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IJPBS |Volume 3| Issue 3 |JUL-SEP|2013|27-32

Research Article
Biological Sciences

HIGH SENSITIVE C-REACTIVE PROTEIN IN PRE-ECLAMPSIA

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ABSTRACT

AIM: *The aim of the study is to whether CRP levels are elevated in the first trimester of pregnancy.* ***MATERIALS AND METHODS:****50 First trimister patients of age below 30 years with gestational age between 10 to 14 weeks of pregnancy, BP ≥130/86 mm of Hg and proteinuria 200mg /L & above were included in the study as cases. Healthy age and gender matched 50 pregnant women were taken as controls.* ***RESULTS:*** *Women with high risk pregnancies are 43.50 times significantly more likely to have elevated hsCRP when compared to Controls ,and also TGL and VLDL are significantly increased in cases with P<0.05.* ***CONCLUSIONS:*** *Thus hsCRP can be used as a predictive marker for pre-eclampsia.*

KEY WORDS

hsCRP, Pre-eclampsia.,Llipid profile.

INTRODUCTION

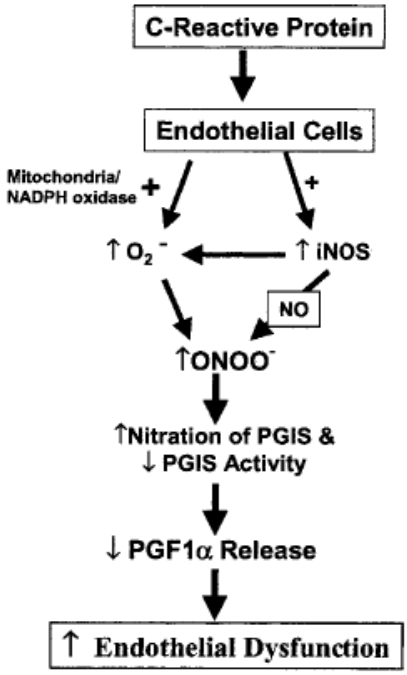
Hypertensive disorders of Pregnancy (HDP) are a frequently encountered complication of pregnancy and has a number of possible etiologies. It may be caused by the pregnancy itself; it may be a long term problem present before the pregnancy began; or it may be a new medical problem, by chance coinciding with pregnancy.

Hypertensive Disorders of Pregnancy (HDP) affects upto 6 - 8% of pregnancies and contribute significantly to still births and neonatal morbidity and mortality [1]. Pre-eclampsia is a common, complication of pregnancy. Symptoms of pre-eclampsia include hypertension and proteinuria and pre- eclampsia are associated with general endothelial dysfunction [2]. Expectant mothers with hypertension are predisposed to potentially lethal complications, notably abruption placenta, disseminated intravascular coagulation, cerebral hemorrhage, hepatic failure, and acute renal failure. In these disorders the fetus is primarily affected through intrauterine growth retardation, preterm birth, low birth weight and perinatal deaths [1]. .

The etiology of pre-eclampsia has been postulated to be part of an exaggerated maternal inflammatory response to pregnancy[3]. Increased production of reactive oxygen species [4] and increased release of inflammatory cytokines, such as Tumor necrosis factor α (TNF α) and Interleukin-6(IL-6)[5 & 6], by activated circulating leukocytes[7 & 8] Also other possible reason is abnormal activation of the clotting system[9] in women with pre-eclampsia.

C-reactive protein (CRP) is an acute phase protein which is increased in systemic inflammation. It was the first acute phase protein to be described and is an exquisitely sensitive systemic marker of inflammation and tissue damage [10]C–reactive protein is a sensitive index of systemic inflammation that predicts adverse

atherosclerotic events, including myocardial infarction, stroke, peripheral vascular disease, and death[11]. Elevated CRP level are correlated with obesity[12]. It is to be known whether C-reactive protein and obesity are associated which predisposes to pre-eclampsia[13]. Systemic maternal inflammatory response to pregnancy is responsible for the endothelial dysfunction which gives the clinical and pathological picture of pre-eclampsia[14] .The association between first trimester C-reactive protein levels and subsequent pre-eclampsia supports the hypothesis that systemic inflammation is involved in the pathogenesis of pre-eclampsia[3].



