

THE RELATIONSHIP BETWEEN OXIDATIVE STRESS AND HIGH SENSITIVE C-REACTIVE PROTEIN IN PREECLAMPSIA

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Abstracts: Background & Objectives: Preeclampsia, being most common medical complication of pregnancy requires early diagnosis and intervention. The aim of present study is to measure and correlate serum MDA level with HS-CRP level in preeclampsia. **Methods:** The present study involves 200 subjects in the age group of 20 to 35 years primigravida, all in their third trimester, recruited from preeclampsia ward and OPD of Mahila Chikitsalaya, Sanganeri gate, Jaipur (Rajasthan). Out of total 200 subjects, 100 were preeclampsia women and 100 were normotensive pregnant women. Data were statistically analyzed by “z” test for comparison of mean and Karl Pearson coefficient of correlation to quantify the association between the variables. **Results:** The levels of serum MDA (nmol/ml) and HS-CRP (mg/l) were significantly elevated ($p < 0.05$) in preeclampsia women (4.97 ± 1.00 and 1.18 ± 0.43) when compared to normotensive pregnant women (2.43 ± 0.51 and 0.66 ± 0.31), respectively. Moreover, in preeclampsia women, a significant positive correlation ($r = 0.732$, $p < 0.05$) between serum MDA and HS-CRP was observed as compared to normotensive pregnant women ($r = 0.160$; $p > 0.05$). **Interpretation & Conclusion:** Elevated serum MDA and HS-CRP in preeclampsia women compared with normal pregnant women suggests that oxidative stress in preeclampsia is associated with increased inflammatory responses.

Key Words: Oxidative Stress; Preeclampsia; Serum high sensitive C-reactive protein (HS-CRP); Serum Malondialdehyde (MDA).

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Introduction:

Hypertensive disorders are the most common medical complications of pregnancy. It is well documented that about 10% of normotensive women and 20-25% chronic hypertensive women, in their first pregnancy suffer from pregnancy induced hypertension¹.

Endothelial dysfunction may play a pivotal role in the genesis of the multisystem disorder developed in preeclampsia. The mechanisms involved in the induction of endothelial cell dysfunction are poorly understood. In preeclampsia oxygenation of both maternal and foetal tissue oscillate frequently which could lead to production of more reactive oxygen free radicals and raised oxidative stress and hence uncontrolled lipid peroxidation².

Impaired function of vascular endothelium in preeclampsia may cause abnormal immune activation causing release of inflammatory agents like cytokines, C-reactive protein etc. The high sensitive C-reactive protein (HS-CRP) is a sensitive marker of tissue damage. Its production is stimulated by inflammatory cytokines such as

Interleukin-6 (IL-6) and α -tumour necrosis factor (α -TNF)³.

The aim of the present study was to measure and correlate serum malondialdehyde (MDA-an index of oxidative stress) level with High sensitive C-reactive protein (HS-CRP-an inflammatory marker) level in preeclampsia as compared to normal pregnant women.

Material and Methods:

The present study was conducted in the upgraded Department of Physiology, SMS Medical College, Jaipur. The present study involves 200 subjects in the age group of 20 to 35 years primigravida all in their third trimester singleton pregnancy, recruited from preeclampsia ward and OPD of Mahila Chikitsalaya, Sanganeri gate, Jaipur (Rajasthan). Out of total 200 subjects, 100 were preeclamptic women and 100 were normotensive pregnant women.

Subjects suffering from any systemic or endocrinal disorder including chronic hypertension, any addiction (Smoking / Alcohol / Tobacco chewing) and taking any medication which can affect antioxidant status

except iron and folic acid were excluded from the study.

The study subjects were informed about the objectives of the study. An informed consent was taken from all the subjects and Institutional ethical committee approval was also taken.

Sample collection:

2 ml of venous blood was collected from subjects using disposable syringe. Serum was separated and analyzed. Blood pressure was recorded by palpatory as well as auscultatory methods after 15 minutes of rest. MDA level was estimated by Thiobarbituric acid (TBA) assay method⁴. Serum high sensitive C-reactive protein (HS-CRP) was estimated by Quantitative determination by turbidimetric immune-assay method^{5,6}.

Statistical analysis:

Data were statistically analyzed by “z” test for comparison of mean and Karl Pearson coefficient of correlation to quantify the association between the variables.

Result:

As depicted from table 1, the mean value of maternal age (years) in preeclamptic and control group was 23.07 ± 2.71 and 22.53 ± 2.18 while gestational age (weeks) was found 31.48 ± 1.83 and 32.01 ± 2.14 , respectively. The mean Systolic BP (mmHg) and Diastolic BP (mmHg) in preeclamptic group were 155.02 ± 11.82 and 99.82 ± 9.33 , while in control group were 119.08 ± 7.56 and 76.04 ± 8.12 i.e. normal, respectively.

Table 2 shows that the levels of serum MDA (nmol/ml) and HS-CRP (mg/l) were significantly elevated ($p < 0.05$) in preeclamptic women (4.97 ± 1.00 and 1.18 ± 0.43) when compared to normotensive pregnant women (2.43 ± 0.51 and 0.66 ± 0.31), respectively.

