Role of biomarker of Oxidative stress in preeclampsia

Smita Bahediya[1,*], Gaurav Modi[2], Shobha Chokshi[3]

[1]Associate Professor, [2]Assistant Professor, [3]Ex. Professor & HOD, AMCMET Medical College, Ahmedabad, Gujarat

***Corresponding Author:**
Email: ashnhlmci@gmail.com

Abstract

Objective: To evaluate the role of biomarker of oxidative stress in predilection of pregnancy induced hypertension.

Material and Methods: A sample of 200 pregnant women was examined at department of Gynecology and obstetrics at tertiary care hospital from the period of July 2008 to march 2010. Pregnant women were divided into three groups including 100 normal healthy pregnant women which were controls. Another 100 pregnant women having increased blood pressure and proteinuria divided into two groups depend on severity on B.P. and urinary proteinuria. Groups were compared for the levels of antioxidant biomarker for the statistical analysis, suitable test for these qualitative variables with 5% significance were used.

Results: Preeclampsia remains a frequent and potentially dangerous complication of pregnancy. The cause remains largely unknown, but oxidative stress and a generalized inflammatory state common are features. In present study, patient with pregnancy induced hypertension shows MDA levels were found significantly higher, while Vitamin C and Vitamin E levels are significantly lower compared with normal healthy pregnant women.

Conclusion: A combination of vitamins C and E administration can be found promising for prevention of preeclampsia. As small study group, our study has a limited statistical power if significance several multicenter randomized clinical trials are further required.

Key Words: Preeclampsia, Oxidative stress, Antioxidants, Free radicals

Access this article online	
Quick Response Code:	Website: www.innovativepublication.com
	DOI: 10.5958/2394-6377.2016.00061.7

Introduction

Preeclampsia affects between 0.4% and 2.8% of all pregnancies in developed countries and many more in developing countries, which cause thousands of pregnancy induced hypertension cases worldwide per year.[1] This common disorder, attributes to more than 90% case of morbidity and mortality, in developing countries more prevalent in first pregnancies.[1] Preeclampsia is defined as more than 90 mm of Hg of diastolic blood pressure, more than 300mg proteinuria per day and elevated urinary protein creatinine ratio.[2] When patients have abnormal liver function, low platelet count, and hemolysis, known as HELLP syndrome.[3]

Pregnancy also one of important reason of oxidative stress, defined as disturbance in balance of pro-oxidant & antioxidant levels. The supplementation with antioxidants protects the fetus and mother from the harmful effect of oxidant stress in pregnancy.[3] Hypertensive medical disorder are the most common medical complications of pregnancy causing morbidity and mortality to both mother and child, with a more than 10% incidence[4]. Pre-eclampsia is a common complication during pregnancy, affecting up to one in seven pregnant women around the world[5]. In India the incidence of PIH according to national standard is 15.2% and the incidence of pre-eclampsia is reported to be 8-10% of the pregnancies[6].

These observations in pre-eclampsia have given rise to increased interest in antioxidants such as Ascorbic acid (Vitamin C), Vitamin E and Uric acid.

Materials and Methods

The study was conducted at Biochemistry and Obstetrics & Gynaecology Department Tertiary medical college and hospital.

Study groups were divided

Group 1 Normal pregnant healthy women (n=100)

Group 2a Pregnant women with mild pre eclampsia (n=75)

Group 2b Pregnant women with Severe pre eclampsia (n=25)

All these cases were studied for lipid peroxide (MDA), Vitamin C and Vitamin E by different standard methods. Subject selection for different study groups were as follows:

Subject selection for Normal Pregnant (Group 1)---

The normal pregnant subjects with obesity, Diabetes mellitus(under medication and untreated diabetes), hypertensive, severely anaemiac and patients of any other systemic disorder, were excluded from the study. All the subjects were having single tone pregnancy and primigravida.

Subject selection for Pre-eclamptic pregnancy(Group 2)--

The diagnosis of Pre-eclampsia was done as per the norms of American college of obstetrics and gynaecologists (1986). Pre-eclampsia was defined as Blood pressure more than 140 mm Hg (systolic)and 90 mm Hg (diastolic), with significant proteinuria (300 mg per 24 h); mild pre-eclampsia (Gr. 2a) was defined as diastolic BP less than 110 mm Hg, with significant proteinuria; and severe preeclampsia (Gr. 2b) as diastolic BP greater than 110mm Hg or massive proteinuria (2 g/24 h) or serum creatinine more than 1.2 mg/dl or when other signs and symptoms of severe pre-eclampsia such as low platelet count, headache, visual difficulties, persistent pain abdomen, (Morris JM et al, 1998).

The cases having past history of diabetes mellitus, hypertension, renal diseases, and liver disorder and with the history of multivitamin intake were excluded. Venous blood samples were collected.

Serum was separated by centrifugation of blood sample and preserved at 4ºC, then used for estimation of various parameters. All the parameter were assessed on UV-VIS Spectrophotometer 1240 (Shimadzu). Institutional Ethics Committee's approval was taken before starting the study. The study was explained to them in brief in a language they can understand. Consent of participants was taken in written informed consent form. Data were collected and analyzed using appropriate statistical tests.

Results

Table 1: Basic descriptive statistics for MDA, Vitamin C and Vitamin E levels with regard to the severity of pre-eclampsia symptoms

Severity of pre-eclampsia symptoms	N	Percent	MDA nmol /ml		Vitamin C mg/dl		Vitamin E mg/dl	
			Median	Min–Max	Median	Min–Max	Median	Min–Max
Normal	100	50	2.89	1.43–3.89	0.8935	0.759-1.19	0.88	0.708-1.192
Mild	75	37.5	5.1	3.45-5.99	0.783	0.612-0.898	0.493	0.396-0.85
Moderate	25	12.5	5.81	4.36-7.54	0.767	0.615-0.843	0.501	0.415-0.602

Table 1 shows serum MDA levels in the pre-eclamptic patient population of women involved in this study were high when compared to the normal, and ranged from 3.45-5.99 nmol/ml, with an average of 5.1 nmol/mL, in mild pre-eclamptic patients. In severe pre-eclamptic patients MDA ranged from 4.36-7.54 nmol/ml, with an average of 5.8 nmol/mL.

