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Original Research Article

Role of C - reactive protein (CRP) In Prediction of Clinical Outcome of Preterm Premature Rupture of Membranes (PPROM)

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Abstract:

Background: C-reactive protein (CRP) is the most extensively studied acute-phase reactant so far in predicting infection. This study was done to evaluate the role of CRP in prediction of clinical outcome in case of PPROM.

Methods: This is a prospective study among 100 pregnant women with PPROM admitted in the department of Obstetrics and Gynecology in Karnataka institute of Medical Sciences & Hospital, Hubballi from December 2019 to May 2021. Pregnant women with PPROM aged more than 18 years with singleton pregnancy and gestational age between 28 to 36 weeks are included. Informed written consent was obtained before collecting the data and examination. Case was evaluated by asking the history, clinical examination, blood grouping and Rh typing was sent. Nitrazine test, fern test, CBC, CRP, Vaginal and cervical swab was sent for culture, urine routine, urine culture and sensitivity was also sent. The information collected was entered in Microsoft Excel and analysed using SPSS 22 software. Chi square test was used to test the association between the variables. Statistical significance was set at 0.05% level of significance ($p < 0.05$).

Results: There were total 100 PPROM woman enrolled for the study. Majority were in the age group of 21-25 years (50%). PPROM was most common among unbooked (75%) cases and among primigravida (56%). Among primi gravida females, 78.57% delivered vaginally after induction and among multigravida the rate of vaginal delivery was 59.09%. Among primi gravida females, 62.5% delivered vaginally after induction and among multigravida the rate of vaginal delivery was 79.55%. After PROM 55.36% of women delivered within 12-24 hrs in primi gravida, whereas 36.36% of women delivered within 12-24 hrs in multi gravida. Mean duration was 23.52hrs with SD of 20.01hrs. Maternal CRP was positive among 46% cases and cord blood was positive for CRP in 39% cases. Maternal morbidity was significant (30%). No maternal mortality in the study. Most common fetal morbidity was sepsis (14%) followed by birth asphyxia (4%).

Conclusion: By educating the women to have regular antenatal care, recognise genital tract infections early, treat appropriately and report at the earliest opportunity, the difficulties associated with PPROM might be lessened. For the purpose of predicting PPROM and averting future problems, CRP can be employed as a diagnostic measure.

Keywords: PPROM, CRP, Maternal morbidity, perinatal morbidity.

Introduction

Preterm premature rupture of the membranes (PPROM), also known as prelabor premature rupture of the membranes before 37th week, is a common obstetric issue that affects 3–5% of all pregnancies. [1] PPROM is a difficulty for the obstetrician and is linked to 30% of neonatal morbidities and fatalities in premature birth. [2,3]

Patients with two or more of the following symptoms are considered to have clinical chorioamnionitis: high body temperature, maternal leukocytosis with bands, foetal tachycardia, uterine discomfort, foul-smelling amniotic fluid, and positive C reactive protein (CRP). [4] The use of maternal serum C-reactive protein (CRP) as a supplemental tool for the detection of subclinical infection in pregnant women who are having preterm labour or preterm membrane rupture has been explored. CRP is an acute-phase protein made in the liver's hepatocytes and is typically found in trace amounts in serum. Following damage and inflammation, the concentration is observed to significantly increase. [5] The biological effects of CRP, which include enhanced phagocytosis, stimulated leukocyte motility, and opsonic effects once it is released, are tied to altered or necrotic membrane structures and suggest a specialised role in tissue regeneration and repair. [6] The endothelium system's macrophages, endogene

pyrogens, and prostaglandins are potential humoral mediators. [7] 24-48 hours after the initiating stimulation, the highest concentrations are visible. The placenta does not allow for the passage of CRP. [8]

Commonly used laboratory indicators including erythrocyte sedimentation rate, white blood cell count, neutrophil count, or vaginal bacterial culture cannot accurately predict early infection. Clinical symptoms including fever and fetomaternal tachycardia typically take time to manifest. [9] Patients with intrauterine infections exhibit elevated CRP concentrations in both their peripheral circulation and amniotic fluid. [10] Infection and prematurity are the most frequent causes of perinatal mortality following PPROM, which can result in unfavourable neonatal outcomes, include intraventricular haemorrhage, periventricular leukomalacia, cerebral palsy, and bronchopulmonary dysplasia. [11]

