International Journal of Reproduction, Contraception, Obstetrics and Gynecology
*Gahlot K et al. Int J Reprod Contracept Obstet Gynecol. 2016 Nov;5(11):4001-4004*
www.ijrcog.org

pISSN 2320-1770 | eISSN 2320-1789

DOI: http://dx.doi.org/10.18203/2320-1770.ijrcog20163878

**Original Research Article**

# To evaluate diagnostic efficacy of maternal serum C - reactive protein to predict preterm labour

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**Received:** 13 September 2016
**Accepted:** 08 October 2016

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## ABSTRACT

**Background:** Preterm birth is a major challenges faced by obstetricians worldwide. Globally, an estimated 13 million babies are born before 37 completed weeks of gestation annually. Preterm birth is the leading direct cause of neonatal death (27%); more than one million preterm newborns die annually. According to report 'India is among the top 10 countries that account for 60 per cent of the world's preterm births. Methods to detect preterm labour early include ultrasound examination of the cervix and detection of biochemical markers of preterm labour in blood (include serum C - reactive protein level) and cervicovaginal secretions. The objective of the study was evaluate diagnostic efficacy of maternal serum C - reactive protein (CRP) to predict preterm labour.
**Methods:** A prospective study comprised of a total of 132 pregnant women with singleton fetus with symptoms of preterm labour. Serum CRP values was taken in all patients. Out of which 17 patients were lost during follow up, 3 patients develop PPROM. Hence study was conducted over 112 patients. Among these 62 patients went in preterm labour and 50 patients delivered at term.
**Results:** For predicting preterm delivery sensitivity, specificity, positive and negative predictive value for serum CRP were 70.9%, 70%, 74.5% and 66% respectively.
**Conclusions:** Serum CRP is good predictor to differentiate the women who were likely to deliver preterm. CRP positivity in early pregnancy is associated with nearly a twofold increased risk of preterm delivery.

**Keywords:** Preterm labor, Prospective study, Serum CRP

## INTRODUCTION

Preterm birth is a major challenges faced by obstetricians worldwide. Globally, an estimated 13 million babies are born before 37 completed weeks of gestation annually. Preterm birth is the leading direct cause of neonatal death (27%); more than one million preterm new-borns die annually.[1] According to report 'India is among the top 10 countries that account for 60 per cent of the world's preterm births**.**

Preterm labour and its subsequent complications makes it the most common, costly and catastrophic complication of pregnancy.[2]Preterm labour is one of the main causes of perinatal mortality and morbidity.[3] Intrauterine infection contributes to 40-50% of all preterm births.[4,5]

C-reactive protein (CRP) was first described in 1930 by Tillet and Francis who observed that sera from patients during acute febrile illness had the ability to precipitate the C-substance (later designated C-polysaccharide, CPS) of pneumococcal cell walls.[6] The serum factor responsible for this reaction was defined as a "C-

precipitin", and later designated "C-reactive". This protein was found to appear in the blood during a variety of reactions of tissue destruction or inflammation and has served as a useful clinical index of this process.[7]

The exact function of CRP in vivo is not known. It is probably an early broad spectrum recognition mechanism to pathogenic microorganisms. The main role of CRP is to recognize in the plasma the potentially toxic autogenous materials released from damaged tissues, to bind to them, and thereby to detoxify them and/or facilitate their clearance.[8]

CRP binds selectively to T-lymphocytes, inhibit their ability to form spontaneous rosettes with sheep erythrocytes and inhibit their response to allogeneic cells in mixed lymphocyte culture reactions. By contrast, CRP does not bind to B lymphocytes, nor does it alter the B - cell functions. CRP also causes inhibition of mixed lymphocyte reactivity and generation of cytotoxic lymphocytes.[9] A CRP specific human complementary probe has been isolated. It is also known that CRP gene is located on chromosome one.[10]

CRP inhibits the aggregation of human platelets stimulated by either modified human immunoglobulin or thrombin. So this property of CRP may play an important role in the control of platelet responsiveness during reaction of inflammation, defense and repair.[11] CRP is a potent activator of the classical complement pathway starting with C1q.[12] CRP, like antibodies can thus bind to ligands, opsonize materials for phagocytosis, and initiate cell damage and inflammatory reactions.[13]

Preterm labour is defined by the world health organization as the onset of labour prior to the completion of 37 week of gestation, in a pregnancy beyond 20 week of gestation. The traditional criteria for preterm labour is persistent uterine contractions accompanied by cervical effacement and dilatation (contraction frequency is six or more per hour, cervical dilatation is 3 cm or more effacement is 80% or more). These criteria have suboptimal sensitivity and specificity because of the common occurrence of symptoms and signs of early preterm labour in normal pregnancy, and the imprecision of digital examination of the cervix, the rate of false positive diagnosis rises to as much as 40%.The practice of initiating tocolytic drugs for contraction frequency without any additional diagnostic criteria results in unnecessary treatment of women who do not actually have preterm labour.