Vitamin C levels are comparatively low, with an average of 7.8 mg/dl and 7.6 mg/dl in mild and severe pre-eclamptic patients respectively, while Vitamin E levels are also low compared to normal populations with an average of 0.49 and 0.50 in mild and severe pre-eclamptic patients.

Table 2: The Kruskal–Wallis test results for the severity of pre eclampsia symptoms depending on MDA, Vitamin C and Vitamin E levels

Severity of preeclampsia **symptoms**	**N**	**Mean rank**	**H**	**p value**
MDA nmol /ml				
Normal	100	50.64	151.538	<0.001
Mild	75	144.51		
Severe	25	167.94		
Vitamin C mg/dl				
Normal	100	138.57	89.619	<0.001
Mild	75	68.32		
Severe	25	44.78		
Vitamin E mg/dl				
Normal	100	150.11	146.958	<0.001
Mild	75	51.61		
Severe	25	48.76		
H is a Kruskal–Wallis test value; p is a level of significance for test value				

Table 2 is showing the analysis of the results performed with the Kruskal–Wallis test demonstrated a statistically significant difference in serum MDA levels, Vitamin E levels, Vitamin C levels between at least two of the analyzed groups with different severity levels of pre eclamptic symptoms ($p < 0.05$).

Table 3 shows The analysis of multiple comparisons demonstrated that the women with mild as well as severe preeclampsia had significantly higher MDA levels and low levels of Vitamin E, Vitamin C than those without preeclamptic symptoms ($p < 0.05$).

Table 3: Multiple comparison test results for the severity of preeclampsia symptoms depending on MDA, Vitamin C and Vitamin E levels

Severity of preeclampsia **symptoms**	**Normal**	**Mild**	**Severe**
p value for multiple comparisons: MDA Independent variable: HYPERTENSION			
H (2, N = 200) = 151.538; p <0.001			
Normal	-	<0.001	<0.001
Mild	<0.001	-	0.001
Severe	<0.001	0.001	-
p value for multiple comparisons; Vitamin C Independent variable: HYPERTENSION H (2, N = 200) = 89.619; p = <0.001			
Normal	-	<0.001	<0.001
Mild	<0.001	-	0.029
Severe	<0.001	0.029	-
p value for multiple comparisons; Vitamin E Independent variable: HYPERTENSION H (2, N = 200) = 146.958; p<0.001			
Normal	-	<0.001	<0.001
Mild	<0.001	-	0.729
Severe	<0.001	0.729	-
H is a Kruskal–Wallis test value; p is a level of significance for test value			

Discussion

Pregnancy is a physiological state accompanied by a high energy demand and an increased oxygen requirement. Various compensatory adaptive changes occur with advancing pregnancy to fulfil the needs of the foetus[8]. Such a condition may be responsible for raised oxidative stress in pregnancy. An Oxidative stress is the presence of free radicals in excess to available antioxidants[9].

In the present study serum malondialdehyde level increases significantly in pregnant women with mild & severe pre-eclampsia compared to Normal pregnant women.

Malondialdehyde levels in patients with pre-eclampsia increase beyond normal pregnancy levels by the second trimester[10]. Rise in MDA could be due to increased generation of reactive oxygen species (ROS) which generates excessive oxidative damage in these patients. These oxygen species in turn can oxidize many other important biomolecules including membrane lipids. The lipid peroxides and free radicals may be important in pathogenesis of preeclampsia[11].

Uncontrolled lipid peroxidation may play an important role in the preeclampsia because of its potential to cause vascular endothelial cell dysfunction which may be the initiator of the pathophysiological events of pre-eclampsia[12]. A number of reports indicate that blood levels of lipid peroxidation products are elevated in women with pre-eclampsia relative to normal pregnancy[13]. Furthermore placental production of lipid peroxides has been demonstrated to be abnormally increased in pre-eclampsia. Consistent with previous studies, in the presents study there is a significant increase in serum MDA levels in the pre-eclampsia patients.

Serum Alpha-tocopharol and Ascorbate levels were decreased which is highly significant in pregnant women with Preeclampsia. Ascorbate oxidizing activity and levels of known circulating markers of oxidative stress (e.g., nitrosothiols, lipid oxidation products, and antibodies to low-density lipoproteins) are increased in women with pre-eclampsia[14].

Many studies confirm that levels of antioxidants such as vitamin C, vitamin E, and other antioxidants are reduced in the sera and placentas of pre-eclamptic women[9]. Sagol et al (1999) observed impaired antioxidant activity in women with pre-eclampsia[15]. Palan et al (2001) found significantly lower levels of beta carotene, lycopene, and xanthenes in the sera and placentas of pre-eclamptic women than in the sera of normotensive women. Although some studies (Zhang C, 2001; Regan CL, 2010) suggested that oxidative stress is important in the development of pre-eclampsia, other studies have found no evidence of lipid peroxidation or reduced antioxidant activity in these women[16,17].

Conclusion

Antioxidant supplementation can decrease the incidence of birth defects and protect both mothers and

the fetous from the damaging and possibly fatal consequences of pregnancy complications.

Further work is needed to support the preliminary findings of the present study to elucidate the lipid peroxidation mechanism(s) involved in the hypertensive disorders of pregnancy.

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