C-REACTIVE PROTEIN IN PREMATURE RUPTURE OF MEMBRANE WITH RESPECT TO FETOMATERNAL OUTCOME

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ABSTRACT

BACKGROUND

The incidence of PROM is about 10% of all pregnancies and 70% of them occur at term. Most of the Indian studies document an incidence of 7-12% for PROM of which 60-70% occurs at term. Rest of the 30-40% is contributed at preterm.

The aim of the study is to study the usefulness of maternal CRP measurements in diagnosis of chorioamnionitis, puerperal endometritis, neonatal infectious morbidities and mortalities among patients with PROM (both term and preterm).

MATERIALS AND METHODS

This is a hospital-based cross-sectional observational study where 100 premature rupture of membrane cases were diagnosed and observed for fetomaternal outcome by doing routine clinical, biochemical and serum CRP examinations.

RESULTS

Maximum number of chorioamnionitis (16%) has developed when duration of rupture was for more than 36 hrs. PROM patients with latent period of ≥36 hrs had poorer neonatal outcome; i.e. 54.83% neonatal morbidity and 84.61% neonatal mortality were seen when duration of rupture was more than 36 hrs. 47.36% of CRP positive PROM women had developed chorioamnionitis during the course of delivery or postpartum. 49.12% of CRP positive PROM women had developed preterm delivery. CRP positive PROM women had poorer neonatal outcome; i.e. 82.35% neonatal morbidity and mortality has noted in babies delivered from CRP positive mother.

CONCLUSION

Careful antenatal monitoring, detection and prompt treatment of infection is necessary. Strict aseptic precautions, appropriate therapy, regular antenatal follow up are important features in the prevention and management of PROM. Evaluation of CRP in blood has helped to predict development of chorioamnionitis and preterm delivery following PROM and also perinatal morbidity and mortality.

KEYWORDS

Preterm, Chorioamnionitis, Fever, PROM.

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BACKGROUND

Spontaneous rupture of membrane at any time beyond 28th weeks of pregnancy, but before the onset of labour is called Prelabour Rupture of Membrane (PROM). When rupture of membrane occurs beyond 37 completed weeks, but before onset of labour, it is called "term PROM", and when it occurs before 37 weeks, it is called "preterm PROM." (PPROM) The incidence of PROM is about 10% of all pregnancies and 70% of them occur at term. Most of the Indian studies document an incidence of 7-12% for PROM of which 60-70% occurs at term.[1] Rest of the 30-40% is contributed by PPROM.

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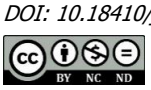


Aetiology- The aetiology of PROM is multifactorial[2] for all practical purposes. The cause of PROM is a reduction in membrane strength. The membranes may lose their tensile strength because of the effect of bacterial proteases. Other products of bacterial metabolism or repeated stretching caused by uterine contraction makes the membrane frail under the effect of normal pressure.

Other factors influencing PROM are cigarette smoking. Alpha1-antitrypsin deficiency of amniotic fluid (Kanayama et al 1985)[3] or may have some genetic influence (Marcil F. 1986).

Complication

The maternal outcome associated with PROM is chorioamnionitis and its squeal. PROM is the most common cause of premature labour, i.e. 20-30% preterm labour

results in premature baby, which leads to organ immaturity and mortality in PPROM.

Neonatal complications include higher incidence of non-assuring Cardiotocography (CTG) patterns (7.9%) due to cord compression subsequent to leaking and higher incidence of sepsis.[4]

In diagnosing PROM, the history and physical examination alone often are inadequate to confirm status of membranes. Fluid may not be present in vagina for evaluation. Furthermore, fluid at times maybe contaminated with urine, cervical mucus, bathwater, vaginal discharge, blood or meconium. Because of these difficulties, multiple cytological, biochemical, calorimetric and sonographic methods have been developed for the detection of rupture membranes. Despite significant advances in technology, no single test has been found to be accurate and diagnosis, still requires an integration of historic factors, physical examination and laboratory testing.[5]

CRP- C-reactive protein is an abnormal serum glycoprotein produced by liver during acute inflammation in response to infection and tissue injury. Its production is regulated by interleukin 1b and 6 and TNF. Also, it had been a measure of acute phase reactions to inflammation. Recently improved high sensitive and standardised quantitative assays in serum and Cerebrospinal Fluid (CSF) had allowed a re-evaluation of its potential as a diagnostic laboratory test. Because it disappears rapidly when inflammation subsides, its detection signifies the presence of a current inflammatory process. Further, by serial measurements, important information can be obtained on the resolution or continuation of the inflammatory process.[6]

This study is designed to be carried out. The diagnostic value of C-Reactive Protein (CRP) in pregnancy complicated by Premature Rupture of the Membranes (PROM) and its fetomaternal outcome.

