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Role of C-Reactive Protein in Preterm Labour and its Association Over Maternal and Neonatal Outcome

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Abstract: ***Aim: To find out role of C-reactive protein in preterm labour and its association over maternal and neonatal outcome. Material and Methods: The prospective study was conducted on 400 antenatal women with preterm labour in MLB Medical College, Jhansi. The study group having preterm labour with CRP positive and control with CRP negative. Result: CRP is an important prediction of preterm labour. CRP positive values patients had more changes of developing clinical chorioamnionitis mothers having raised CRP values have babies with low birth weight and neonatal septicemia.***

Keywords: CRP, LSCS, CL, PROM

1. Introduction

Preterm labour is defined by the World Health Organization as the onset of labour prior to the completion of 37 weeks of gestation, in a pregnancy beyond 20 weeks of gestation. Preterm labour may either be a physiological process that has occurred too soon or a pathological process following an abnormal stimulus. The earlier the onset of labour, the more likely is that a pathological process like infection is implicated. Infection is implicated as the aetiological factor in 40-50% of cases of preterm labour at early gestations (<30 weeks). Infection induces an intra-amniotic inflammatory response involving the activation of a number of cytokines and chemokines which in turn trigger preterm contractions, cervical ripening and rupture of the membranes. Human C-reactive protein (CRP) is the classical acute phase reactant, the circulating concentration of which rises rapidly and extensively in a cytokine-mediated response to tissue injury infection and inflammation. Recently improved high sensitive and standardized quantitative assays in serum and cerebrospinal fluid (CSF) have allowed a re-evaluation of its potential as a diagnostic laboratory test.

Aims and Objectives

1) To diagnose the cases with preterm labour.
2) To evaluate cases with preterm labour for C-reactive protein as biomarker.
3) Study the association of C-reactive protein over maternal and neonatal outcome.

2. Material and Methods

The study was conducted on 400 antenatal women with preterm labour in the department of Obstetrics and Gynaecology in cooperation with department of Pathology in MLB Medical College, Jhansi. This is a prospective cohort study and followed through pregnancy, delivery and early perperium till discharge.

Study group: 200 antenatal women having preterm labour with CRP positive

Control group: 200 antenatal women having preterm labour with CRP negative

Inclusion criteria: Cases of antenatal women with symptoms of preterm labour between >20 week to < 37 week gestational age without any systemic disease.

Exclusion criteria: Cases of antenatal women with gestational diabetes, diabetes mellitus, essential hypertension, preeclampsia, antepartum hemorrhage and systemic illness and chronic infections are excluded from the study.

All antenatal women taken in the study were examine for preterm labour by perabdomen and pervaginal examination
All women were subjected to quantitative high sensitive CRP test.

On level of CRP, patient were divided into two groups :-

1) Case with C-reactive protein positive (CRP level >6mg/dl)
2) Case with C-reactive protein negative (CRP level <6mg/dl)

Monitoring after delivery:
Parameters studied were – maternal pulse rate, maternal temperature, C-reactive protein.

Monitoring after delivery
Parameters for follow up were – maternal pulse rate, maternal temperature and C-reactive protein determination of both mother and newborn. Baby is followed for –

1) Birth weight
2) Early neonatal sepsis

After delivery

a) Mother and newborn were followed up for evidence of sepsis.
b) Newborn evaluation done for sepsis and all routine blood investigation were send.

Investigations

A. Maternal investigation:

1) Routine blood examination : Hb%, TLC, DLC, ESR, Urine (routine and microscopy), urine (Culture and sensitivity)
2) Maternal C-reactive protein value by using Latex agglutination method by Beacon Kit.
3) Maternal vaginal culture.

B. Investigation of newborn:

Routine blood examination - Hb%, TLC, DLC.

C. Data analysis

All the data were calculated using chi square test ($\chi 2$), degree of freedom and p values are calculated.

3. Results

Table 1: Distribution of patients according to their Gestational age

Gestational age (wks)	Case	Percentage	Control	Percentage
20-24	26	13.0	6	3.0
24-28	30	15.0	60	30.0
28-32	86	43.0	83	41.5
32-36	58	29.0	51	25.5
Total	200	100	200	100
χ^2 = 23.003 df = 3 and p = 0.00004				

Above table depicts that most common gestational age for study group in our study was 28-32 weeks (43%) followed by 32-36 wks (9%) and the least incidence of study group was in 20-24 wks of gestational age. There is highest association seen between C-reactive protein positive (study group) and gestational age 25-32 weeks. P value = 0.00004 which is highly significant. The value is found to be highly statistically significant.

