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Original Research Article

Study to detect infection and diagnose chorioamnionitis to aid in management of cases of preterm premature rupture of membranes in a tertiary care centre of Jharkhand

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ABSTRACT

Background: The present study undertaken is to identify the risk factors causing Preterm premature rupture of membranes (pPROM) and to study fetal and maternal outcome associated with pPROM, to diagnose and manage chorioamnionitis associated with pPROM and to evaluate levels of C reactive protein (CRP).
Methods: This study was conducted in the department of obstetrics and gynaecology, Rajendra institute of medical sciences from March 2019 to February 2020.50 cases of confirmed preterm premature rupture of membrane before 35 weeks of pregnancy were taken as cases and 50 cases of normal pregnancy (28-40 weeks) were taken as controls.
Results: Highest incidence of premature rupture of membrane was among 20–25-year (68%) age groups**.** Incidence of premature rupture of membrane was more in low socioeconomic status (72%)**.** Maximum incidence of premature rupture of membrane in 31-33 weeks gestational age (52%). Most cases of premature rupture of membrane in 24–48-hour group (38%). Most of study group (90%) and control group (80%) delivered by vaginal route. 11 study cases with clinical chorioamnionitis had elevated CRP (43.5 mg/l). One presented with clinical chorioamnionitis. CRP was most sensitive (92%). Total maternal morbidity was due to puerperal pyrexia (22%). Four patients with neonatal sepsis had CRP>6 mg/l. CRP and presence of polymorphs in gastric aspirate have 100% association with septicemia in neonates.
Conclusions: Preterm premature rupture of membrane can be associated with adverse foetal and maternal outcome if immediate measures are not taken.

Keywords: Preterm, Chorioamnionitis, Septicemia, Neonate, Morbidity

INTRODUCTION

Preterm premature rupture of fetal membranes (pPROM) is defined as the onset of amniotic fluid leakage from the vagina before the onset of uterine contractions at less than 37 weeks of gestational age.[1]

pPROM occurs in 2-3% of all pregnancies leading to 30-40% of preterm births. pPROM is a multifactorial process including certain risk components such as pPROM in previous pregnancy, smoking, socioeconomic status, poor nutrition (e.g. body mass index below 19.8 kg/m^2, copper and ascorbic acid deficiencies), prior cervical conization, cervical cerclage, second- and third trimester bleeding, acute pulmonary disease and prior episodes of preterm contractions, infection (bacterial vaginosis), amniocentesis, polyhydramnios and multiple gestation but in most of the cases, the cause remains unknown and is not apparent at the time of membrane rupture.[2]

Foetal membrane rupture is a physiologic process at term, but when it occurs preterm, it results from abnormal structural weakening of the membranes in the region of the internal cervical OS where it is initiated by membrane stretch and involves local inflammation and ascending bacterial colonization.[1]

The weakening of membranes is directly caused by bacterial collagenases and proteases, but a number of other pathways are also involved like increased maternal cytokines or an imbalance in MMPs and TIMPs in response to microbial colonization, trauma, and uterine over-distension.[3]

Genital tract 2 pathogens that have been associated with pPROM include *Neisseria gonorrhoeae*, *Chlamydia trachomatis*, *Trichomonas vaginalis*, and group B β hemolytic *Streptococcus* (GBS). When fluid leakage occurs after amniocentesis, resealing of the membranes is usual (86-94%), but it is usually uncommon after preterm premature rupture of membranes. The latent period from membrane rupture to delivery is typically brief after pPROM. If pPROM occurs before 34 weeks of gestation, more than 90% of women will deliver within 1 week. Near the limit of viability, about two thirds of women will deliver within 1 week of membrane rupture, but with expectant management, a latency of four weeks or more can be achieved in one in five cases.[1]

Currently most authorities accept a plan of active management which includes prevention of infection, delay of delivery until foetal maturity is achieved and active intervention by induction if labour is no longer preventable or if early infection is suspected.[4]

The present study undertaken is to identify the risk factors causing pPROM and to study fetal and maternal outcome associated with pPROM, to diagnose and manage chorioamnionitis associated with pPROM and to evaluate levels of CRP.

Aims and objectives

Aim and objectives were to detect infection and diagnose chorioamnionitis to aid in management of cases of pPROM and to evaluate levels of CRP in cases with clinical and subclinical chorioamnionitis.

METHODS

This study was conducted in the department of obstetrics and gynaecology at Rajendra institute of the medical sciences**.**

Study duration

Study conducted from March 2019-February 2020.

Study place

Study carried out at Labour and indoor wards, department of obstetrics and gynaecology, RIMS, Ranchi.

Study type

Study type was prospective cross-sectional study.