Body Mass Index is a validated, independent risk factor for pre-eclampsia[15] .It is suggested that BMI and C-reactive protein might share a common pathway linking obesity to pre-eclampsia. It has been seen that increase in BMI causes increase in the levels of C-reactive protein[12]. Physiologically, pre-eclampsia is characterized by elevated circulating levels of TNF-α and IL-6, where IL-6 are the major source from adipose cells. Thus they are the principle determinants of hepatic C-reactive protein production. Therefore C-reactive protein might be an intermediary in the pathway between BMI and pre-eclampsia. Present study is done to investigate whether CRP. Levels are elevated during the first trimester (10-14 Weeks) in women who subsequently develop pre-eclampsia.

MATERIALS AND METHODS

It is a case control type of study was done on patients who attended the Out Patient Department of Obstetrics & Gynaecology for regular check up. Ethical committe approved protocol and also written consent was taken. Levels are elevated during the first trimester (10-14 Weeks) in women who subsequently develop pre-eclampsia

Inclusion Criteria:

Cases comprised of 100 Primi pregnant women, aged below 30 years, who were of 10 to 14 weeks of pregnancy. The blood pressures of these pregnant women were ≥130Systolic pressure and ≥ 86 Diastolic pressure and Proteinuria~200mg/l and above who attended the outpatient department .50 Age matched healthy primi pregnant women who are normotensive and without proteinuria were taken as controls.

Exclusion criteria

Pregnant women with family history of Hypertension, Diabetes mellitus, Ischaemic Heart. Disease and any renal, cardiovascular, neurological complication.

Specimen Collection:

Fasting venous blood samples were collected from cases and controls and the samples were centrifuged

for the estimation of serum total cholesterol and serum triglycerides, HDL cholesterol and high sensitive C-reactive protein. Correspondingly urine sample of the patient was taken for urine sugar and urine protein. All routine investigations were done.

High sensitive C-reactive protein is based on the principle of agglutination reaction for the ultrasensitive determination of C – reactive protein in human serum by Turbidimetric Immunoassay. Serum triglyceride was estimated by GPO-PAP method, Serum total cholesterol ,Serum HDL – cholesterol was estimated by Enzymatic End point method using in the Randox Daytona auto analyzer.

The Statistical software namely SPSS 15.0 were used for the analysis of the data and Microsoft word and Excel have been used to generate graphs, tables etc.

Table 1: Comparison of BMI and Gestational age for Controls and Cases

Basic characteristics Mean ± SD	Controls	Cases	P value
BMI in kg/m2	23.04±1.53	24.83±1.35	P<0.001**
Gestational Age in weeks	12.13±1.46	12.47±1.26	0.297

Table 2: hs CRP (mg/L) levels for Controls and Cases

hs-CRP	Controls	Cases
Range(mg/L)	1.21-2.25	2.25-7.0
Mean ± SD	1.60±0.31	2.68±1.43
95% CI	1.45-1.70	2.31-3.24

