Research Article

Study of serum hsCRP and lipid profile in pre-eclampsia

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Abstract

Objectives: The aim of the study is to determine the role of serum hsCRP as a pro inflammatory marker in preeclampsia and to evaluate the role of serum lipids (T.Cholesterol,non HDL, Triglycerides) in the pathogenesis of preeclampsia, as because the reports on lipid abnormalities in preeclampsia were inconsistent. **Materials and method:** It is a cross sectional study conducted in the Department of Biochemistry, RRMCH. The study group includes 50 preeclamptic women and age matched (18-35years) 50 healthy pregnant women. Study group were selected according to inclusion and exclusion criteria. Fasting blood samples were collected to perform serum hsCRP, T. Cholesterol, Triglyceride, and non HDL as calculated according to formula (T cholesterol-HDL C). **Results:** The data was analyzed using students t test, p value of <0.05 considered statistically significant. The mean value of serum hsCRP was statistically significant with p value<0.0001 ie values high in cases when compared with controls. Expect LDL other parameters like T. Cholesterol, Non HDL, Triglycerides were statistically significant (p value0.0001) with values being high in preeclamptic groups than in healthy pregnant women. HDL values were less in the case group than in control group. **Conclusion:** The significantly high levels of serum hsCRP in preeclampsia could be due to an exaggerated systemic inflammation which could be a marker of pathological uteroplacental perfusion, a characteristic feature of preeclampsia. Abnormal lipid profiles may have a role in promotion of oxidative stress and maternal endothelial dysfunction which is a classic hallmark of preeclampsia. Hence early detection of these parameters may aid in better management, providing a better maternal and fetal outcome.

Keywords: Preeclampsia, hsCRP, Triglycerides, Non HDL, Total Cholesterol.

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INTRODUCTION

Pre-eclampsia is a pregnancy specific disorder that affects virtually every organ system, characterized by host of abnormalities resulting in vascular endothelial damage and subsequent vasospasm, leading to the development of hypertension and proteinuria that occurs after 20 weeks of gestation in a previously normotensive or nonproteinuric women[1]. According to International Society for Study of Hypertension in pregnancy (ISSHP), hypertension in Pre-eclampsia is defined as systolic BP ≥ 140mm of Hg (or) and diastolic BP ≥ 90mm of Hg measured at 2 occasions at least 4 hours apart. Proteinuria is defined as ≥ 300mg /day in a 24 hour sample or ≥ +1 on urine dip stick on 2 random sample at least 4 hours apart[2].The incidence of Pre-eclampsia worldwide is 4-7%[3]. In India the incidence is reported as 8-10% of pregnancies[4]; being 10% in primigravida, 5% in multigravida. Pre-eclampsia is associated with high maternal mortality and morbidity as well as risk of perinatal death, pre-term birth and IUGR[3]. The pathophysiological mechanism of Pre-eclampsia is unclear, but the origin of condition is recognized as lying in the placenta as Pre-eclampsia resolves with delivery of placenta[3]. The pathogenesis of Pre-eclampsia is complex with genetic, immunologic and environmental factors interacting[5]. Pre-eclampsia is a two stage disorder. First stage is characterized by altered formation of placenta.

