

Predictive value of C - reactive protein levels during pregnancy in adverse pregnancy outcomes: One year study at Swaroop Rani Nehru Hospital & Kamla Nehru Hospital (Motilal Nehru Medical College Allahabad)

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Abstract

Objective: To evaluate the association, if any, between serum CRP levels in first and early second trimester of pregnancy and adverse pregnancy outcomes.

Materials and Methods: The present study was carried out in 300 antenatal cases attending the department of Obstetrics and Gynaecology at Swaroop Rani Nehru Hospital & Kamla Nehru Hospital (Motilal Nehru Medical College Allahabad), over a period of one year.

Inclusion Criteria: Pregnant women < 20 weeks.

Exclusion Criteria: Multiple gestation, previous H/O PTL or mid trimester abortions, endocrine disorder, medical illnesses, HIV infection and substance abuse. Serum C-Reactive protein levels were tested and the participants were divided into 2 groups. Group1 included all pregnant ladies with CRP level > 5mg/L (Study Group) and Group2 with CRP level < 5mg/L (Control Group). These patients were followed till delivery and pregnancy outcomes like preterm labour, PPRM, fetal growth restriction, preeclampsia, mode of delivery, low birth weight, still births and neonatal intensive care unit admissions were noted. The statistical significance of differences of variables were made out by calculating the p-value.

Result: Raised level of serum CRP had positive correlation with adverse pregnancy outcomes and effect of elevated CRP level was maximum on PPRM (p value-0.002), preeclampsia (p value-0.004) and low birth weight (p value-0.002). Elevated CRP had no significant impact on still birth (0.06).

Conclusion: Early detection of higher level of serum CRP in pregnancy can be used as predictor of inflammation and may help in early intervention and follow up of the patients to minimize adverse maternal and fetal complications.

Keywords: C - reactive protein, Preterm labour, Fetal growth restriction, Preeclampsia, Low birth weight, Still births.

Introduction

C-reactive protein (CRP) is an annular (ring-shaped), pentameric protein found in blood plasma. The name is credited to an acute phase reactant produced by the hepatocytes that reacted with the somatic 'C' carbohydrate antigen of Pneumococcus¹ in patients with inflammation that was first identified in the year 1930.² Its level rises in response to a wide range of acute and chronic inflammatory conditions such as bacterial, viral, or fungal infections; rheumatic and other inflammatory diseases; malignancy; and tissue injury and necrosis due to secretion of inflammatory cytokines such as interleukin-1 and interleukin-6 by macrophages, T cells and fat cells (adipocytes). Its physiological role is to bind to lysophosphatidylcholine expressed on the surface of dead or dying cells and some types of bacteria in order to activate the complement system via the C1q complex,³ promoting phagocytosis by macrophages, which clears necrotic and apoptotic cells and bacteria. Thus it plays a role in innate immunity as an early defense system against infections.

CRP rises within two hours of the onset of inflammation, up to a 350-400 mg/L and peaks at 48 hours.⁴ Its half-life of 18 hours is constant, and therefore its level is determined by the rate of

production and hence the severity of the precipitating cause. CRP is thus a screen for inflammation. Higher levels of CRP are found in mild inflammation and viral infections (10-40 mg/L), active inflammation, severe bacterial infections and burns (>200 mg/L).⁵

CRP as a measure of diagnosing asymptomatic subclinical infection during pregnancy will definitely help us to predict various infection related morbidities and complication during pregnancy.

Materials and Methods

Place of Study: Department of Obstetrics and Gynaecology at Swaroop Rani Nehru hospital, Allahabad and Kamala Nehru Memorial hospital, Allahabad.

Duration of Study: One year; 2016-2017.

Type of Study: Interventional

Sample Size: 300

Sample Collection Method: Incidental sampling.

Inclusion Criteria: All antenatal cases attending OPD were included in the study except the cases as specified in exclusion criteria.

Exclusion Criteria:

1. ANC with >20weeks of gestation.
2. Patients with multiple gestation.

3. Patient with increased BMI (>25kg/sq.m).
4. Patient with medical disorders like cardiovascular diseases, chronic hypertension, chronic kidney diseases, chronic lung diseases etc.
5. Endocrine disorders such as Diabetes Mellitus and Thyroid Disorders.
6. Immunocompromised and HBsAg Reactive patients.
7. Patient diagnosed as preeclampsia.
8. Patient with previous history of preterm delivery and cervical incompetence.
9. Patient with addiction to alcohol and smoking.

