Scholars Journal of Applied Medical Sciences (SJAMS) **ISSN 2320-6691 (Online)**
Sch. J. App. Med. Sci., 2014; 2(6D):3092-3096 **ISSN 2347-954X (Print)**

(An International Publisher for Academic and Scientific Resources)
www.saspublishers.com **DOI:** 10.36347/sjams.2014.v02i06.051

Research Article

The Relationship between Oxidative Stress and Atherogenic Index (A.I.) in Preeclampsia

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Abstract: Preeclampsia is the most common medical complication of pregnancy. About 10% of normotensive women and 20-25% chronic hypertensive women, in their first pregnancy suffer from pregnancy induced hypertension requires its early diagnosis and intervention. The aim of the study is to measure and correlate serum malondialdehyde (MDA) level (an index of oxidative stress) with Atherogenic Index (A.I.) in preeclampsia as compared to normal pregnant women. The present study involves 200 subjects in the age group of 20 to 35 years (devoid of diabetes, urinary tract infections, renal or liver disorders) 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 preeclamptic 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. The levels of serum MDA (nmol/ml) and Atherogenic Index (A.I.) were significantly elevated ($p<0.05$) in preeclamptics (4.97±1.00 and 5.66±0.89) when compared to normotensive pregnant women (2.43±0.51 and 3.69±0.46), respectively. Moreover, a significant ($p<0.05$) positive correlation of MDA with A.I. in preeclamptic group ($r=0.638$) was seen in comparison of controls ($r=0.108$). Present study concluded that elevated serum MDA and Atherogenic Index (A.I.) in preeclamptic women compared with normal pregnant women suggest that oxidative stress in preeclampsia is associated with increased risk of future cardiovascular events.
Keywords: , Oxidative stress, Preeclampsia, Serum malondialdehyde (MDA), Serum Total Cholesterol (TC), High Density Lipoprotein-Cholesterol (HDL-C), Atherogenic Index (A.I.)

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 hypertension [1].

According to the Society of Obstetricians and Gynaecologists of Canada-Blood pressure ≥ 140/90 mm Hg after 20 weeks gestation with proteinuria (≥ 300 mg/24hrs) is defined as preeclampsia. Preeclampsia is the leading cause of maternal mortality in developed countries and in developing countries like India, Bangladesh, Pakistan etc and is associated with a five-fold increase in perinatal mortality [2].

Although the exact pathophysiologic mechanism of preeclampsia is not clearly understood, evidences from last many years indicate that preeclampsia is primarily a placental disorder. Many pathophysiological features of preeclampsia such as increased sensitivity to pressor agents, activation of the coagulation cascade and increased vascular permeability suggest that vascular endothelial dysfunction is an important component of this disorder. It has been postulated that free radical mediated lipid peroxidation may be involved in this process of vascular endothelial dysfunction [3].

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 peroxidation [4].

Since the cell membrane consists primarily of lipids, uncontrolled lipid peroxidation causes cell injury and

death via membrane damage [5]. It also causes evolution of toxicity produced metabolites especially reactive aldehydes, capable of reacting molecular targets at a distance [6]. Among the different aldehydes formed, the most intensively lipid peroxidation product malondialdehyde (MDA) is the sensitive marker of oxidative stress. It is used as a biochemical marker for the assessment of lipid peroxidation because it is a major breakdown product split off from lipid peroxides. Uncontrolled lipid peroxidation is a key contributing factor to pathophysiologic condition of preeclampsia. Reactive oxygen species (ROS) formed in lipid peroxidation process cause damage at distant tissues and endothelial cells of arterial vessels [7].

Reactive oxygen species (ROS) may also be responsible for the fatty deposition in the vessel walls; this may predispose them for coronary heart disease in future. Atherogenic index is the useful predictor of coronary heart disease. Atherogenic Index indicates the relationship or proportion between the Atherogenic and the antiatherogenic lipid fraction, which can be calculated by using the formula, Total Cholesterol/High Density Lipoprotein-Cholesterol [8].

Adiga U *et al*. [8] conducted a study on 35 preeclamptic and 25 normal pregnant women. They found atherogenic index was significant high in preeclamptic women. The study conducted by Cong KJ *et al*. [9] has also shown elevated levels of lipids. Kokia E *et al*. [10] also found the same result in their study. There are very few studies which represent relationship between oxidative stress and A.I.

The aim of the present study was to measure and correlate serum malondialdehyde (MDA) level (an index of oxidative stress) with Atherogenic index (A.I.) in preeclampsia as compared to normal pregnant women.

METHODOLOGY

Study Design

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 (devoid of diabetes, urinary tract infections, renal or liver disorders) primigravida, all in their third trimester singleton pregnancy, recruited from preeclampsia ward and OPD of Mahila Chikitsalaya, Sanganeri gate, Jaipur. 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. Malondialdehyde (MDA: an index of oxidative stress) level was estimated by Thiobarbituric acid (TBA) assay method [11].