Table 2: Distribution of patients according to duration of rupture of membrane

Duration (hr)	Study group	Percentage	Control group	Percentage
<12	17	15.8	15	40.5
12-24	26	24.29	12	32.4
> 24	64	59.8	10	27.1
Total	107	100	37	100
χ^2 = 13.95; df = 2 and p = 0.0001				

Patient with CRP positive had 64 cases (59.8%) duration of leaking for more than 24 hours with PROM followed by 26 cases (24.29%) having leaking >12-24 hrs followed by 17 cases (15.8%) having leaking for less than 2 hrs. while in control group highest percentage of leaking found in 15 case (40.5%) for less than 12 hrs. There is significant association seen between study group and control group and duration of leaking (p=0.0001). This value is found to be statistically highly significant.

Table 3: Distribution of patients according to Chorioamniotis with PROM (n=107)

	Study group	Percentage	Control group	Percentage
features of clinical chorioamnionitis present	24	23.5	3	8.2
features of clinical chorioamnionitis Absent	83	77.5	34	91.8
Total	107	100	37	100
χ^2 = 3.702; df = 1 and p = 0.004				

Patient with CRP positive with PROM had highest percentage of patient developing chorioamnionitis than control group. 24 case (23.5%) developed clinical chorioamnionitis in CRP positive group with PROM while only 3 cases (8.1%) in control group developed clinical chorioamnionitis. There is significant association between CRP positive patients with chorioamnionitis. Patient with CRP positive had develop features of clinical chorioamnionitis is highly percentage (p=0.004). This value is found to be statistically highly significant.

Table 4: Distribution of patients according to cervical length (cm)

Cervical length (cm)	*Study group*	*Percentage*	*Control group*	*Percentage*
<2.5	113	56.5	72	36.0
> 2.5	87	43.5	128	64.0
Total	200	100	200	100
χ^2 = 16.9; df = 1 and p = 0.00003				

In our study, it was found that study group had high percentage of 113 (56.5%) case. With cervical length (<2.5cm) while control group had 128 case (64%) with CL (>2.5cm). There is highly significant association between CRP positive preterm patient with cervical length (p=0.00003). This value is statistically highly significant

Table 5: Distribution of patients according to mode of delivery

Fetal outcome	Study group	Percentage	Control group	Percentage
Normal Vaginal delivery	68	56.6	61	59.2
Forceps	0	0	0	0
LSCS	52	43.3	42	40.7
Total	120	100	103	100
χ^2 = 0.14; df = 1 and p = 0.69				

In our study, no. of vaginal delivery were 68 cases (56.6%) out of 120 deliveries while in control group 61 cases (59.2%) had vaginal deliveries. Cases with CRP positive had more no. of LSCS (cesarean delivery) than control group. In case group 52 cases (43.3%) had LSCS while in control group 42 case (40.7%) had LSCS. There is no significant association found between CRP with mode of delivery (p=0.69) in our study.

Table 6: Distribution of patients according to fetal outcome

Fetal outcome	Study group	Percentage	Control group	Percentage
Live birth	98	81.6	86	83.9
Fetal demise	22	18.3	17	16.5
Total	120	100	103	100
χ^2 = 0.12; df = 1 and p = 0.7				

In our study, out of 120 babies, 98 babies (81.6%) were live birth and 22 babies (18.3%) had fetal demise while in control group 17 babies (16.5%) had fetal demise out of 103 babies. There is no significant association between CRP with fetal outcome in our study (p=0.7).

Table 7: Distribution of patients according to fetal weight at birth

Fetal weight	Study group	Percentage	Control group	Percentage
VLB	27	22.5	15	14.5
LBW	63	52.5	42	40.7
EBW	30	30.8	46	44.6
Total	120	100	103	100
$\chi^2 = 9.75$; df = 2 and p = 0.007				

In our study, study group had high percentage of baby with LBW (low birth weight) 63 babies (52.5%) had LBW out of 120 babies, while in control group, 42 babies were LBW and only 15 were VLBW. There is significant association with CRP with baby birth weight (p=0.007). This value is statistically highly significant.