Levels of interleukin-6 (IL-6) in the amniotic fluid larger than 1500 Pg/ml exhibit a highly significant connection with plasma CRP concentrations greater than 1.5 mg/dl. The risk of an early delivery can be predicted and detected using the C-reactive protein as a screening test. [12] Despite the continual rise (and decline) of new infection markers, C-reactive protein (CRP) is the most thoroughly researched acute-phase reactant to date. Its wide availability and its quick, easy, and affordable determination make it one of the preferred indices. [13] Hence this study was done to evaluate the role of CRP in predicting the clinical outcome of PPROM.

Objective:

To evaluate the role of C - reactive protein (CRP) in predicting the clinical outcome of preterm premature rupture of membranes (PPROM).

Materials and Methods:

This was a hospital based prospective study conducted in the department of Obstetrics and Gynecology in Karnataka Institute of Medical Sciences & Hospital, Hubballi, Karnataka from December 2019 to May 2021 among 100 pregnant women with PPROM (Premature Prelabour Rupture of Membranes)

Inclusion criteria:

1. Pregnant women aged 18years or more
2. Pregnant women with singleton pregnancy
3. Gestational age between 28wk-36wks+6days with PPROM

Exclusion Criteria:

1. Pregnant women with medical disorders like gestational hypertension, preeclampsia, thyroid disease, gestational diabetes
2. Congenital anomalies in the fetus, fetal growth restriction
3. Gross vaginal bleeding, fever
4. Pregnancy less than 28wks and multiple gestation
5. Procedures that may result in PPROM like cervical encirclage
6. Cervical incompetence

100 pregnant women were selected for the study, considering the 90% sensitivity of CRP in chorioamnitis [14] with absolute precision. Total sample size calculated was 73 which extended to 100. Written informed consent was obtained from the study participants. PPROM was diagnosed by history taking and physical examination. Other methods used were nitrazine test (nitrazine paper turns blue) and fern test.

Gestational age was determined by LMP and 1st trimester scan. Investigations like CBC, CRP, vaginal and cervical swab was sent for culture and sensitivity. The information collected was entered in Microsoft Excel and analysed using SPSS 22 software. Chi-square test was used to test the association between variables and statistical significance was set at 0.05% level of significance ($p < 0.05$).

Results:

In our study 100 women with preterm prelabor rupture of membrane (PPROM) participated. Among them 12 had history of PPROM in previous pregnancy. Majority belonged to the age group of 21-25 years i.e. 50% followed by less than 20 years (26%) and 26-30 years (23%). Mean age was 23.09 years with standard deviation of 3.16 years. 75% study populations in our study were unbooked and 56% were primigravid. When socio-economic status was studied, majority of the study participants belonged to low socio-economic status (74%). [Table 1]

Table 1: Clinico-social Characteristics of study participants

Variable		Frequency	Percentage
Age	<20 years	26	26%
	21-25 years	50	50%
	26-30 years	23	23%
	31-35 years	1	1%
Regstration status	Booked	25	25%
	Unbooked	75	75%
Gravida	Primigravida	56	56%

	Multigravida	44	44%
Socio-economic status	High	1	1%
	Middle	25	25%
	Low	74	74%

Table 2: Obstetric details of the study participants

Variable		Primi (56)	Multi (44)	P value
Mode of delivery	Vaginal delivery	35 (62.5%)	35 (79.55%)	0.06
	LSCS	21 (37.5%)	09 (20.45%)	
PROM to Delivery interval	<6hr	00	01 (02.27%)	0.633
	6-12hr	10 (17.86%)	13 (29.55%)	
	12-24hr	31 (55.36%)	16 (36.36%)	
	24-48hr	12 (21.43%)	11 (25%)	
	>48 hr	03 (05.35%)	03 (06.82%)	

Among primi gravida females, 62.5% delivered vaginally after induction and among multigravida the rate of vaginal delivery was 79.55%. After PROM 55.36% of women delivered within 12-24 hrs in primi gravida, whereas 36.36% of women delivered within 12-24 hrs in multi gravida. Mean duration was 23.52hrs with SD of 20.01hrs. [Table 2]