Aims and Objectives

To study the usefulness of maternal CRP measurements in diagnosis of chorioamnionitis, puerperal endometritis, neonatal infectious morbidities and mortalities among patients with PROM (term and preterm).

MATERIALS AND METHODS

This is a hospital-based cross-sectional observational study conducted in the Department of Obstetrics and Gynaecology, VIMSAR, Burla, for the duration of two years, i.e. from November 2014 to October 2016. A total of 100 patients with pregnancies after 28 completed weeks of gestation with complaint of watery vaginal discharge (leaking membrane) with at least one hour of latent period (i.e., rupture of membrane to onset of labour) with having normal CTG findings at the time of admission were recruited for the study serially till the 100 numbers of cases achieved.

After admission to indoor or labour room, detailed history, general examination, examination of other systems and abdominal examination was recorded in all cases.

Confirmation of rupture of membrane done by looking gross leakage of amniotic fluid through cervical canal during coughing or sneezing and by estimation of pH of collected fluid from the posterior fornix (vaginal pool) by litmus or nitrazine paper test, then gentle per vaginal examination was done.

A routine haematological examination and 2 cc of blood of each patient was drawn for estimation of C-reactive protein. It was considered positive when the serum C-reactive protein value was more than 8 mcg/dL. Urine was sent for routine microscopy and culture and sensitivity test.

All cases with a diagnosis of premature rupture of membrane are given antibiotics, i.e. Inj. Ceftriaxone (1 gm) IV steroids and tocolysis if necessary.

Then, the patients were kept under observation. The progress of labour was observed. Mode of delivery was as per indication warranted. Any maternal complications during was noted and managed.

After birth of the baby weight, sex, Apgar score at 1 minute and 5 minutes were recorded. The babies delivered from mother with PROM were given antibiotics, i.e. Inj. Ceftriaxone (125 mg) IV. Then, the baby was closely observed and followed to detect any complication during first week of survival.

All these cases were compiled and only important and relevant factors were taken into consideration.

Statistics- The data were processed on computer software package SPSS version 11. The "Chi-square test with p value" and "Odds ratio" were calculated. The association between maternal C-reactive protein and fetomaternal outcome was expressed in term of "Odds ratio" and its significance in terms of "p value." 95% confidence interval ($p < 0.05$) was considered as significant.

OBSERVATION

Age Group in Yrs.	Number of Cases	Percentage
≤20	17	17%
21-25	16	16%
26-30	30	30%
31-35	17	17%
≥36	20	20%
Total	**100**	**100.00%**

Table 1. Age Incidence

Maximum number of cases belong to age group 26-30 years and minimum number of cases belong to age group 21-25 years.

Gravida	Number of Cases	Percentage
G1	40	40%
G2	32	32%
G3	20	20%
G4	4	4%
≥G5	4	4%
Total	**100**	**100%**

Table 2. Parity Incidence

Majority of PROM patients are primigravida and rest 60% constitutes multigravida.

Antenatal Checkup	Number of Cases	Percentage
Booked cases	73	73%
Unbooked cases	27	27%
Total	**100**	**100%**

Table 3. Antenatal Checkup (Booked/Unbooked Cases)

Gestational Age in Weeks	Number of Cases	Percentage
<37	37	37%
≥37	63	63%
Total	**100**	**100%**

Table 4. Period of Gestation

Maternal Complications	Study Group (100)	
	Number of Cases	Percentage
Anaemia	40	40%
Abruptio placentae	1	1%
Breech	4	4%
Chorioamnionitis	28	28%
IUGR	4	4%
Oligohydramnios	10	10%
Previous CS	2	2%
PIH	3	3%
Twin	2	2%

Table 5. Associated Pregnancy Complication

In the study group, 64% patients had various complications as mentioned in the table above. Among which, anaemia is most common, seen in 40% cases, followed by chorioamnionitis (28%) and oligohydramnios (10%).

Mode of Delivery	Total Number of Cases	Primigravida		Multigravida	
		Number of Cases	Percentage	Number of Cases	Percentage
VD	64	31	48.44%	33	51.56%
Instrumental VD	4	1	25%	3	75%
LSCS	32	8	25%	24	75%

Table 6. Mode of Delivery

Indication of C.S.	No. of Cases	Percentage
CPD	4	11.11%
Foetal distress	21	58.33%
Oligohydramnios	1	2.78%
Previous CS	3	8.33%
Primi, breech	2	5.56%
Twin, 1st breech	1	2.78%
Unfavourable cervix	4	11.11%
Total	**32**	**100%**

Table 7. Indications of Caesarean Section

In the study group, foetal distress 21 cases (58.33%) was the main indication of caesarean section.