During placentation a defective invasion of extravillous trophoblast cells of spiral arteries has been shown. This contributes to reduced utero-placental blood flow that can result in foetal IUGR. A growing body of evidence suggest that oxidative stress further aggravates vascular function in placenta which in-turn gives rise to insufficient perfusion, inflammatory apoptosis and structural damage. Second stage is characterized by the clinical manifestations of hypertension and proteinuria[2,5].The association of altered lipid profile in essential hypertension is well documented. In early pregnancy there is increased body fat accumulation associated with increased lipogenesis and also early pregnancy dyslipidemia is associated with an increased risk of preeclampsia[6]. In normal pregnancy this feature is not atherogenic and is believed to be under hormonal control[7]. Pregnancy is a physiological stress, the stress being laid on biochemical changes which becomes exaggerated in complications of pregnancy like preeclampsia. The most common factor associated with preeclampsia is placental vasculopathy. Triglyceride related vasculopathy may be one possible etiological factor in a multifactorial disorder like preeclampsia. In healthy pregnancy adaptive changes takes place in women's physiology to meet the demand of rapidly developing fetus but in pregnancy complicated by preeclampsia these normal adaptive metabolic response are further exaggerated affecting the functions of various organs involved in lipid and lipoprotein metabolism[8] Pregnancy is associated with physiological hyperlipidemia. Different lines of evidence indicate that abnormal lipid metabolism is not merely a manifestation of preeclampsia, but that it is directly involved in its pathogenesis[7]. An abnormal lipid profile is known to be strongly associated with atherosclerotic cardiovascular diseases and has a direct effect on endothelial dysfunction[9]. Gohil *et al* in a one year study showed that concentration of total cholesterol, LDL and triglycerides concentrations were significantly increased in preeclamptic females as compared to normal pregnant women[10]. Recently there is increasing interest in the use of non HDL cholesterol as a marker of atherogenesis. Laboratory diagnosis of lipid disorders should be based on the use of indicators which present full impact of all plasma lipid components. Non HDL -C is the sum of cholesterol accumulated in all lipoproteins except HDL ,such as chylomicrons ,VLDL and their remnants, IDL, LDL and Lp(a). The concentration of non HDL is calculated using a simple equation as Non HDL - C(mg/dl)= TC – HDL C[11] , all of which have a potential to deliver cholesterol to arterial wall .This measure thus reflects atherogenic risk not captured by LDL-C measurement alone, particularly in context of elevated triglyceride[12]. CRP is a acute phase reactant produced by the liver in response to placental proinflammatory cytokines, especially IL6 and TNF α. CRP is an objective and sensitive marker of overall inflammation in the body. The etiology of endothelial dysfunction in preeclampsia could be postulated as a part of an exaggerated maternal inflammatory response to pregnancy. Increased production of reactive oxygen species and increased release of inflammatory cytokines, leads to increase in CRP levels showing it as a proinflammatory marker[13]. Increased inflammatory response in pregnancy may be explained by different stimuli occurring at different phases of pregnancy like placental ageing, increasing estrogen levels. However factors like age, smoking, labor may be associated with raised hsCRP concentration[14], but in the current study all participants were non smokers, and with no history of preterm labor.

Serum hsCRP is one of the suitable markers for low grade inflammation evaluation. This marker rises subsequent to stress which are accompanied by endothelial dysfunction and lead to peripheral vascular remodeling, decreased compliance and vascular stiffness[15]. Inflammation is considered to have a crucial role in pathophysiologic mechanism of preeclampsia and endothelial dysfunction is accompanied by elevated levels of inflammatory markers. Levels of hsCRP have been suggested to provide better sensitivity in establishing inflammation than levels of CRP[14]. Thus the current study was taken up to evaluate the role of lipids in the pathogenesis of preeclampsia and to determine the changes in levels of serum hsCRP which acts as a proinflammatory marker.

MATERIALS AND METHODS

Study population

The study was conducted in the department of biochemistry in collaboration with Department of obstetrics and Gynecology, RajaRajeswari Medical college and Hospital, Bangalore. The study was approved by the ethical clearance committee of Rajarajeswari medical college and hospital. Patients satisfying the inclusion criteria were enrolled in the study. Informed consent was taken from all subjects included in the study. A complete medical history was taken and physical examination was performed for each individual. The study comprised of fifty cases diagnosed with preeclampsia and fifty normal healthy pregnant women.

Inclusion criteria: Women diagnosed with pre-eclampsia according to criteria defined by ISSHP, aged between 18 to 35 years were included in the study.