Moreover, a significant positive correlation ($r = 0.732$; $p < 0.05$) between serum MDA and HS-CRP was observed in preeclamptic group as compared to controls ($r = 0.160$; $p > 0.05$) (Table 3).

Table: 1 Demographic profile of studied population

S.No.	Parameters	Preeclamptic group n=100		Control group n=100	
		Mean	±SD	Mean	±SD
1.	Age (years)	23.07	2.71	22.53	2.18
2.	Gestational Age (weeks)	31.48	1.83	32.01	2.14
3.	Systolic Blood Pressure (mmHg)	155.02	11.82	119.08	7.56
4.	Diastolic Blood Pressure (mmHg)	99.82	9.33	76.04	8.12

(n=Total number of subjects)

Table:2 Comparison of serum Malondialdehyde (MDA) concentration (nmol/ml) and High sensitive C-reactive protein (HS-CRP) concentration (mg/l) between two groups.

S.No.	Parameters	Preeclamptic Group		Control Group		z
		Mean	±SD	Mean	±SD	
1.	MDA (nmol/ml)	4.97	1.00	2.43	0.51	*21.49
2.	HS-CRP (mg/l)	1.18	0.43	0.66	0.31	*11.09

(* $p < 0.05$: Significant)

Table: 3 Correlation of Serum Malondialdehyde (MDA) (nmol/ml) with High sensitive C- reactive protein (mg/l) between two groups.

Parameter s	Preeclamptic group		Control group	
	r	p	r	p
High Sensitive-C Reactive Protein (mg/l)	0.732	<0.05	0.160	>0.05

($p < 0.05$: Significant)

Discussion:

Preeclampsia is a complex condition, which cannot be attributed to any single cause. The primary cause to develop a disease may be due to insufficient invasion by trophoblast cells in uterine wall in early pregnancy. There is no unifying scientific evidence to explain the pathophysiology of disease. But, a possible hypothesis for its pathogenesis is reduced placental perfusion as a result of shallow invasion of trophoblast cells, this leads to increased lipid peroxidation and the release of oxygen radicals without counter regulation by antioxidants⁷.

Present study demonstrated a significant ($p < 0.05$) increase in concentration of serum MDA (nmol/ml) in preeclamptic group (4.97 ± 1.00) as compared to normal pregnant women (2.43 ± 0.51). Present finding is in agreement with studies of many workers^{8,11}. But some studies had reported that there was no evidence of increased lipid peroxidation in preeclampsia¹².

During pregnancy, free radicals and other damaging reactive oxygen species such as the superoxide anions and peroxide ions are formed in oxidative metabolic processes; their activation is increased during preeclampsia. These reactive oxygen species (ROS) interacts with polyunsaturated fatty acids (PUFA). Since biological membrane are rich in PUFA, therefore membrane lipids are susceptible to peroxidative attack, this attack initiates a complex series of reactions resulting the formation of MDA. That is why, serum MDA level increases in preeclampsia and signifies the lipid peroxidation¹³.

Preeclampsia is associated with profound inflammatory changes. Many studies have shown that markers of endothelial activation or inflammation have an active role in preeclampsia¹⁴. Present study also shows serum level of HS-CRP (mg/l), a sensitive marker of tissue damage and inflammation was significantly elevated ($p < 0.05$) in preeclamptic women (1.18 ± 0.43) when compared to normotensive pregnant women (0.66 ± 0.31) (Table 2).

Present findings correlate with the previous reports of Belo L et al¹⁵, Ustun Y et al¹⁶, and Kumru S et al¹⁷. Present results are also similar with the findings of Mirzaie F et al¹⁸ and Bargale A et al¹⁹, who proposed that persistent and exaggerated systemic inflammation during pregnancy leads to endothelial dysfunction and further preeclampsia. In 2010, Ertas IE et al measured serum HS-CRP level and found that elevated HS-CRP level is a useful marker in predicting severity of preeclampsia²⁰.

Present results are in contrast to the studies of Savvidou MD et al²¹, Stefanovic M et al²² and Kristensen K et al²³, who found no significant difference in the levels of the HS-CRP in preeclamptic women as compared to normotensive pregnant women.

Further in present study, a significant ($p < 0.05$) positive correlation of serum MDA with HS-CRP level was found in preeclampsia ($r = 0.732$) in comparison of control group ($r = 0.160$; $p > 0.05$) as shown in table 3, which reflects that oxidative stress synergizes with inflammation in preeclampsia, which increases the disease severity. Result of Sathish BM et al²⁴ favours present study. Present results support the hypothesis that systemic inflammation is involved in the pathogenesis of preeclampsia and serum HS-CRP level may be a marker to predict severity of disease.

Conclusion:

Elevated serum MDA and HS-CRP in preeclamptic women compared with normal pregnant women suggest that preeclampsia is characterized by exaggerated maternal systemic inflammatory response. So, serum MDA and HS-CRP levels can be utilized as marker of disease severity in preeclampsia and early detection of these parameters is going to aid in better management of preeclampsia cases which is important to improve the maternal and fetal outcome in preeclampsia.

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