Maternal Complications	Study Group (100)	
	No. of Cases	Percentage
Chorioamnionitis	28	28%
Abruptio placentae	1	1%
Oligohydramnios	10	10%
Preterm delivery	37	37%

Table 8. Maternal Complications

High Vaginal Swab Culture	Number of Cases	Percentage
Escherichia coli	28	28%
Klebsiella	9	9%
Pseudomonas	2	2%
Streptococcus	3	3%

Table 9. Bacteriology of High Vaginal Swab Culture

Out of 100 high vaginal swabs, Escherichia coli was recovered from 28% patients, Klebsiella from 9%, Streptococcus hemolyticus from 3% and Pseudomonas from 2% patients. Rest other samples were sterile and no patients had more than one pathogen in her high vaginal swab culture.

Perinatal Morbidity and Mortality	No. of Diseased	%	No. of Deaths	%
Stillbirths	3	8.82%	3	23.07%
RDS	12	35.29%	8	61.53%
Pneumonia	1	2.94%	0	0%
Gastroenteritis	6	17.64%	2	15.38%
Jaundice	5	1.49%	0	0%
Conjunctivitis	3	8.82%	0	0%
Neonatal sepsis	0	0%	0	0%
PUO	4	11.76%	0	0%
Total	**34**	**100%**	**13**	**100%**

Table 10. Neonatal Morbidity and Mortality

Duration of Rupture of Membrane to Labour	Study Group (100)	Percentage
	Number of Cases Developing Chorioamnionitis	
0-12 hrs.	2	2%
13-24 hrs.	3	3%
25-36 hrs.	7	7%
Above 36 hrs.	16	16%

Table 11. Duration of Rupture Membrane to Labour and Incidence of Chorioamnionitis

The incidence of chorioamnionitis has increased when the duration of rupture of membrane has increased. Maximum number of chorioamnionitis (16%) has developed when duration of rupture was more than 36 hrs.

Duration of Rupture of Membrane in Hours	LB	SB	Neonatal Morbidity		Neonatal Mortality	
	No. of Cases	No. of Cases	No. of Cases	Percentage	No. of Cases	Percentage
<12 hrs.	56	1	8	25.80%	2	15.39%
13-24 hrs.	10	0	2	6.45%	0	0
25-36 hrs.	7	0	4	12.90%	0	0
>36 hrs.	16	2	17	54.83%	11	84.61%
Total	**89**	**3**	**31**	**100%**	**13**	**100%**

Table 12. Duration of Rupture of Membrane and Neonatal Outcome

This table shows relation between C-reactive protein and incidence chorioamnionitis.

Chorioamnionitis	Total Cases	CRP Positive		CRP Negative	
		No. of Cases	P%	No. of Cases	%
Positive	28	27	47.36%	1	2.32%
Negative	72	30	52.63%	42	97.67%

Table 13 (a). CRP and Chorioamnionitis

x^2 = 24.66, D.F. = 1, P value = 0.00000068, Odds ratio = 37.800 CI @95% (4.865-293.691).

G.A. at Time of Delivery in Weeks	Total	CRP Positive		CRP Negative	
		Number of Cases	Percentage	Number of Cases	Percentage
Preterm (<37)	37	28	49.12%	9	20.93%
Term (≥37)	63	29	58.87%	34	79.06%