Hs CRP is significantly elevated in cases (student=4.43, P<0.001

Figure -1: Bar diagram showing hs CRP levels in cases and controls

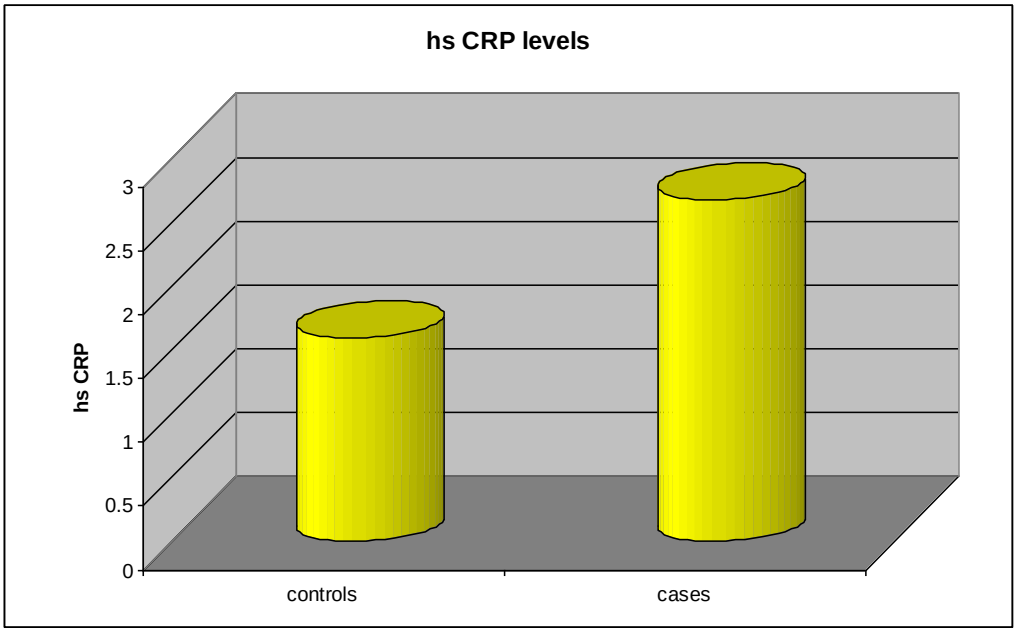


Table 3: hsCRP (mg/L) in high risk pre-eclampsia

(95th percentile of controls is 2.0)

hsCRP(mg/L)	Controls	Cases
CRP <2.0	48(96.7%)	20 (40.0%)
CRP >2.0	2 (3.3%)	30 (60.0%)
Total	50	50

$\chi 2=23.776$, $P<0.001$

Women with high risk pregnancies are 43.50 times significantly more likely to have elevated hsCRP when compared to Controls.