Sampling method

Inclusion criteria

The 50 cases of confirmed pre-tem premature rupture of membrane before 35 weeks of pregnancy were taken as cases. 50 cases of normal pregnancy [28-40 weeks] were taken as controls.

Exclusion criteria

Any associated comorbidity [diabetes, hypertension]and patient on drugs for those morbidity, infection of any sort, rheumatoid arthritis, systemic lupus erythematosus were excluded from this study.

Detailed history was taken followed by complete general and obstetrical examination.

Liquor was confirmed by the following: Gross pooling from posterior fornix, positive ferning, nitrazine paper test and evaporation test.

Daily monitoring of parameters [maternal pulse, temperature, foetal heart rate, total leucocyte count, differential leucocyte count, ESR, CRP] was done for all cases.

Foetal heart rate, maternal temperature, contractions or uterine tenderness was assessed 8 hourly in confirmed cases of PROM. Corticosteroid coverage was done with 2 doses of injection betamethasone 12 mg intramuscular 12 hours apart. Tocolytics were administered for enabling complete corticosteroid coverage. Conservative management was stopped in the scenario of onset of labour or development of chorioamnionitis [maternal temperature>100.4°F uterine tenderness, foul smelling vaginal discharge, abnormal foetal heart rate<100 bpm or >160 bpm], during which labour was augmented with dinoprostone gel [dose according to stage and progress of labour]. If necessary lower segment caesarean section was also done according to maternal and foetal condition.

After delivery cord blood was taken for estimation of neonatal CRP. Mother and neonate were assessed for evidence of sepsis.

Investigations

Maternal investigations were TLC, DLC, ESR, maternal CRP and high vaginal swab.

Statistical analysis was done by SPSS software.

RESULTS

This study was undertaken in the department of obstetrics and gynaecology, Rajendra institute of medical sciences, Ranchi.

Table 1: Age wise and socioeconomic status distribution of study and control group.

Variables	Study group		Control group	
	N	%	N	%
Age group (In years)				
20-25	34	68	30	60
25-30	13	26	18	36
30-35	3	6	2	4
Socioeconomic status				
Low	36	72	20	40
Middle	10	20	17	34
Upper	4	8	13	26
Total	50	100	50	100

Table 1 shows that the highest incidence of premature rupture of membrane was among 20-25 year (68%) followed by 25-30 (26%) and 30-35 (6%) year age groups**.** Higher incidence of the pre-mature rupture of membrane in the low socioeconomic status (72%) as well as least among the upper socioeconomic group (8%) in the study group**.**

Table 2: Obstetrical history.

Gravidity	Study group		Control group	
	N	%	N	%
Primi-gravida	5	10	8	16
Second gravida	5	10	10	20
Multi gravida	40	80	32	64
Total	50	100	50	100

Table 2 shows higher incidence of premature rupture of membrane in multigravida (80%), followed by primigravida and second gravida (5% each).

Table 3: Gestational age.

Gestational age (In weeks)	Study group		Control group	
	N	%	N	%
28-30	12	24	0	0
31-33	26	52	0	0
34-36	12	24	0	0
37-39	0	0	36	72
40-41	0	0	14	28
Total	50	100	50	100

Table 3 shows maximum incidence of premature rupture of membrane in 31-33 weeks gestational age (52%) followed by 28-31 and 34-36 weeks (12% each).

Table 4 shows most cases of premature rupture of membrane in 24-48 hour group (38%), followed by 96-120 hours (22%), 48-72 hours (20%), 72-96 (10%) and >120 hours group (10%) respectively.

Table 4: Duration of premature rupture of membrane.

Duration of premature rupture of membrane (in hours)	Study group	
	N	%
24-48	19	38
48-72	10	20
72-96	5	10
96-120	11	22
>120	5	10
Total	50	100

Table 5: Mode of delivery.

Mode of delivery	Study group		Control group	
	N	%	N	%
Vaginal delivery	45	90	40	80
C-section	5	10	10	20
Total	50	100	50	100

Table 5 shows most of study group (90%) and control group (80%) delivered by vaginal route.

Table 6: Mean CRP and its correlation with chorioamnionitis.

Diagnostic group	Study group		Mean CRP
	N	%	
Clinical chorioamnionitis with elevated CRP	11	22	43.5 mg/l
Elevated CRP without clinical chorioamnionitis	21	42	18.1 mg/l
Clinical chorioamnionitis with normal CRP	1	2	<6 mg/l
No clinical chorioamnionitis and normal CRP	17	34	<6 mg/l

Table 6 shows that 11 study cases with clinical chorioamnionitis had elevated CRP (43.5 mg/l), 21 study cases had elevated CRP (18.1 mg/l) but no clinical chorioamnionitis. One presented with clinical chorioamnionitis with normal CRP and 17 study cases had no clinical chorioamnionitis or elevated CRP.