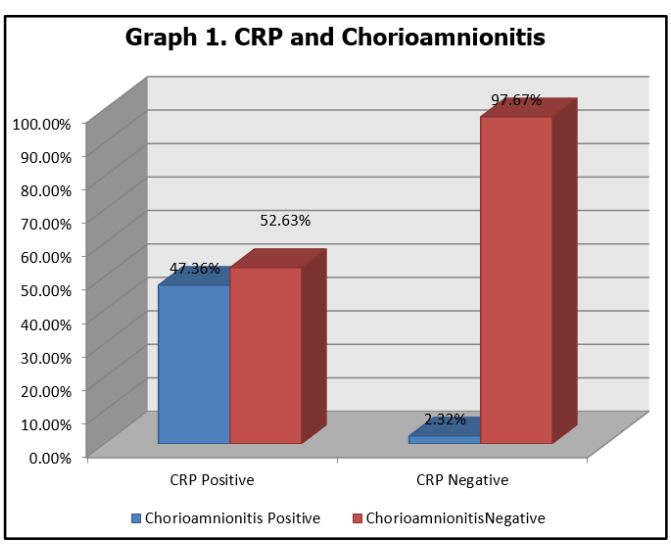
Table 13 (b). CRP and Preterm Labour

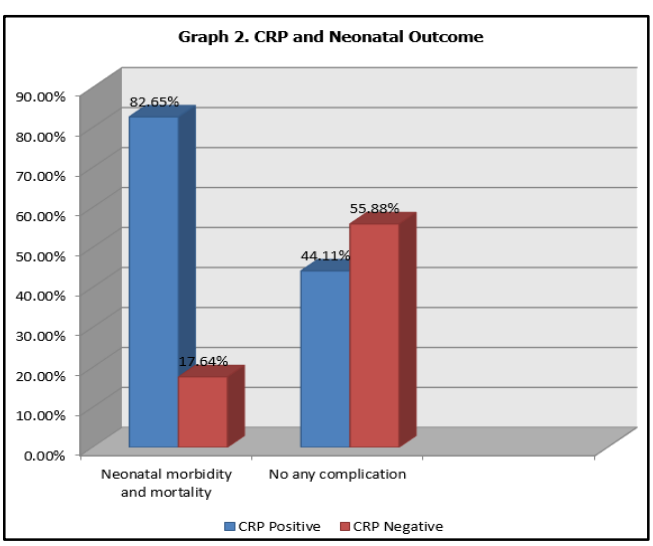
x^2 = 8 .35, D.F. = 1, p value = 0.003, Odds ratio = 3.674 CI @95% (1.483-8.968).

Neonatal Outcome	Total Births	CRP Positive		CRP Negative	
		Number of Cases	Percentage	Number of Cases	Percentage
Neonatal morbidity and mortality	34	28	82.35%	6	17.64%
No complication	68	30	44.11%	38	55.88%
Total	**102 Births**				

Table 14. CRP and Neonatal Outcome

x^2 = 13.50, D.F. = 1, p value = 0.0001, Odds ratio = 5.911; CI @95% (2.167-16.121).





DISCUSSION

Age Group- The age group coincides with that of House et al (1974).[7] They have found that 40.6% patients belong to age group 25-35 years. Akhter et al found 40.33% of 300 cases of PROM belong to age group between 21-25%.

Parity Incidence- In his study, primigravida were more vulnerable to PROM, which is similar to findings of Akhtar et al[8] who found 45% primigravida with PROM and S Akter 2010 found 38% of primigravida with PROM in their study.

Antenatal Checkup- Majority of PROM cases were found in booked cases. There was no significant correlation between the antenatal care and incidence of PROM.

Gestational Period- Out of 100 cases of study group, incidence of preterm PROM was 37%. Similar incidence was found in Danforth DN study[9] who noted 30% of preterm PROM in his study.

Associated Pregnancy Complications- The most common obstetrical complication associated with PROM met during this study was anaemia. 40% of the patients suffered from anaemia, which was mostly mild and moderate.

Duration of Labour- In the present study, 51% PROM cases were in labour for less than 8 hours and within 16 hours of labour 83% delivered. House et al 1974,[7] 455 PROM cases had almost similar finding. In their series, over 75% patients were in labour for less than 10 hours. So, the result of the present study compares well with that of House et al.

Mode of Delivery- In the present series, there were 64% vaginal deliveries, 4% instrumental vaginal delivery, 32% caesarean section. There was an incidence of 20% caesarean delivery in Tahir et al study[10] and 14% in Shehla et al[11] study.

Indication of LSCS- Caesarean section was done in 32 cases. The main indication of caesarean section was foetal distress (58.33%) followed by CPD (11.11%) of cases. Wilson et al (1951)[12] reviewed 143 women with PROM in whom CS was required in 31 cases (22%). Out of 31 cases CS was done in 18 (58%) for breech presentation.

There were 28% cases of chorioamnionitis, Artal K study[13] noted 3-13% cases of chorioamnionitis.

Bacteriology of High Vaginal Swab Culture- In this study, high vaginal swab culture was done and E. coli was found in 28% cases followed by Klebsiella in 9% cases and pseudomonas and streptococcus in 2% and 3% cases, respectively. Similar was the findings of Santosh et al (1984)[14] who from 100 cases of PROM isolated E. coli with highest incidence of 22% followed by Pseudomonas.