Figure: 2 Bar diagram representing hs CRP in subjects of cases and controls

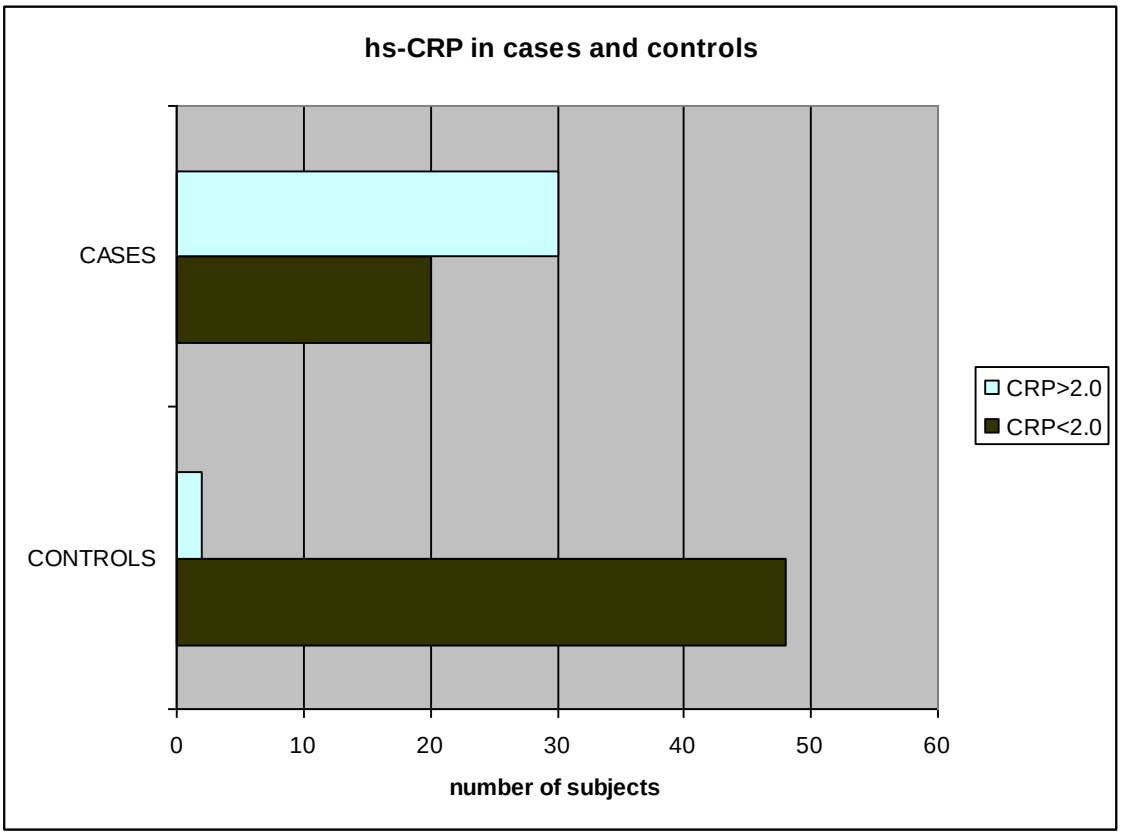


Table 4: Lipid profile in cases and controls

Lipid profile Mean ± SD	Controls	Cases	P value
Total Cholesterol mg/dl	203.13±41.38	220.15±42.13	0.326
HDL mg/dl	41.77±8.20	44.18±7.79	0.216
LDL mg/dl	119.53±31.27	130.98±39.51	0.187
TG mg/dl	183.23±41.36	211.98±46.47	0.015*
VLDL mg/dl	35.43±8.35	43.93±10.47	0.007**

TGL and VLDL are significantly increased in cases with P<0.05

DISCUSSION

Pre-eclampsia is a multifactorial and multisystem disorder of human pregnancy. Clinically characterized by hypertension, proteinuria, and edema. Pathophysiologically, the hallmark of pre-eclampsia include increased vasoconstriction resulting in maternal hypertension and reduced uteroplacental blood flow, disturbed vascular endothelial integrity with increased vascular permeability, and activation of the coagulation cascade[16].

C-reactive protein (CRP) is a marker of tissue necrosis and inflammation. CRP are elevated in pre-eclampsia, but there is still a debate about its usefulness as marker for pre-eclampsia during the first and second trimester of pregnancy.

In present study there is increase in hs CRP levels in women with high risk pregnancies are 43.50 times significantly than that of controls correlates with study done by Myles Wolf et al, in Boston showed that high resolution CRP assays were performed on first trimester serum samples in women who developed pre-eclampsia [13].

Mean Body Mass index among cases is significantly elevated in cases. Our findings are consistent with the studies by Chung Fang Qiu et al,who have reported that lean women BMI ≤ 25 kg / m2 and elevated CRP were associated with a 2.5 fold increased risk of pre-eclampsia. But no similar association was observed in overweight women[17].

Compared with women who had normal pregnancy, the first trimester C reactive protein levels were significantly higher among women in whom pre-eclampsia developed. The findings of Wolf M et al.[13] is consistent with our study.

In the present study the mean Triglycerides and VLDL cholesterol levels are significantly increased in cases as compared to controls .The mean HDL cholesterol levels were within normal limits in cases. In line with the present study, the studies of Hirschfield et al., have reported high triglycerides and VLDL cholesterol in high risk pre-eclamptic pregnant women. Human CRP is a calcium dependent ligand binding protein with highest affinity to phosphocholine residues in plasma lipoproteins; this forms the basis for the observations.

C-reactive protein is a sensitive index of systemic inflammation that predicts adverse atherosclerotic events, including myocardial infarction, stroke, peripheral vascular disease and death[11].Elevated CRP levels are correlated with obesity, an association that might explain part of the excess cardiovascular risk linked to obesity[12].Systemic inflammation has been implicated in the pathogenesis of pre-eclampsia. Whether elevated C-reactive protein levels measured early in pregnancy, are associated with the subsequent development of pre-eclampsia is not clearly known. It is also not known whether C-reactive protein and obesity are similarly associated in pregnancy, and if so, whether inflammation might be one pathway through which obesity predisposes to pre-eclampsia [13].

The etiology of pre-eclampsia is still to be determined. Among many hypotheses, a few hypotheses deserve a lot of attention. The Genetic hypothesis, the Placental ischemia hypothesis and Immune dysfunctionhypothesis[18] are particularly noteworthy.

Thus, this present study indicates that High Sensitive C - reactive protein can be used as a predictive factor for pre-eclampsia.

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