Table 8: Distribution of patients according to Neonatal septicemia

Septicemia	Study group	Percentage	Control group	Percentage
Present	31	31.6	17	16.5
Absent	67	68.3	86	83.5
Total	98	100	103	100
$\chi^2 = 6.32$; df = 1 and p = 0.011				

In our study, out of 98 live birth babies, 31 babies (31.6%) develops neonatal septicemia in study group while in control group, 17 babies (16.5%) out of 103 babies develops neonatal septicemia. Babies born to mothers with CRP positive had more incidence of developing neonatal septicemia as compared to mother with CRP negative. There is significant association seen between CRP and newborn developing neonatal septicemia (p=0.01). This value is statistically highly significant.

4. Discussion

1) Above table depicts that most common gestational age for study group in our study was 28-32 weeks (43%) followed by 32-36 wks (9%) and the least incidence of study group was in 20-24 wks of gestational age. (Table – 3). There is highest association seen between C-reactive protein positive (study group) and gestational age 25-32 weeks. P value = 0.00004 which is highly significant. The value is found to be highly statistically significant.
2) Patient with CRP positive had 64 cases (59.8%) duration of leaking for more than 24 hours with PROM followed by 26 cases (24.29%) having leaking >12-24 hrs followed by 17 cases (15.8%) having leaking for less than 2 hrs. while in control group highest percentage of leaking found in 15 case (40.5%) for less than 12 hrs. There is significant association seen between study group and control group and duration of leaking (p=0.0001). This value is found to be statistically highly significant.
3) Patient with CRP positive with PROM had highest percentage of patient developing chorioamnionitis than control group. 24 case (23.5%) developed clinical chorioamnionitis in CRP positive group with PROM while only 3 cases (8.1%) in control group developed clinical chorioamnionitis. There is significant association between CRP positive patients with chorioamnionitis. Patient with CRP positive had develop features of clinical chorioamnionitis is highly percentage (p=0.004). This value is found to be statistically highly significant.
4) In our study, it was found that study group had high percentage of 113 (56.5%) case. With cervical length (<2.5cm) while control group had 128 case (64%) with CL (>2.5cm). There is highly significant association between CRP positive preterm patient with cervical length (p=0.00003). This value is statistically highly significant.
5) In our study, no. of vaginal delivery were 68 cases (56.6%) out of 120 deliveries while in control group 61 cases (59.2%) had vaginal deliveries. Cases with CRP positive had more no. of LSCS (cesarean delivery) than control group. In case group 52 cases (43.3%) had LSCS while in control group 42 case (40.7%) had LSCS. There is no significant association found between CRP with mode of delivery (p=0.69) in our study.
6) In our study, out of 120 babies, 98 babies (81.6%) were live birth and 22 babies (18.3%) had fetal demise while in control group 17 babies (16.5%) had fetal demise out of 103 babies. There is no significant association between CRP with fetal outcome in our study (p=0.7).
7) In our study, study group had high percentage of baby with LBW (low birth weight) 63 babies (52.5%) had LBW out of 120 babies, while in control group, 42 babies were LBW and only 15 were VLBW. There is significant association with CRP with baby birth weight (p=0.007). This value is statistically highly significant.
8) In our study, out of 98 live birth babies, 31 babies (31.6%) develops neonatal septicemia in study group while in control group, 17 babies (16.5%) out of 103 babies develops neonatal septicemia. Babies born to mothers with CRP positive had more incidence of developing neonatal septicemia as compared to mother with CRP negative. There is significant association seen between CRP and newborn developing neonatal septicemia (p=0.01). This value is statistically highly significant.

5. Conclusion

- CRP is an important predictor of preterm labour.
- Good correlation was observed between raised CRP values and gestational age.
- PROM is more common in patients having raised CRP values.
- CRP is found to be an important parameter in patients developing chorioamnionitis. Patients having CRP positive values had more chances of developing clinical chorioamnionitis.
- Positive correlation between raised CRP values and short cervical length (<5cm) predictor of PTL.
- Tocolytics are more beneficial in patient having CRP negative value. CRP positive patient have more failure rate with tocolytics.
- As far as fetal prognosis are concerned mother with raised CRP values have babies with LBW and neonatal

septicemia may be useful marker for early detection of neonatal sepsis.

- Hence CRP may be used a quick, easy, economic test and could be performed in minimally equipped laboratory in peripheral health centres and hospitals.

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