Original Research Article

Study of oxidative stress and uric acid in preeclampsia

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Abstract

Aims: This study is aimed to evaluate oxidative stress and antioxidant uric acid levels in preeclampsia. **Methods:** Serum malondialdehyde levels, serum uric acid levels and serum superoxide dismutase activities were evaluated in 40 cases of women with preeclamosia (Group I) and compared with 40 healthy normotensive pregnant women (Group II) as controls. **Results:** In preeclamptic group lipid peroxidation product malondialdehyde (MDA) (10.45 ± 5.65 v/s3.65 ± 0.72nmol/l) is significantly increased than in normotensive pregnant (control group). The serum superoxide dismutase activity (1.08 ± 0.36 v/s 2.70 ± 0.70 u/ml) is significantly decreased in preeclamptic group than in controls while uric acid level (5.82 ± 2.47 v/s 3.20 ± 0.65mg/dl) is significantly higher in cases preeclamptic women as compared to normal pregnant women. **Conclusion:** Increased malondialdehyde and decreased superoxide activity with higher uric acid level due to endothelial dysfunction are contributing for oxidative stress in preeclampsia.

Key Words: Preeclampsia, malondialdehyde (MDA), antioxidant, superoxide dismutase (SOD), uric acid.

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INTRODUCTION

Preeclampsia is most common pregnancy specific disorder and is the main cause of maternal and perinatal mortality and morbidity. Amongst all hypertensive disorders of pregnancy preeclampsia affects 5 - 10% of all pregnancies.[1-2] In spite in advances in treatment, there is no decline in rate of occurrence of preeclampsia.[3] Pregnancy is a physiological stress in which more biochemical changes occur in blood in normal pregnancy which get exaggerated in complications of pregnancy like preeclampsia.[4] Preeclampsia occurs in second or third trimester of pregnancy. Preeclampsia is defined according to the international society for the study of hypertension in pregnancy classification (ISSHP) as systolic blood pressure ≥ 140mmHg or diastolic blood pressure higher than 110mmHg on one occasion or ≥ 90mmHg on repeated measures accompanied by new onset proteinuria defined as ≥ 0.3 g/24h, or ≥ 1+ proteinuria on dipstick testing on repeated measures, after the 20th week of gestation.[5] Preeclampsia has been characterised as the disease of theories[(6)] Pregnancy induced hypertension is associated with endothelial dysfunction and the normal protective role of vascular endothelial layer becomes severely compromised[7-9]. Endothelial cells being target and source of free radicals which are constantly formed in vascular system. Reactive oxygen species (ROS) particularly superoxide anions evoke endothelial cell activation through multiple pathways.[10] Oxidative stress increases during preeclampsia and results in increased production of lipid peroxide products primarily measured as thiobarbituric acid reacting substances (which include malondialdehyde a major breakdown product of lipid peroxidation), reactive oxygen species and superoxide radicals to cause endothelial injury and dysfunction,

platelet and neutrophil activation.[11-12] These findings in preeclampsia attracted increased interest in antioxidants such as uric acid, Vit c, Vit e etc. In this context the present study is an attempt to determine changes in serum levels of lipid peroxide products malondialdehyde and antioxidants namely superoxide dismutase activity and uric acid levels in women with preeclampsia.

MATERIAL AND METHODS

Study population: In present study 40 cases of preeclampsia (Group I) and 40 healthy normotensive pregnant women (Group II) from Swami Ramanand Teerth Rural Government Medical College and Hospital Ambajogai, Dist. Beed were selected. Both cases and controls were primi between 18 - 30 years of age having more than 29 weeks of gestation. The study was performed under approval of ethics committee of SRTRGMCH Ambajogai and written informed consent was obtained from pregnant women under study. Clinical and ultrasonological evaluation were used to diagnose normal pregnant women and all of these presented a normal course of pregnancy. All subjects with any history of pregestational Diabetes Mellitus, gestational Diabetes Mellitus, hypertension, cardiovascular disease, renal and liver diseases as well as cases of fetal anomolies and maternal and/or fetal infection and history having multivitamin intake were excluded from the study. History and examination findings of both cases and controls were noted.

Sample collection: With all aseptic precautions fasting venous blood samples were collected in plain bulb which were centrifuged at 1000 rpm for 15 min for serum separation and samples were analysed immediately for following parameters.

Malondialdehyde (MDA): Malondialdehyde was estimated as thiobarbituric acid reacting substances (TBARS) by Kay Satoh method[12]. The samples were treated with thiobarbituric acid under hot acidic condition and pink colour formed was read at 532nm using spectrophotometer. The lipid peroxide concentration was expressed as nmol/ml.

Serum superoxide dismutase (SOD) activity: Superoxide dismutase activity in serum was measured by using method of Marklund and Marklund modified by Nandi *et al* which is based on inhibition of auto oxidation of pyrogallol in aqueous or alkaline medium and read at 430nm.[13] Fifty percent inhibition was defined as 1 unit of superoxide dismutase activity.

Serum Uric acid levels: The serum uric acid levels were measured by method of Caraways at 730nm using spectrophotometer.[14].

Statistical Analyses: Statistical analysis was carried out using standard statistical methods using statistical software. Data was expressed as mean ± standard deviation. Differences between mean were compared by Students t test whenever parameters presented a Guassian distribution. A p value lower than 0.05 (P <0.05) was considered statistically significant. Normality was assessed by Shapero Wilk Test.