Duration of Latent Period and Incidence of Chorioamnionitis- In the present study, chorioamnionitis was detected in 28 cases out of 100 cases (28%). With duration of 0-12 hours of rupture, there were 2% cases of chorioamnionitis, but as duration of rupture increased, the incidence of chorioamnionitis also increased, i.e. in between 12-24 hours, there were 3% cases between 24-36 hours, 7% cases, and above 36 hours, 16% cases.

The incidence was more or less similar to the finding of (House and Pathak)[7] 25%, 1979.

Duration of Rupture of Membrane and Neonatal Outcome- Maximum neonatal morbidity, i.e. 17 (54.83% of total morbidity) and mortality, i.e. 11 (84.61% of total mortality) are seen when duration of rupture was more than 36 hrs. But, there was no such association of increased duration of rupture of membrane and increased number of neonatal morbidity and mortality found in this study.

CRP and Maternal Outcome

(a) CRP and Chorioamnionitis

In this study, 57 patients of PROM were CRP positive, out of which, only 27 cases, i.e. 47.36% developed chorioamnionitis. Likewise, 1 patient (2.32%) developed chorioamnionitis out of rest 43 patients who were CRP negative.

The results of this study are similar to that of Evans et al (1980),[15] which stated that an elevated C-reactive protein serves as an early indicator of infection in PROM. Hawrylyslyn et al (1983)[16] stated that CRP is superior to available clinical and laboratory investigations in predicting infection.

(b) CRP and Preterm Delivery

In this study, 57 patients of PROM were CRP positive, out of which only 28 cases, i.e. 49.12% developed preterm delivery. Likewise, 9 patients, i.e. 20.93% developed preterm delivery, out of rest 43 patients who were CRP negative.

This result is similar to that of Halder A et al (2013).[17] They found that women with CRP positive is associated with nearly a two-fold increased risk of preterm delivery.

CRP and Neonatal Outcome

In this study, poor neonatal outcome was seen in 34 births, out of total 102 births, out of which 28 births had delivered from 28 CRP positive PROM women and 6 births had delivered from 6 CRP negative PROM women. Likewise, there were 30 births who were delivered from 29 CRP positive PROM women and 38 births who were delivered from 37 CRP negative PROM women.

Halder A et al (2013)[17] noted neonates born to CRP positive mother had more poor neonatal outcome than those born to CRP negative mother in their study.

Summary

1. Maximum number of cases was in the age group 26-30 years.
2. The primigravida (40%) were more prone to PROM.
3. Majority were booked cases (73%).
4. Preterm PROM cases were 37% and term PROM cases were 63%.
5. In this study, 51% cases of PROM were in labour for less than 8 hours and 83% within 16 hours of labour.
6. The most common obstetrical complications associated with PROM encountered during pregnancy in this study was anaemia (40%).
7. There were vaginal deliveries in 68% cases and caesarean section in 32% cases.
8. The main indication for caesarean section was foetal distress (58.33%).

9. 37% PROM women underwent preterm delivery and 28% PROM women developed chorioamnionitis.
10. High vaginal swab reveals E. coli in 28% cases followed by Klebsiella in 9% cases.
11. Perinatal morbidity was seen in 30.39% and perinatal mortality was seen in 12.74%, out of total 102 births.
12. Maximum number of chorioamnionitis (16%) has developed when duration of rupture was more than 36 hours.
13. PROM patients with latent period of ≥36 hours had poorer neonatal outcome; i.e. 54.83% neonatal morbidity and 84.61% neonatal mortality were seen when duration of rupture was more than 36 hrs.
14. 47.36% of CRP positive PROM women had developed chorioamnionitis during the course of delivery or postpartum.
15. 49.12% of CRP positive PROM women had developed preterm delivery.
16. CRP positive PROM women had poorer neonatal outcome; i.e. 82.35% neonatal morbidity and mortality has noted in babies delivered from CRP positive mother.

CONCLUSION

In this observational study, maximum patients (58%) had a latent period of 0-12 hrs. and there was a high incidence of perinatal morbidity and mortality of 30.39% and 12.74% respectively and ill effects were directly proportional to the latent period.

PROM is a significant obstetric problem and it poses a huge challenge to the obstetrician who is caught in a dilemma due to the jeopardising effect of premature rupture of membrane on both maternal and foetal health. Hence, all cases of premature rupture of membrane should be treated early and energetically to minimise the adverse maternal and foetal effects of premature rupture of membrane.

Careful antenatal monitoring, detection and prompt treatment of infection is necessary. Strict aseptic precautions, appropriate therapy, regular antenatal follow up are important features in the prevention and management of PROM.

Evaluation of CRP in blood has helped to predict, which case will develop chorioamnionitis and preterm delivery following PROM and also perinatal morbidity and mortality.

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