Exclusion criteria: Women with history of diabetes mellitus, previous hypertension, thyroid disorders, any evidence of kidney, liver disease, recent history of fever, any chronic inflammatory diseases, h/o smoking were

excluded from the study. Fasting venous blood samples were collected from antecubital vein in Clot Activator tubes from both study and control group under full aseptic precautions. The samples were allowed to clot and Serum separated from the blood after centrifugation.Spot random urine sample was collected for urine albumin determination by dipstick method. BP was measured with sypgmomanometer in supine relaxed position. The patients were not in labour when samples were collected. The following investigations were performed by fully automated analyser.

a. Serum hsCRP by Immunoturbidimetry method
b. Serum cholesterol by CHOD method
c. Serum HDL by Immunoinhibition method
d. Serum Triglycerides by GPO method
e. Serum LDL by Immunoinhibition method
f. Non HDL calculated as T.Cholesterol minus HDL

RESULTS AND DISCUSSION

The data collected was tabulated and analysed using descriptive statistics.

The results are presented as mean ± SD. Statistical method applied was students t test. A p value of <0.05 was considered to be statistically significant.

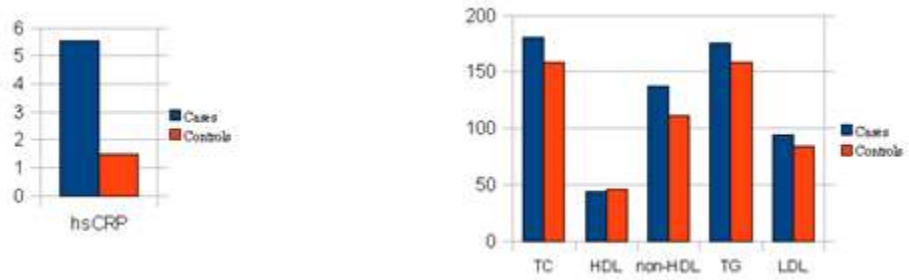

Figure 1: Srum hsCRP and Lipid profile in study groups

Table 1: Age distribution among study groups

Age in yrs	Preeclamptic cases (n=50)	Normal controls (n=50)
≤20	13	3
21-25	27	28
26-30	8	17
≥31	2	2
Mean ±SD	**23.5±3.96**	**24.66±2.99**

Table 2: Demographic characteristics among case and control group

	Cases n=50	Controls n=50	p value
Age (yrs)	23.5±3.96	24.66±2.99	0.1(NS)
Gestational age (weeks)	32.96±3.2	32.18±3.6	0.25(NS)

Abbreviation: NS, not significant

Table 3: Comparison of clinical and biochemical characteristics of study groups

	Cases n=50	Controls n=50	p value
FBS(mg/dl)	87±1.41	86±5.66	0.22
Systolic Blood Pressure (mmHg)	150.3±13.9	115.96±6.96	<0.0001
Diastolic Blood Pressure(mmHg)	100.56±9.24	75.84±5.58	<0.0001
hsCRP(mg/L)	5.55±5.6	1.5±0.96	<0.0001
T.Cholesterol(mg/dl)	180.9±29.49	158.08±26.81	0.0001
HDL(mg/dl)	43.52±4.48	46±5.27	0.01
LDL(mg/dl)	93.96±26.41	84.4±30.56	0.09
Non-HDL(mg/dl)	137.38±29.94	111.46±28.28	<0.0001
Triglycerides(mg/dl)	175.16±24.61	157.94±15.84	<0.0001

Abbreviations: **FBS**: Fasting blood sugar; **hsCRP:** High sensitive C reactive protein **HDL:** high density lipoprotein; **LDL:** low density lipoprotein