The total cholesterol (TC) was estimated by the CHOD-PAP method [12]. HDL-C was also estimated similarly after precipitating the chylomicrons LDL and VLDL [13]. Atherogenic Index (A.I.) can be calculated by using the formula TC/HDL-C [8].

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.

RESULTS

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 a significant rise ($p<0.05$) in TC levels in preeclampsia (237.9±33.16) as compared to normal pregnancy (206.9±15.43) and a significant fall ($p<0.05$) in HDL-C in preeclampsia cases (42.18±2.44) was seen when compared with control women (56.41±4.68).

The levels of serum MDA (nmol/ml) and Atherogenic Index (A.I.) were significantly elevated ($p<0.05$) in preeclamptic women (4.97±1.00 and 5.66±0.89) when compared to normotensive pregnant women (2.43±0.51 and 3.69±0.46), respectively.

Moreover, a significant positive correlation ($r=0.638$; $p<0.05$) between serum MDA and A.I. was observed in preeclamptic group as compared to controls ($r=0.108$; $p>0.05$) (Table 3).

Table 1: Demographic profile of studied population

Sl. No.	Parameters	Preeclamptic group (Mean±SD) n=100	Control group (Mean±SD) n=100
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) (nmol/ml) and other parameters between two groups

Sl. No.	Parameters	Preeclamptic Group (Mean±SD)	Control Group (Mean±SD)	z	p
1.	MDA (nmol/ml)	4.97±1.00	2.43±0.51	21.49	<0.05
2.	TC (mg/dl)	237.9±33.16	206.9±15.43	8.62	<0.05
3.	HDL-C (mg/dl)	42.18±2.44	56.41±4.68	-27.20	<0.05
4.	A.I.	5.66±0.89	3.69±0.46	20.98	<0.05

(p<0.05: Significant)

Table 3: Correlation of Serum Malondialdehyde (MDA) (nmol/ml) with Atherogenic Index (AI) between two groups

Parameter	Preeclamptic group		Control group	
	r	p	r	p
Atherogenic Index (A.I.)	0.638	<0.05	0.108	>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 antioxidants [14].

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 Utoila JT *et al*. [15], Jain SK *et al*. [16], Madazil R *et al*. [18] and Kaur G *et al*. [18]. But some studies had reported that there was no evidence of increased lipid peroxidation in preeclampsia [19].

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 peroxidation [20].

Moreover, there was a significant rise (p<0.05) in TC levels in preeclampsia (237.9±33.16) as compared to normal pregnancy (206.9±15.43) in present study, which was similar to results of Potter JM *et al*. [21], Hubel CA [22] and Adegoke OA *et al*. [23]. However, Sattar N *et al*. [24] and De J *et al*. [25] reported no alteration in TC levels [24-25]. A significant fall (p<0.05) in HDL-C in preeclampsia cases (42.18±2.44) was seen when compared with control women (56.41±4.68). Estrogen is responsible for induction of HDL-C but in preeclampsia there is a fall in estrogen levels as compared to normal pregnancy. Hence the low HDL-C in preeclampsia is due to hypoestrogenemia and insulin resistance [26]. Present result is in agreement with the previous report of Luis B *et al*. [27].

Present study portrays the fact that Atherogenic Index (A.I.) is significantly elevated (p<0.05) in preeclampsia (5.66±0.89) over the normal pregnant state (3.69±0.46). Present results are in agreement with studies of Kokia E *et al*. [10], Cong KJ *et al*. [19] and Adiga U *et al*. [8]. A significant (p<0.05) positive correlation of MDA with A.I. in preeclamptic group (r=0.638) was seen in comparison of controls (r=0.108). Reactive oxygen species (ROS) may also be responsible for the fatty deposition in the vessel walls; this may predispose them for coronary heart disease in future.

Atherogenic index is the useful predictor of coronary heart disease [8].

Elevated TC level, reduced HDL-C level and increased A.I. in the present study indicate the presence of dyslipidemia and may contribute to the pathophysiology of preeclampsia. Pregnancy challenges the lipolytic activity of lipoprotein lipase as there is marked reduction in its activity during pregnancy. The changes in the lipid levels could be related to the decrease in hepatic lipase activity during gestation [28]. Activities of lipoprotein lipase and hepatic lipase are substantially decreased during normal pregnancy and are attributed to the heightened insulin resistance and raised estrogen levels respectively [29]. Physiological insulin resistance is exaggerated in preeclamsia [30]. Gestational insulin resistance may accentuate the suppression of lipoprotein lipase activity and increase mobilization of free fatty acids from visceral adipocytes. These facts explain the hypercholesterolemia in preeclampsia [31].

CONCLUSION

Moreover, increased oxidative stress is associated with augmented cardiovascular risk factors. The dyslipidemia found in hypertensive pregnant patients could be associated with enhancement of pathological lipid deposition in predisposed vessels leading to endothelial dysfunction. The raised atherogenic index is a risk factor in causing coronary heart disease in future. These patients need to be followed up till the lipid levels normalize. Interventional studies are needed to determine whether pre-pregnancy weight reduction and dietary modification can lower the risk of preeclampsia.

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