Table 7 shows comparison of CRP with parameters such as maternal temperature, TLC, DLC, ESR and Foetal heart rate. CRP was most sensitive (92%), but less specific (58%). Maternal temperature, TLC, DLC, ESR and foetal heart rate were more specific than sensitive. ESR (100%) was most specific followed by maternal temperature (91%) and DLC (91%). Foetal heart rate was least sensitive (35%) followed by DLC (50%), TLC (55%), maternal temperature (75%) and ESR (88%).

Table 7: Comparison of CRP and other parameters determining clinical chorioamnionitis.

Test	Without clinical chorioamnionitis		With clinical chorioamnionitis		Specificity	Sensitivity
	Normal	Abnormal	Normal	Abnormal		
CRP	17	21	1	11	58%	92%
Maternal temperature	36	2	4	8	91%	75%
TLC (>12000)	32	6	6	6	87%	55%
DLC	34	4	9	3	91%	50%
ESR	38	0	2	10	100%	88%
Fetal heart rate	32	6	8	4	81%	35%

Table 8: Maternal morbidity in premature rupture of membrane.

Causes	Study group n=50			
	N	%	Positive cervical swab	Raised CRP>6 mg/dl
Puerperal pyrexia	11	22	5	5
Puerperal sepsis	05	10	5	5
Idiopathic	06	12	0	0
Postpartum hemorrhage	0	0	0	0

Total maternal morbidity was due to puerperal pyrexia (22%), the main cause was chorioamnionitis because of late coming of patients to the hospital.

Table 9: Correlation between CRP and neonatal morbidity in premature rupture of membrane.

Causes of neonatal morbidity	Study group (n=50)			
	N	Avg. value of CRP	No. of cases with CRP>6 mg/l	% cases with CRP>6 mg/l
Neonatal sepsis	4	21.8	4	8
Neonatal hyper-bilirubinemia	8	<6	-	-
Neonatal respiratory distress	2	<6	-	-
Neonatal intra-ventricular hemorrhage	1	<6	-	-

Table 9 shows correlation between CRP and neonatal morbidity in premature rupture of membrane. 4 patients with neonatal sepsis had CRP>6 mg/l. Rest patients with neonatal hyperbilirubinemia, neonatal respiratory distress and neonatal intraventricular haemorrhage had average value of CRP<6 mg/l.

Table 10 shows correlation between neonatal sepsis and various tests to diagnose the same. CRP and presence of polymorphs in gastric aspirate have 100% association with septicemia in neonates. TLC and DLC have non specific association with neonatal sepsis and may be elevated in conditions of non septicemia as well.

Table 10: Correlation of CRP levels accuracy with other tests in diagnosing neonatal sepsis in study group.

Tests	Septicemic babies, n=4		Non septicemic, n=46	
	N	%	N	%
CRP>6 mg/l	4	100	-	-
TLC <5000/cumm	3	75	1	2.17
DLC (polymorphs<50%)	3	75	-	-
Presence of polymorphs in gastric aspirate >20 polymorphs/ HPF	4	100	-	-

DISCUSSION

Expectant management in cases of preterm premature rupture of membrane is by far the most accepted treatment modality. The approach should always be a meticulous watch over signs and symptoms of impending infection in order to save the mother from danger of chorioamnionitis. Laboratory parameters like TLC, DLC, ESR are quite unreliable since they often fluctuate in pregnancy and with associated stress. CRP is the most sensitive marker as it has a short half life (less than 24 hours) and is diagnostic of early stages of infection. The purpose of this study is to detect infection and diagnose chorioamnionitis and also to determine CRP levels in cases of Clinical and sub clinical chorioamnionitis.

In this study we have included 50 cases of confirmed preterm premature rupture of membrane (<35 weeks) as study group and 50 cases of normal pregnant women (28-40 weeks) as control group.

Table 1 shows that the highest incidence of premature rupture of membrane was among 20-25-year (68%) followed by 25-30 (26%) and 30-35 (6%) year age groups.