Intervention: All participants underwent blood sample examination for C-reactive protein level which was done by Latex turbidimetry method. After these participants were assigned into 2 study groups and group 2 served as control group.

Group 1: Pregnant ladies with CRP level > 5mg/L (Study Group).

Group 2: Pregnant ladies with CRP level < 5mg/L (Control Group).

Statistical Analysis

The statistical significances were measured by calculating P value (P Value<0.05). These patients were followed with defined schedule of visits that is monthly up to 28 weeks, fortnightly up to 36 weeks and weekly thereafter along with general examinations and systemic examinations, routine investigations and ultrasonography till delivery. Gestational age at time of delivery and pregnancy outcomes such as intrauterine growth restriction, premature rupture of membrane, preterm labor, mode of delivery, low birth weight, still births, neonatal deaths, neonatal intensive care unit admissions were noted. Parameters of the two groups were compared and data analyzed by P-value.

Result

Out of 300 patients 98 patients had serum CRP level > 5 mg/L and 202 patients had serum CRP level < 5 mg/L (Table 1) which means 32.6% of sample size was attributed to Group I(study group) and rest of them that is 67.4 were assigned to Group II(control group). Among 98 patients of Group I maximum number of patients(59.1%) had S.CRP level between 10-14.9 mg/L and 20.4% had their S.CRP levels between 5 - 9.9 mg/L and ≥ 15 mg/L. Average mean level of S.CRP came to be 12.5 ± 3.22 mg/L. The mean age of patients of Group I was 22.2 ± 3.8 years and in Group II it was 22.9 ± 4.7 yrs with P-value = 0.60. In both, Group I and Group II, maximum number of patients (89.7%) and

(60.3%) respectively were primigravida (Table 2). When variables of Group I were compared, increased CRP level was significantly common in primigravida (p value- 0.02). Same was the situation with Group II but when variables of both the groups were compared to each other there was no significant difference. Highest mean CRP (14.2 ± 2.3 mg/L) level belonged to primigravida in group 1 which was statistically significant with p value of 0.02 when compared to other gravidas whereas in group 2, highest level of mean CRP (2.3 ± 1.1 mg/L) was found in G3 and lowest level(1.41 ± 0.5 mg/L) in gravid 2 with no significant statistical difference among variables of group 2. Highest level of mean CRP in study group was 14.8 ± 2.3 mg/L, found to be present in lower socioeconomic class which was statistically significant with p value of 0.01. Similarly, in control group significantly high level of mean value of CRP was 2.3 ± 1.1 mg/L, found in lower socioeconomic class with p value of 0.04. Amongst Group I maternal complications (Table 3), incidence of Preeclampsia was 78.5% that of preterm delivery was 73.4% while that of Premature Rupture of Membrane was 50% and incidence of IUGR was 71.4%. In Group II incidence of respective complications were 7.9%, 3.9%, 4.9% and 9.9%. When compared among both the groups, the incidences of all adverse maternal outcomes were significantly high in group I (higher mean CRP level) and statistically significant p value of 0.01, suggesting positive correlation of adverse maternal outcome with raised CRP levels.

In Group I out of 98 patients 28.4% delivered vaginally and 71.4% delivered by Caesarean Section. When variables of Group I compared statistically, rate of delivery by caesarean section was significantly high with the p value of 0.01. In Group II 67.3% patients delivered vaginally and 32.3% by Caesarean Section with statistically significant high number of vaginal mode of delivery with p value of 0.03. On comparing variables of both the groups, the difference of mode of delivery was significant with the p-value of 0.01(<0.05). Babies borned to mothers with raised CRP had following birth weight distribution (Table 4), 20.4% babies had weight <1.5kg followed by 62.2% babies with weight lying between 1.6-2.4 kg and 17.3% babies were of ≥ 2.5 kg with the mean weight of 2 ± 0.3 kg. In group II 3.9% babies had weight <1.5kg followed by 23.7% babies with weight lying between 1.6-2.4 kg and 72.2% babies were of ≥ 2.5 kg with the mean weight of 2.6 ± 0.3 kg respectively. On calculating statistical difference among the mean weights of both the groups, difference was significant with the P-value of 0.04(<0.05).

