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RESEARCH ARTICLE

ROLE OF MATERNAL PLASMA CRP LEVELS IN EARLY AND MID-PREGNANCY AS A DIAGNOSTIC MARKER FOR PREDICTING PRETERM DELIVERY- A CLINICAL STUDY

***Dr. Anupriya**

Civil Hospital, Ludhiana, Punjab, India

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ABSTRACT

Recently the measurement of C-reactive protein in maternal serum has been suggested to have a predictive value in the diagnosis of preterm labour. CRP can prove useful in identifying early infection which could lead to preterm labour. Study is to assess the role of maternal plasma CRP levels in early and mid-pregnancy as a diagnostic marker for predicting preterm delivery.

Material and Method: The present study comprised of a total of 100 pregnant women with singleton fetus with gestational age less than 28 weeks. CRP levels in maternal blood were measured in both groups in early and mid-pregnancy. Patients were followed subsequently to see how many go into pre-term labor. Study group comprised of 50 cases who delivered pre term while control group comprised of 50 cases who delivered at term (≥37 weeks).

Result: In the study group, mean CRP level was 11.32±3.66 mg/L whereas in control group mean CRP level was 6.63±2.69. Thus mean CRP level in study group was significantly higher than control group. The ideal cut off value of CRP is 8.0 mg/L according to our data. In CRP positive cases (CRP≥8mg/L) the percentage of cases delivering preterm was higher (76.36%) than in CRP negative cases (17.77%). The sensitivity, specificity, PPV and NPV of CRP was 84%, 74%, 76%, 82% respectively.

Conclusion: Very high levels of maternal CRP (≥8mg/L) in early and mid-pregnancy were associated with increased risk of preterm delivery.

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INTRODUCTION

Preterm labour is defined as and when labour is started after the 20th week of pregnancy but before the 37 completed weeks. The etiology of preterm birth is multifactorial though in majority of cases the cause is unknown; infection is thought to play an important role in a high proportion of cases. Recently the measurement of C-reactive protein in maternal serum has been suggested to have a predictive value in the diagnosis of preterm labour. CRP can prove useful in identifying early infection which could lead to preterm labour. C-reactive protein (CRP) is an acute phase protein (globulin) secreted by the liver in response to inflammation. It was first described by Tillet and Francis in 1930. Serum levels of C-reactive protein increase with inflammatory process, infection and tissue necrosis. Hvilsom *et al*. (2002) reported a significant association of elevated serum CRP levels with a nearly twofold increased risk of delivery before 37 weeks gestation.

MATERIAL AND METHODS

The present study comprised of a total of 100 patients consisting of pregnant women with singleton fetus with gestational age less than 28 weeks of which 50 were of the study group and 50 of the control group. In both groups, 50 percent were less than 20 weeks gestation and 50 percent were between 20-28 weeks gestation.Study group was the set of patients who delivered pre term(<37weeks) while control group was of those who were in labour at term (≥37 weeks). Patients were examined for built, weight, fever and local and systemic examination to rule out any signs of infection and inflammation. Maternal non-fasting blood sample were collected in 10 ml vacutainer tubes in early and mid pregnancy and were sent to lab for all basic routine ANC investigations. Along with it plasma CRP samples were taken and sent to laboratory for estimation. CRP levels in maternal blood were measured in both groups - study and control by latex agglutination method. In this study CRP level <8mg/L were taken normal.

Patients were compared on the basis of CRP into three groups:

Group - A Patients with normal CRP.
Group - B Patients with increased CRP up to 20 weeks of gestation.
Group - C Patients with increased CRP in 20 – 28 weeks of gestation.

Corresponding author: Dr. Anupriya,
Civil Hospital, Ludhiana, Punjab, India.

Patients with increased CRP were followed subsequently to observe how many patients went into pre-term labor.

RESULTS

Table 1 shows range and mean CRP value in both study and control groups. In study group range of CRP level was 1-18 mg/L and mean CRP level was 11.32±3.66 mg/L whereas in control group range and mean CRP level was 1-13.5 mg/L and 6.63±2.69 mg/L respectively. Thus, both range and mean CRP level in study group was significantly higher than control group. Table 2 shows range and mean BMI value in both study and control groups.

There is no statistically significant difference in BMI distribution in two groups. In table 3, ROC curve analysis was used to determine the cutoff point of CRP to predict perinatal outcome (term/preterm). Area under ROC curve is 0.844 (95% CI 0.758- 0.909) which shows that CRP is a very good discriminator for predicting preterm delivery. The sensitivity and specificity of CRP is almost equal at CRP value= 8.0 mg/L (sensitivity=78%, specificity=80%). Therefore ideal cut off value of CRP is 8.0 mg/L according to our data. Table 4 shows range and mean CRP value in both groups. In less than 20 weeks group range of CRP level was 1-18 and mean CRP level was 11.64±3.98 mg/L whereas in 20-28 weeks group range and mean CRP level was 5-16.1mg/L and 10.99±3.35 mg/L respectively.