Methods to detect preterm labour early include ultrasound examination of the cervix and detection of biochemical markers of preterm labour in blood and cervicovaginal secretions.

The objective of the study was evaluating diagnostic efficacy of maternal serum C - reactive protein (CRP) to predict preterm labour.

## METHODS

This prospective study was conducted in GSVM Medical College, Kanpur, department of obstetrics and gynaecology and radio diagnosis.

### *Inclusion criteria*

132 patients with a singleton pregnancy admitted to our hospital with symptoms of preterm labour were included in this study. Others inclusion criteria involve no history of apparent genitourinary infection, normal pre pregnancy BMI, Previous history of preterm labour and with history of threatened abortion.

### *Exclusion criteria*

Patients with Cervical dilation >2cm, Multiple gestation, premature rupture of membrane, Antepartum haemorrhage, sign of fetal distress, any foetal congenital anomaly and intrauterine death, Metabolic syndrome and Cardiovascular disease, History of cervical incompetence, cone biopsy, history Cervical circlage, previous machester repair and History of associated infection and inflammation were excluded from study.

### *Methodology*

After taking thorough history& complete examination (general, systemic, per speculum and vaginal), all basic routine ANC investigations along with it plasma CRP samples were taken and sent to laboratory. CRP levels in maternal blood were measured by latex agglutination method after abdominal ultrasound to confirm the foetal maturity, amount of liquor and congenital anomaly. The receiver operating characteristic curve analysis was applied to determine the optimal cut-off values of serum CRP for predicting delivery before 37 completed gestational weeks. These patients were followed by delivery.

Out of total 132 patients included in study, 17 patients were lost during follow up, 3 patients develop PPROM. Hens study was conducted over 112patients .Among these 62 patients went in preterm labour and 50 patients delivered at term.

On the basis of CRP level Patients were divided into two groups:-

- Patients with normal CRP level (<8mg)
- Patients with increased CRP (>=8mg/l)

Logistic regression analysis, Hanley & McNeil ROC curve analysis, independent sample t-test were used to analyse the data using Medcalc and Instat statistical software.

## RESULTS

Regarding age distribution, majority of patients delivered preterm i.e. 34 (54%) was between 21-25 years and minimum 4 (6.4%) patients were >30 years. Regarding parity incidence of preterm delivery were higher in primigravida (56.4%) than multigravida (43.5%).

**Table 1: Difference between the mean CRP value in term and preterm groups.**

| | Term | Preterm | P value |
|---|---|---|---|
| Mean cervical length (mm) | 32.59± 4.0 | 24.83±6 | 0.0001 |
| Total no. of patients | 50 | 62 | |

Among patients delivered preterm (n=62) maximum 23 (37%) patients had gestational age < 24 weeks on admission. Mean CRP value on admission and mean gestational age of delivery were 13.2 ± 3.5 mg/l and 26.5 ± 2.5 weeks respectively with increase gestational age at admission mean CRP value decrease.

**Table 2: Mean CRP value in different gestational age groups in patients delivered preterm.**

| Gestational Age on admission | No. of cases | | Mean CRP value ± SD (mg/l) | Mean GA of delivery(weeks) |
|---|---|---|---|---|
| | No. | % | | |
| <24 weeks | 23 | 37 | 13.2 + 3.4 | 26.53±2.5 |
| 24 - 28 weeks | 14 | 22.5 | 10.5 + 3 | 28.22±1.7 |
| 28 - 32 weeks | 13 | 21 | 7.83 + 1.4 | 30.48±1.9 |
| >32 weeks | 12 | 19.3 | 6.11 + 1.2 | 36.17±0.75 |

Competitive ROC curve analysis was used to define serum CRP to predict preterm delivery (Figure 1). Area under ROC curve for serum CRP (p value = 0.0001) (Table 3). Sensitivity and specificity of PTL <34 weeks was higher for Serum CRP (93% vs. 89%) (Table 5).

## DISCUSSION

Preterm birth is a major cause of perinatal mortality and morbidity. Prediction of preterm delivery by simple technique will help in early intervention and subsequent prevention of preterm labour. This is especially important in a country like our where intensive care unit facilities are often not available or may be financially not possible.