Naeye et al reported that advanced maternal age was a risk factor for preterm premature rupture of membrane which was not consistent with our study.[5]

As per study by Romen et al mean age of patients with preterm premature rupture of membrane was 25.2±0.7 years which was again not in accordance with our study. This may be attributed to study sample received by us during the study period.[6]

Table 1 shows higher incidence of preterm premature rupture of membrane in low socioeconomic status (72%) and least among upper socioeconomic group (8%) in the study group. Our findings are consistent with those of Artal et al who found that poor nutritional status associated with preterm premature rupture of membrane in low socio economic status.[6]

Table 2 shows higher incidence of premature rupture of membrane in multigravida (80%), followed by primigravida and second gravida (5% each). Our observation is consistent with study by Rush et al who found correlation between preterm premature rupture of membrane and multigravida.[7]

Similar findings have been seen in Romen et al, Ismail et al.[6,8]

Table 3 shows maximum incidence of premature rupture of membrane in 31-33 weeks gestational age (52%) followed by 28-31 and 34-36 weeks (12% each). Romen et al found similar results in their study.[6]

Ismail et al found mean gestational age in case of preterm PROM to be 31 weeks which is consistent with our study.[8]

Table 4 shows most cases of premature rupture of membrane in 24-48 hour group (38%), followed by 96-120 hours (22%), 48-72 hours (20%), 72-96 (10%) and >120 hours group (10%) respectively. Our results were not in accordance to those by Lowensohn et al who found mean duration of preterm rupture of membrane to be 150 hours. This may be attributed to early referral of patients during our study period at our centre.[8]

Table 5 shows most of study group (90%) and control group (80%) delivered by vaginal route. Study by Ismail et al found 47% normal vaginal delivery, whereas Devi et al had 42.3% normal delivery rate which was far less than our study.[8,9] This may be attributed to the study population during our study period and good intrapartum monitoring by our resident doctors on duty.

Table 6 shows that 11 study cases with clinical chorioamnionitis had elevated CRP (43.5 mg/l), 21 study cases had elevated CRP (18.1 mg/l) but no clinical chorioamnionitis.1 presented with clinical chorioamnionitis with normal CRP and 17 study cases had no clinical chorioamnionitis or elevated CRP. Our findings support those of Romen et al, Mathur et al who also found that CRP is a good predictor of clinical chorioamnionitis.[6,10]

Table 7 shows comparison of CRP with parameters such as maternal temperature, TLC, DLC, ESR and Foetal heart rate. We compared CRP with other indicators of infection like maternal temperature, TLC, DLC, ESR and foetal heart rate and was found to be more sensitive (92%), but less specific (58%). Maternal temperature, TLC, DLC, ESR and Foetal heart rate were more specific than sensitive. ESR (100%) was most specific followed by maternal temperature (91%) and DLC (91%). Foetal heart rate was least sensitive (35%) followed by DLC (50%), TLC (55%), maternal temperature (75%) and ESR (88%). Our results are consistent with those of Farb et al who found sensitivity 56% and specificity 73% in diagnosing clinical chorioamnionitis.[11]

Our study results are different from those of Evan et al who found sensitivity 82% and specificity 100%.[12]

Our findings are also consistent with Romen et al who found CRP to be most accurate in diagnosing clinical chorioamnionitis as compared to TLC and DLC.[6]

Our findings are also in accordance with studies by Ismail et al who found sensitivity of CRP to be 82% and specificity to be 55%.[8]

Total maternal morbidity (Table 8) was due to puerperal pyrexia (22%), the main cause was chorioamnionitis because of late coming of patients to the hospital. Out of total 11 cases of puerperal pyrexia, 5 were due to puerperal sepsis and rest 6 were due to idiopathic causes. Hawrylyshyn et al found maternal morbidity rate to be 16.7%.[13]

Devi et al found it to be 20.19%.[9] Our findings are consistent with those of Mathur et al who found maternal morbidity to be 20%.[10]

Table 9 shows correlation between CRP and neonatal morbidity in premature rupture of membrane. 4 patients with neonatal sepsis had CRP>6 mg/l. Rest patients with neonatal hyperbilirubinemia, neonatal respiratory distress and neonatal intraventricular haemorrhage had average value of CRP<6mg/l. Our findings are consistent to those of Thompson et al who found that elevated CRP (>8 mg/l) was associated with neonatal septicemia and neonatal morbidity.[14]

Table 10 shows correlation between neonatal sepsis and various tests to diagnose the same. CRP and presence of polymorphs in gastric aspirate have 100% association with septicemia in neonates. TLC and DLC have non specific association with neonatal sepsis and may be elevated in conditions of non septicemia as well. Boyle et al have suggested that count <10000/cumm is associated with infection. Philip et al suggested that count <5000/cumm to improve specificity of the test.[15]

Our findings are consistent with those of Singh et al who found out that TLC< 7000/cumm, CRP 8 mg/l and gastric aspirate with polymorphs >20/HPF have sensitivity of 75% and specificity of 100% in diagnosing neonatal septicemia.[16]

Limitations

Results in this study were representative of the cross section of population we got in this study.

CONCLUSION

Preterm premature rupture of membrane can be associated with adverse foetal and maternal outcome if immediate measures are not taken. Hence every step should be taken to look for risk factors for preterm premature membrane rupture. Antenatal care starting from grassroot levels should be stringent so that no lady is denied the care and early referral if needed at the earliest.

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