Table 1

	Control group (CRP <5mg/L)	Study group (>5mg/L)
Number of patients	202	98
Percentage of patients (%)	67.4	32.6
Mean CRP \pm SD (mg/L)	1.5 ± 0.78	12.5 ± 3.4

Table 2: Difference between mean CRP in relation to gravidity

Gravida	Control Group(n=202) CRP level < 5 mg/L			Study Group(n=98) CRP level > 5 mg/L		
	Number of patients	% of patients	Mean CRP	Number of patients	% of patients	Mean CRP
G1	122	60.3	2.15 ± 1.1	88	89.7	14.2 ± 2.3
G2	50	24.7	1.41 ± 0.5	8	8.1	8.2 ± 1.2
G3	20	9.9	2.3 ± 1.1	2	2	11.8 ± 2.4
≥G4	10	4.9	2.05 ± 0.6	0	0	0
p-value	0.04(<0.05)		0.02(<0.05)	0.02(<0.05)		0.02(<0.05)

Table 3

Maternal complications	Group I (Study Group) (n=98) CRP level > 5 mg/L		Group II (Control Group) (n=202) CRP level < 5 mg/L		P-value
	No.	%	No.	%	
PE	77	78.5	16	7.9	0.001(<0.05)
PROM	49	50.0	8	3.9	0.003(<0.05)
PTL	72	73.4	10	4.9	0.001(<0.05)
IUGR	70	71.4	20	9.9	0.003(<0.05)
Mode of Delivery					
Vaginal	28	28.5	136	67.3	0.01(<0.05)
Caesarean Section	70	71.4	66	32.3	0.01(<0.05)
p-value	0.01		0.03		
Fetal outcomes					
LBW	81	82.6	56	27.7	0.001(<0.05)
Still birth	2	2	3	1.4	0.6 (>0.05)
NICU Admission	74	36.6	82	83.6	0.01(<0.05)

Table 4

Birth Weight(Kg)	Control Group (n=202) CRP level < 5 mg/L		Control Group (n=202) CRP level < 5 mg/L	
	No.	%	No.	%
≤1.5	20	3.9	8	20.4
1.6-2.4	61	23.7	48	62.2
≥2.5	17	72.2	146	17.3
Mean ± SD	2.6±0.3		2±0.3	
P-value	0.04(<0.05)			
APGAR Score at 1 mint				
	No.	%	No.	%
0 -3	9	4.4	17	17.2
4-6	28	13.9	37	37.8
7-10	163	81.2	44	45
Mean ± SD	7.02 ± 1.2		5.86 ± 1.7	
P value	0.04 (<0.05)			
APGAR Score at 5 mints				
0 -3	4	1.9	4	4.1
4-6	17	8	18	18.4
7-10	181	92	76	77.5
Mean ± SD	8.1 ± 1.23		7.34 ± 1.36	
P value	0.06(>0.05)			

Discussion

In cases of normal pregnancy, physiological inflammatory changes occurring as a result of foreign conceptus and its implantation are tolerated well by the

women as a result of increase in T- helper cells that counteract the adverse effects of inflammatory cytokines released from the conceptus and pregnancy gets established uneventfully. Pathologically infection

anywhere in the body may cause release of endotoxins and activation of cell mediate immunity and release of several cytokines and interleukins-6 which may also act locally on the decidua's and fetal membranes leading to arachidonic acid stimulation and synthesis of prostaglandin E₂ (PGE₂) and F₂ acting in a paracrine fashion. This results in various adverse pregnancy outcomes like pregnancy induced hypertension, intra uterine growth retardation, preterm labour, premature rupture of membrane, low birth weight, Still birth etc. In similar fashion as infection; metabolic disease, cardiovascular disease and cancers also induce array of increased pro-inflammatory cytokines and production of acute phase reactants adversely affecting pregnancy. Maximum risk of adverse pregnancy outcome is documented when there is local urogenital infection either symptomatic or asymptomatic. They release bacterial products and endotoxins leading to cell mediated immunity activation within the decidua tissue and fetal membranes. A cascade of events occur locally producing local prostaglandin (PGE₂ and F₂) that stimulate myometrium contractions and cause preterm labour and then preterm delivery.⁶

Measuring serum CRP as a marker of non-evident or subclinical infection and inflammation anywhere in the body and/or exaggerated inflammatory response to pregnancy in absence of infection to predict adverse pregnancy outcomes seems promising.

The utility of the measuring CRP in the blood and prediction of pregnancy complications may enable us to identify those pregnant women who are prone to have complications, and hence they can be managed in a keener and more appropriate way with multidisciplinary approach for happy pregnancy outcome with safe mother and baby. The cost effectively of this simpler test further enhances its utility as a predictor of many adverse pregnancy outcomes.

Conclusion

Early detection of higher level of serum CRP in pregnancy can be used as predictor of inflammation related adverse pregnancy outcomes and may help in early intervention, timely referral and tertiary care of the patients to minimize devastating maternal and fetal complications.

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