Maternal CRP was positive among 46% cases and cord blood was positive for CRP in 39% cases. Even culture was sent and compared with the outcome in both mother and neonate. It was seen that most common postnatal complication was fever followed by wound infection, PPH, UTI, LRTI and sepsis. Among 17% study participants who were positive for CRP, 14% positive for cord blood CRP and 13%, 14% & 12% with culture positive in their blood, cervical swab and vaginal swab were febrile after delivery. And these findings were related with even wound infection. [Table 3]

Table 3: Factors affecting maternal outcome of the study participants

Variable		Healthy	Febrile	LRTI	URTI	PPH	UTI	Sepsis	Wound infection
Maternal CRP	**Positive**	21	17	1	0	2	2	1	2
	Negative	49	2	0	1	0	1	0	1
Cord blood CRP	**Positive**	18	14	1	0	2	1	1	2
	Negative	52	5	0	1	0	2	0	1
Cordblood culture	**Positive**	14	13	1	0	2	0	1	1
	Negative	56	6	0	1	0	3	0	2
Cervical swab culture	**Positive**	16	14	0	1	1	1	1	3
	Negative	54	5	1	0	1	2	0	0
Vaginal swab culture	**Positive**	18	12	1	0	2	2	1	3
	Negative	52	7	0	1	0	1	0	0

Table 4: Factors affecting fetal outcome of the study participants

Variable		Healthy	Birth asphyxia	Sepsis	LRTI	MAS	RDS
Maternal CRP	**Positive**	27	3	11	2	2	1
	Negative	50	1	3	0	0	0
Cordblood CRP	**Positive**	24	2	11	1	0	1
	Negative	53	2	3	1	2	0
Cordblood culture	**Positive**	15	5	8	2	2	0
	Negative	62	1	4	0	0	1
Cervical swab culture	**Positive**	22	3	10	1	1	0
	Negative	55	3	2	1	1	1
Vaginal swab culture	**Positive**	19	6	10	2	2	0
	Negative	58	0	2	0	0	1

Most common fetal complication was Sepsis followed by birth asphyxia, LRTI, MAS and RDS. Among 11% study participants who were positive for CRP, 11% positive for cord blood CRP and 8%, 10% & 10% with culture positive in their blood, cervical swab and vaginal swab had sepsis after delivery. And these findings were related with even birth asphyxia and LRTI. [Table 4]

Table 5: Factors associated with neonatal outcome of the study participants

Variable		Live	Neonatal Death	Total	p value
Maternal CRP	Positive	42	4	46	0.29
	Negative	52	2	54	
Cordblood CRP	Positive	35	4	39	0.316
	Negative	59	2	61	
Cord blood culture	Positive	29	3	32	0.601
	Negative	65	3	68	
Cervical swab culture	Positive	34	3	37	0.806
	Negative	60	3	63	
Vaginal swab culture	Positive	34	5	39	0.06
	Negative	60	1	61	
ROM duration	<6hr	30	1	31	0.98
	6-12hr	32	1	33	
	12-24hr	23	2	25	
	24-48hr	4	1	5	
	>48 hr	5	1	6	

There were total 6 neonatal deaths. Few variables were correlated to test the association between the neonatal death and others like maternal CRP, cord blood CRP, cord blood culture, cervical swab culture, vaginal swab culture and ROM duration. It was found that novariables were affecting the outcome significantly [Table 5]

Table 6: Comparison of different variables with mode of delivery

Variable		VD	LSCS	p value
Maternal CRP	Positive	32	14	0.92
	Negative	38	16	
Cordblood CRP	Positive	27	12	0.893
	Negative	43	18	
Cordblood culture	Positive	21	11	0.51
	Negative	49	19	
Cervical swab culture	Positive	24	13	0.39
	Negative	46	17	
Vaginal swab culture	Positive	25	14	0.30
	Negative	45	16	

Maternal CRP, Cord blood CRP, Cordblood CRP, Cord blood culture, cervical swab culture and vaginal swab culture were not significantly associated with the mode of delivery.[Table 6]

Discussion:

The most sensitive acute phase protein, C-reactive protein, appears to rise in less than 24 hours, making it an ideal marker for early-stage infection diagnosis. Presently, expectant management is a recognised therapy for PPROM. The mother's risk of developing chorioamnionitis remains the primary clinical concern, though.