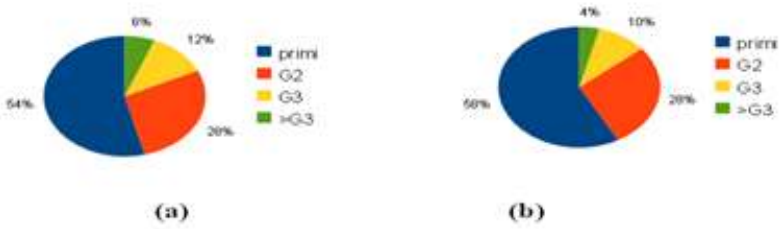

Figure 2: Showing parity among (a) cases and (b) controls groups

RESULT AND DISCUSSION

The present study enrolled 100 pregnant women; 50 cases and 50 controls. Table.1 depicts the age distribution among the study groups. Table.2 shows the demographic characteristics. There was no significant difference in maternal age and the gestational age between cases and controls Chart.1 shows the parity of the subjects in case and control groups and among cases 54% and among controls 58% were primigravida. Table.3, shows the lipid profile and hsCRP levels and it is seen that the mean± SD of hsCRP and the lipid levels like T.cholesterol, Triglycerides and non HDL were significantly elevated in preeclampsia as compared to controls (p value of 0.0001).Serum HDL levels were decreased in cases as compared to controls (p value 0.01).Serum LDL levels were not statistically significant between the study groups(p value 0.09.) Preeclampsia being a complex pathophysiological condition the regulatory systems of inflammation and endothelial functions are stimulated beyond the physiological limits of normal pregnancy where lipids could play an important role in modifications of endothelial function and structure[10]. Although all the major class of biomolecules may be attacked by free radicals but lipids are probably the most susceptible one. The lipid peroxides formed as a result of oxidative destruction are known to injure the cell membrane[16]. HDL cholesterol is one of the major lipoprotein involved in exchange of cholesterol, cholesterol esters and TG between tissues. HDL facilitates reverse cholesterol transport to liver where it can be excreted. Decreased HDL may compromise this function. The decreased HDL levels in our study is consistent with the study conducted by Gohil *et al*. In a study conducted by Nanda *et al*, hsCRP levels were elevated in preeclampsia as compared to controls wherein they suggested that serum hsCRP could act as a predictor of preeclampsia.

H S Hwang *et al* study concluded that serum levels of hsCRP were higher in women with preeclampsia when compared with normal pregnancy and could also be a marker of severity of the condition. Study by Pradnya Phalak *et al*[6] and Singh *et al*[17] observed a significantly increased serum Triglyceride, Total Cholesterol and a decreased level of HDL in cases as compared to controls, our results were in accordance with their study. The TG related vasculopathy may be one possible etiological factor. Women with preeclampsia have higher levels of circulating serum triglycerides which is an essential step in lipid mediated endothelial dysfunction[8]. One of the mechanism involved in pathological process of preeclampsia is via dysregulation of lipoprotein lipase resulting in a dyslipidemic lipid profile[17], the net effect of which will be an increase in circulating triglycerides[6]. The presence of a proatherogenic lipoprotein profile, is characterized by increased small dense LDL and is exclusive to a subset of preeclamptic patients with high TG levels[18] According to study by Mustafa *et al*[7] and C K Eman *et al*[19], they reported that Total cholesterol values didn't change significantly in preeclampsia when compared with the control group. LDL levels between preeclamptic and control group were not statistically significant in our study. This could be due to shift of large LDL particle to smaller dense particles which are intrinsically more susceptible to oxidative changes. This scenario could be explained with increased TG levels along with decreased HDL, causing inhibition of endothelium dependent relaxation and vasoconstriction as demonstrated by Kazuhiro ogura *et al* study[20]. Thus in our study though serum LDL were not significantly different quantitatively but the qualitative changes in LDL in the form of small dense LDL cannot be ruled out which can also contribute to atherogenic characteristics. In the present study we found dyslipidemic profile in preeclamptic patients when compared to normal pregnant women. This study supports the role of atherogenic lipid profile in preeclampsia which contributes to endothelial dysfunction. Dyslipidemia and oxidative stress may play a role in pathogenesis of preeclampsia through increased susceptibility to lipid peroxidation.

CONCLUSION

Thus from the current study we conclude that serum hsCRP is significantly elevated in preeclampsia suggesting preeclampsia to be an exaggerated inflammatory condition when compared to normal pregnancy. The elevated lipid levels like Total cholesterol, non HDL, Triglycerides with decreased HDL

have a greater part in endothelial dysfunction which could be due to abnormal lipid peroxides. Evaluation of the above parameters may help in understanding the pathophysiology and increase the diagnostic criteria in preeclampsia. Hence early detection of these parameters may aid in better management, providing a better maternal and fetal outcome.

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