Maternal CRP has been studied extensively as an adjunct in the diagnosis of sub clinical infection among pregnant women with preterm labour or PROM.[14] Studies have shown that median CRP values in normal pregnancy appear to be higher than standardized value for non-pregnant individuals and CRP value is further elevated in labour. Although a chorioamniotic infection or inflammation may be associated with preterm labour and delivery, it remains unclear whether elevated CRP level is a response to infection or to labour.

**Table 3: Comparative statistical analysis of ROC curve of serum CRP.**

| | Serum CRP |
|---|---|
| Area under ROC curve | 0.88 |
| Standard error | 0.0306 |
| 95%confidence interval | 0.806 to 0.934 |
| Z statistics | 12.43 |
| Significant level (p value) | <.0001 |

**Table 4: Diagnostic accuracy of serum CRP in predicting delivery <37 weeks.**

| | Sn | Sp | PPV | NPV |
|---|---|---|---|---|
| Cervical length | 82.2% | 74% | 79.6% | 77% |

**Table 5: Diagnostic accuracy of cervical length and CRP in predicting delivery <34 weeks.**

| | Sn | Sp | PPV | NPV |
|---|---|---|---|---|
| CRP | 93% | 72% | 58% | 96% |

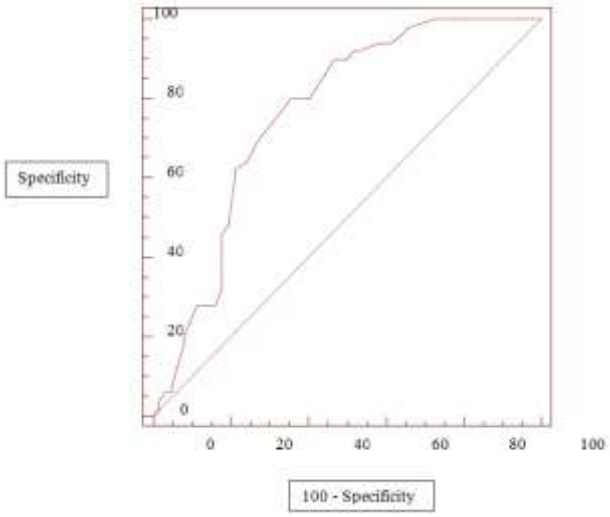


**Figure 1: CRP ROC curve.**

In present study we found a statistical significant difference between mean CRP value of patients delivered preterm and term (p=0.001) at cut off value 8 mg/L. Our finding are consistence with Lohsoonthorn et al who found that elevated serum CRP was associated with an increased risk of spontaneous preterm labour (OR=2.15, 95%; CI: 0.85-5.42) and very preterm delivery (OR=20.6, 95%; CI: 2.53-168.03).[15] Hvilsom et al reported a significant association of elevated serum CRP levels with a nearly twofold increased risk of delivery before 37

weeks' gestation.[16] Ghezzi et al found no relation between circulating CRP levels and preterm delivery.[17]

It was observed in the present study that sensitivity and specificity for serum CRP was 70.9% and 70.0%. Serum CRP can be used as a screening tool for prediction of preterm labour but negative predictive value is 66%.But for predicting early preterm birth (<34 weeks) serum CRP had higher sensitivity (93%) and specificity (72% ).

## CONCLUSION

Based on this study it can be concluded that serum CRP are good predictor for preterm delivery. Raised CRP level (>8mg/dl) in early pregnancy in the absence of any medical/surgical or obstetric complication can predict high likelihood of preterm labour. The limitation of the study lies in the fact that CRP is raised in response to both pathological as well as physiological conditions. Hence widespread applicability of CRP as a predictor of poor pregnancy and neonatal outcome needs further supportive evidence. This information may help patients avoid unnecessary interventions of unproven value such as tocolysis, hospitalization, and activity restriction in patients presenting with symptoms of preterm labour. The limitation of the study lies in the fact that CRP is raised in response to both pathological as well as physiological conditions. Hence widespread applicability of CRP as a predictor of poor pregnancy and neonatal outcome needs further supportive evidence.

## ACKNOWLEDGEMENTS

Authors would like to thank Dr. Sikha Pandey, Dr. Nidhi Mishra, Dr. Sheela Jain and Dr. Sona Singh as consultant in Department of Obstetrics And Gynaecology, BMC, Sagar, MP, India to guide in preparing this manuscript. Authors also acknowledge Mr. Indal Singh for his assistance in statistical work.

*Funding: No funding sources*
*Conflict of interest: None declared*
*Ethical approval: The study was approved by the Institutional Ethics Committee*

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**Cite this article as:** Gahlot K, Pandey K, Singh PP, Gahlot V, Mourya R. To evaluate diagnostic efficacy of maternal serum C - reactive protein to predict preterm labour. Int J Reprod Contracept Obstet Gynecol 2016;5:4001-4.