100 patients in all were evaluated for the current study. With a mean age of 23.09 years and an SD of 3.16 years, the majority (50%) belonged to the 21–25 age groups. Anjana Devi et al. at JIPMER Pondicherry [15] found that 76.9% of the study participants were in the age range of 20-29 years, while Tian C et al. in China [16] found that the mean age of the study participants was 26+2 years. BS Kodkany at JNMC Belgaum [17] found that 46% of the study participants were in the 21–25 year age range. In our study, PPROM occurs more frequently in unbooked patients than in booked situations. In the study by Anjana Devi et al. [15], 52% of the PROM group's reservations were made as opposed to 63% in the control group. 56% of Primigravida in this study had PPROM compared to 44% of Multigravida. In contrast to this conclusion, 63.5% of women in similar research done in Bihar by Sinha A et al [18] and 53.7% of women in a study conducted in Japan by Ima et al were multigravida. 71% of the women in [19] Parul Garg's study in Mathura were multivores. [20]

In the study group, there were 31% caesarean sections, compared to 12% in the control group, according to Swati Pandey [21]. Comparable to the Swati Pandey study, 30% of the participants in the current study underwent caesarean sections. In contrast to the current study, the rates of caesarean sections were greater in the studies by Anjana Devi15 and Singhal [22] and lower in the studies by Piya Ray [23] and Kamala J [24].

46% of cases had positive maternal CRP levels, while 39% had positive cord blood CRP levels. This result was consistent with research done in Bihar by Sinha A et al. [18] where 46.5% of

participants tested positive for CRP, and research done in Mathura by Parul Garg et al. [20] where the CRP positivity rate was 83.8%, a very high rate compared to our study. 28.75% of participants in a Korean study by Yoon BH et al. were positive for cord blood CRP. [25]

An increased risk of maternal morbidity is linked to PROM. The length of the ROM increases maternal morbidity. The most frequent morbidity identified in our investigation was femoral morbidity. Maternal morbidity was observed in 21% of patients in the Kodkany [17] research. Puerperal pyrexia was observed in 19% of the individuals in this study. Singhal [22], in comparison, revealed a maternal morbidity of 4%. Maternal morbidity in Kamala Jayaram's [24] study was 4%. Maternal morbidity in the current research was 30%.

It is concerning how ROM and the resulting foetal risk are related. When membranes tear, the infection clock begins to run. Additionally, a higher percentage of prenatal death has been linked to PROM (Akhter et al., 1980).26 In our research, sepsis (14%) was the most frequent consequence, followed by birth asphyxia (4%), LRTI (2%), MAS (2%) and RDS (1%). Perinatal morbidity was 32% and death was 5% in the Sanyal [27] research. Perinatal morbidity in Kodkany [17] was 39.8%, with birth asphyxia accounting for 29.5% of those cases. The perinatal death rate in Anjana Devi's [15] study was 4.8%. It was 2.5% in Piya Ray's [23] study. Perinatal morbidity was 23% and death was 6% in the current study. Fetal morbidity increases with increase in PROM to delivery interval.

Conclusion:

PPROM is a dangerous condition that raises the possibility of both maternal and foetal morbidity. It makes 5–10% of pregnancies more difficult. With a decrease in gestational age and an increase in the latent period, complications rise. The diagnosis of PPROM, the identification of etiological variables, and their therapy present challenges. In 46% of instances, the CRP was positive, and in 30% of cases, maternal morbidity was present. Fetal morbidity was seen among 23% cases.

Most common postnatal complication was fever (19%) followed by wound infection (3%), UTI (3%), PPH (2%), LRTI (1%), URTI(1%) and sepsis (1%). Most common fetal complication was Sepsis (14%) followed by birth asphyxia (4%), LRTI (2%), MAS (2%) and RDS (1%). Neonatal mortality rate in our study was 6%. Therefore, the most accurate marker for early preterm delivery prediction in PPROM is the detection of maternal CRP at admission in cases of PPROM.

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