	
Apgar score	<6	14 (46.3%)	5 (55.56%)	9 (42.61%)	1(4.17%)	0.256[cs]
	>6	40(64.7)	0	14(68.4)	25 (96.3%)	

CS-Chi-square test.

Table 3. Indications for LSCS in PPROM cases.

Sno	Indication for LSCS	No. of cases(%)
1	Breech	08 (27.5%)
2	Fetal distress	06 (20.68%)
3	Failed induction	04 (13.79%)
4	Transverse lie	03 (10.34%)
5	Suspected chorioamnionitis	03 (10.34%)
6	HELLP syndrome	01 (3.44%)
7	Severe oligoamnios	01 (3.44%)
8	Precious pregnancy	01 (3.44%)
9	severe preeclampsia	01 (3.44%)
10	Abruptio placenta	01 (3.44)%
	Total	29

Enterococcus faecalis was the most common culture isolate in our study. Antibiotic sensitivity to Amikacin and Imipenem in gram negative isolates and Vancomycin and Linezolid for gram positive isolates was noted.

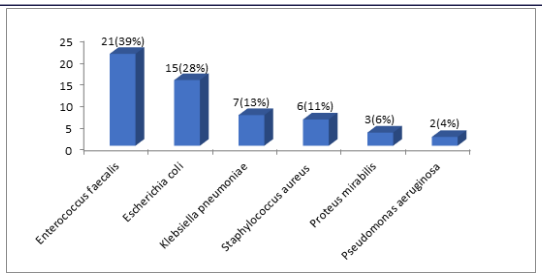

Figure 1-Bacterial isolates of cases with PPROM.

Table 4-Antibiotic sensitivity in gram positive isolates-

	Antibiotics	Sensitivity No.(%)
First line drugs	Ampicillin(AMP)	10(37.0%)
	Penicillin(P)	5(18.5%)
	Erythromycin(E)	4(14.8%)
Second line drugs	Linezolid(LZ)	19(70.3%)
	Vancomycin(VA)	15(55.5%)
	Tetracyclin(TE)	7(25.9%)
	Clindamycin	14(51.8%)
	Ciprofloxacin(CIP)	8(29.6%)

Table 5- Antibiotic sensitivity in gram negative isolates-

Antibiotics		Sensitivity pattern No.(%)
First line drugs	Gentamicin(GEN)	5(18.5%)
	Ampicillin (AMP)	4(14.8%)
Second line drugs	Imipenem (IMP)	22(81.4%)
	Amikacin(AK)	18(66.6%)
	Meropenem(MRP)	17(62.96%)
	Amoxyclav(AMC)	11(40.7%)
	Ciprofloxacin(CIP)	11(40.7%)
	Ceftriaxone(CTX)	10(37.0%)
	Piperacillin+Tazobactam	8(29.6%)
	Cefuroxime(CXM)	5(18.5%)
Third line drugs	Aztreonam	6(22.2%)
	Ceftazidime(CAZ)	4(14.8%)

Among 54 live birth cases, 36 needed NICU (Neonatal intensive care unit) admission most commonly for RDS and LBW. Apgar score <6 was seen more commonly in extreme preterm. Lower Apgar was associated with higher NICU admissions. Fresh still births and Neonatal death cases of which 4 are due to extreme prematurity and 1 each are due to LBW, LBW & RDS.

Table 6- Causes NICU admission.

Sno.	Reason for NICU admissions	PPROM (according to GA)		
		Group1 (n=5)	Group 2 (n=23)	Group 3 (n=26)
1	RDS	5	14	2
2	LBW	5	10	1
3	Congential heart disease	0	2	1
4	Hypoglycemia	0	3	1
5	Primary pulmonary hypertension	--	2	0
6	Hyperbilirubinemia	--	19	6
7	Neonatal sepsis	2	4	1
8	Necrotising enterocolitis	--	1	0

Mean TLC and hs-CRP levels in PPROM are 12.65 ± 4.26/mm^3 and 2.84± 0.7 mg/dl respectively. Using Welch Anova, the mean TLC and hs-CRP are not significantly different over gestational ages. 4 mothers had chorioamnionitis in whom the TLC was high hs-CRP was borderline. Mean birth weight was 2.1 □ 0.92 kgs. Most common cause of neonatal death was respiratory distress followed by sepsis. There were no maternal deaths in our study.

Table 7- Correlation of TLC and hs-CRP levels between the groups.