Table 1. CRP level in both study and control group

Group	No.	Range of CRP (mg/L)	Mean CRP value±SD (mg/L)	95% CI	't' = 7.299 'p' <0.0001
Study group	50	1-18	11.32±3.66	10.28-12.36	
Control group	50	1-13.5	6.63±2.69	5.87-7.40	

Table 2. Average BMI in both group

Group	No.	Range of BMI(kg/m^2)	Mean	't'	'p'
Study group	50	18.5-23.8	20.89±1.37	0.079	0.937 (NS)
Control group	50	18.5-23.6	20.87±1.41		

Table 3. Hanley & McNeil ROC curve

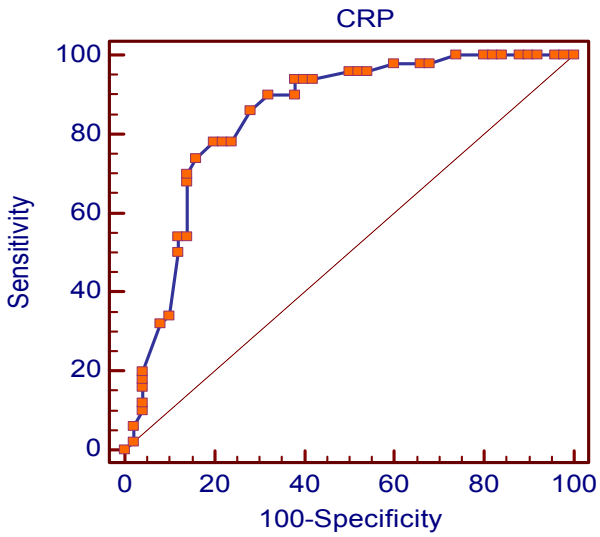

Table 4. Distribution of CRP level in study group according to gestational age at which CRP is done

Gestational age at which CRP is done	No.	Range of CRP (mg/L)	Mean CRP value±SD (mg/L)	't'	'p'
Less than 20 weeks	25	1-18	11.64±3.98	0.626	0.534
20-28 weeks	25	5-16.1	10.992±3.35		(N.S.)

Table 5. Distribution of sample according to CRP cut off value (8mg/L)

Group (Total =100)	Pregnancy outcome	
	Term (n=50)	Preterm (n=50)
A (n= 45)	N= 37	N= 8
(CRP negative)	%= 82.22	%= 17.77
B (n= 28)	N= 6	N=22
(CRP positive at gestational age less than 20 weeks)	%= 21.42	%= 78.57
C (n=27)	N= 7	N=20
(CRP positive at gestational age 20-28 weeks)	%= 25.92	%= 74.07

CRP positive ≥8mg/L

Table 6. Comparisonof sample according to CRP cut off value (8mg/L)

Group	Term	Pre term	Total
A (CRP negative)	37 (82.22%)	8 (17.77%)	45
B+C (CRP positive)	13 (23.63 %)	42 (76.36 %)	55

Although CRP was raised in both groups difference in CRP levels was not statistically significant. (p=0.534). Table 5 shows that the number of cases delivering preterm is comparable in CRP positive group B (n=22,%= 78.57) and C (n= 20, %= 74.07). Table 6shows that in CRP positive cases (B+C, n= 55) the percentage of cases delivering preterm is higher (n=42, %=76.36) than in CRP negative cases (A, n= 45) where the percentage of cases delivering preterm is 17.77% (n=8).Thus it shows that incidence of preterm deliveries is significantly higher in CRP positive cases (B+C) when compared with CRP negative cases. (A)

DISCUSSION

In our study both range and mean CRP level in study group was significantly higher than control group. In our study the sensitivity and specificity of CRP is almost equal at CRP value= 8.0 mg/L (sensitivity=78%, specificity=80%). Therefore ideal cut off value of CRP is 8.0 mg/L according to our data. Ghezzi *et al*. (2002), Lohsoonthorn *et al*. (2007), Pitiphat *et al*. (2005) found that elevated CRP levels ($\geq$ 8 mg/l) had a greater higher risk of preterm deliveries. We found that sensitivity, specificity, PPV and NPV of CRP was 84%, 74%, 76%, 82%. Our study was comparable with Saini *et al*. (2003) and Ibarra Chavaria *et al*. (1989).

Conclusion

Both range and mean CRP level in study group was significantly higher than control group. Sensitivity and specificity of CRP was 84% and 74% respectively. The positive predictive value was 76% and negative predictive value was 82%. CRP is a very good discriminator for predicting preterm delivery. Ideal cut off value of CRP is 8.0 mg/L according to our data.

There is no statistically significant difference in incidence of pre term labour in cases where CRP is raised before 20 weeks of pregnancy and in cases where CRP is raised between 20-28 weeks of pregnancy. Incidence of preterm deliveries is significantly higher in CRP positive cases when compared with CRP negative cases.

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