Parameter	Overall	Group 1	Group 2	Group 3	p-value
TLC	12.65 ± 4.26	13.78 ± 3.10	13.03 ± 3.91	11.73 ± 4.98	0.3735[A]
hs-CRP	12.84 ± 18.32	16.04 ± 28.75	14.98 ± 18.94	8.69 ± 12.17	0.5973[A]

A- Anova

Table 8 -Causes for neonatal deaths

Sno.	Cause of death	PPROM (according to GA)		
		Group 1 (n=5)	Group 2 (n=4)	Group 3 (n=1)
1	RDS	3	2	0
2	Pulmonary haemorrhage	1	0	0
3	Congenital heart disease	0	1	0
4	Neonatal sepsis	1	1	0
5	Meconium aspiration	0	0	1

DISCUSSION-

PPROM is the rupture of amniotic membrane less than 37 weeks of gestation[2,3,5]. Most cases of PPROM were in women less than 25yrs. This is due to the younger age at marriage in our population. The incidence of PPROM was more between 34-36 weeks as compared to lesser gestational ages which is similar in most studies[5,6]. Infections being the leading cause of PPROM which is evident by positive cultures in most cases in the study. Higher incidence was also found in low socio-economic status which is similar to a study by Rani S et al[17]. Infections of urinary tract and genital tract being more common in low socioeconomic groups.There was no statistically significant difference in the groups with respect to gravidity and parity.

The mean latent period from admission to delivery was longer in group 1 for action of antenatal steroids and increase in birth weight. Conservative management was tried in all cases in group 1. In group 2 and 3 most of the pregnancies were terminated after steroid admisinstration. This was because the risk of chorioamnionitis and better neonatal outcome if delivered as compared to conservative management.

Induction of labour was commonly performed for most cases. Vaginal route was the commonest mode of delivery. Cesarean section was performed in indicated cases. Fetal malpresentations was the most common indication concurring with other studies[7,8]. Fetal distress secondary to cord compression and oligoamnios was second most common indication which is again similar to study by Noor et al[5]. Transverse lie, chorioamnionitis, severe preeclampsia and related complications, precious pregnancy were other indications for Cesarean section.

PPROM complicated with obstetric and medical complications like can further increase the maternal and neonatal morbidity[10]. The fetal outcome was directly correlated with gestational age and expected birth weight. Poorer fetal outcome was seen with lesser gestational ages which is similar to other studies[8,9,12,13]. Despite the use of steroids, neonates with gestational age less than 28weeks fared poorly. This emphasizes the need for efficient NICU care for these babies.

Enterococcus faecalis was the most common culture isolate in our study in contrast to other studies where E.Coli was the commonest organism[18,19]. Enterococcus faecalis infections are known for being more resistant to antibiotics and causing atypical sepsis presentations. Antibiotic therapy needs to be changed as per the culture and sensitivity pattern of organisms as empirical antibiotics will not cover enterococcus.[9,10].

TLC and hs-CRP levels did not show any significant correlation though both were used as markers for diagnosing maternal chorioamnionitis in comparison with other studies by Nageeb et al and Noor et al[2,5]. Neonatal sepsis was found to be higher when maternal TLC and hs-CRP levels were raised. The commonest indication for NICU admissions was RDS, similar to most studies. LBW, hyperbilirubinemia was other common complications.

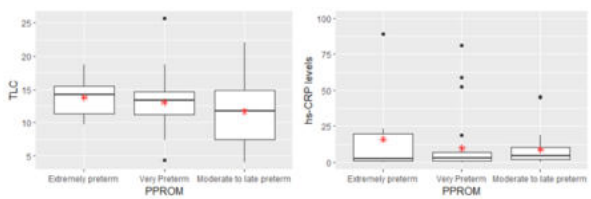

Figure 2- Comparison of TLC and hs-CRP Levels.

CONCLUSION-

PPROM is most commonly caused by vaginal infections. Effective screening for vaginal infections and treatment with appropriate antibiotics will go a long way in its prevention. Microbiological resistance to antibiotics is an emerging problem as vaginal infections with newer organisms is posing challenges in management. Early diagnosis and in-utero referral to tertiary care helps in better feto-maternal outcome. Lesser the gestational age in pregnancies complicated by PPROM, poorer the outcome. The neonates born to mothers with PPROM are at higher risk of RDS and infection related morbidity. Larger studies are needed to establish protocols for antibiotic therapy in PPROM.

Abbreviations- RDS- respiratory distress syndrome, LBW- low birth weight, TLC- total leucocyte count, hs-CRP- highly sensitive C-reactive protein, NICU- neonatal intensive care unit.

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