RESULTS

Table 1: Blood pressures and BMI (Body mass index) of cases and controls

		Cases (n=40)	Controls (n=40)	P value
BP	SBP mmHg	154 ± 10.56	125 ± 7.81	P < 0.01
	DBP mmHg	97.73 ± 5.7	75.45 ± 3.25	P < 0.01
BMI (Kg/M^2)		26.83 ± 3.28	25.53 ± 3.08	P > 0.05

Values are mean ± S.D., Blood Pressure, SBP Systolic Blood Pressure, DBP Diastolic Blood Pressure, BMI Body mass Index

Blood pressures and BMI (Body mass Index) of cases and controls is shown in table 1.Values are mean ± S.D. The mean value of SBP (Systolic blood pressure) in cases is 154.67 ± 10.56 mmHg and in control is 125.3 ± 7.81 mmHg; there is significant difference (p,0.01) between cases and controls. The DBP (diastolic Blood Pressure) in cases and controls is 97.73 ± 5.7 mmHg and 75.45 ± 5.25 mmHg respectively. There is significant difference (p<0.01) between cases and controls. The mean BMI of controls is 25.53 ± 3.08 $kg/M^2$and in study group 26.83± 3.28 kg/M^2. p value is more than 0.05 which is not significant.

Table 2: The biochemical parameters to assess lipid peroxidation and antioxidant status of cases and controls

Parameter	Cases (n=40)	Controls (n=40)	P value
MDA (nmol/ml)	10.45 ± 5.65	3.65 ± 0.72	P < 0.001
Serum SOD (units /ml)	1.08 ± 0.36	2.70 ± 0.70	P < 0.001
Serum URIC acid (mg/dl)	5.82 ± 2.47	3.20 ± 0.65	P < 0.001

The biochemical parameters to assess lipid peroxidation and antioxidant status of cases and controls are shown in table 2. The mean MDA in cases and in controls is 10.45±5.65nmol/ml and 3.65±0.72nmol/ml respectively. The MDA is significantly increased in preeclampsia patients as compared to controls (p<0.001). The mean superoxide dismutase activity in cases and controls is 1.08 ± 0.36 u/ml and 2.70 ± 0.70 u/ml respectively which is significantly decreased in cases (p<0.001).The mean serum uric acid level in cases and controls is 5.82 ± 2.47mg/dl and 3.20 ± 0.65 mg/dl respectively which is significantly increased in cases (p<0,0001).

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DISCUSSION

Very little information is available about pathophysiology of preeclampsia. The clinical course of pregnancy induced hypertension is progressive and continuous. Delivery is the only treatment once disease has occurred. Detection of disease in early stages and appropriate management of such cases may improve outcomes of mothers and babies.[4] The genesis of preeclampsia has its roots in deficient trophoblast invasion and failure of uterine artery remodelling leading to placental hypoxia /ischaemia during early gestation. Placental hypoxia results in release of products into maternal circulation which initiates the maternal physiological changes in preeclampsia.[15-17] Recent studies suggest that PIH (pregnancy Induced Hypertension) is associated with endothelial dysfunction and normal protective role of the vascular endothelial layer becomes severy compromised.[11,18] This compromised fetoplacental unit may be the constant source of free radicals and other damaging reactive oxygen species such as superoxide anions.[19,20] Free radicals are the important pathological factors for preeclampsia. The antioxidants are used up to combat these free radicals. Insufficient antioxidants /antoxidant capacity leads to oxidative stress which is a mediator for endothelial dysfunction.[21-23] The present study shows that increase in serum levels of MDA ($p<0.001$) in preeclamptic patients when compared with normal pregnancy in agreement with previous reports which indicate increased lipid peroxidation products in women with preeclampsia as compared to normal pregnancy.[11,18,19,22,24] Malondialdehyde is one of the thiobarbituric acid reacting substances which is a biomarker of lipid peroxidation and its increased level in maternal circulation indicates the contribution of oxidative stress in the pathogenesis of preeclampsia.[23] Another important factor suggested to be responsible for the increased lipid peroxidation is an insufficiency in antioxidative defence.[11,27,31] In present study antioxidant defence is measured in terms of superoxide dismutase (SOD)activity in serum. In agreement with previous studies this study noted a significant decrease in serum superoxide dismutase activity in ($P<0.001$) preeclamptic pregnancies as compared to normal pregnancy. Several studies have demonstrated decreased serum levels of Superoxide dismutase activity in preeclamptic pregnancy as compared to normal pregnancy.[26-28] In preeclampsia there is increased consumption of antioxidants. SOD, natural free radical scavenger is first line defence against oxidative stress. The present study noted a significant rise in serum uric acid in preeclamptic women than in normotensive pregnancies in agreement with previous studies.[4] Uric acid is water soluble weak antioxidant present in plasma. Hyperuricemia in preeclampsia is ineffective to protect against free radical activity and placental dysfunction[18,19,31] The aetiology for hyperuricemia is multifactorial which has contribution from renal diminution of uric acid clearance and oxidative stress.[29] There is increased production of uric acid at hypoxic placenta and at hypoxic fetal tissues which enters in maternal circulation.[26] The rise in uric acid impairs nitric oxide generation in endothelial cells and can induce endothelial dysfunction.[30]

CONCLUSION

In conclusion our study supports the lipid peroxidation is important to understand pathophysiology of preeclampsia. Antioxidants by their quinching ability to absorb free radical generated energy act as homeostatic buffer to control lipid peroxidation resulting in reduction in plasma antioxidant levels. Increased malondialdehyde levels and decreased serum superoxide dismutase activity with higher uric acid level due to endothelial dysfunction are contributing for oxidative stress in preeclampsia.

Compliance with ethical standards

Ethical approval: All procedures performed in studies involving human participants were in accordance with ethical standards of institutional and national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent: Informed written consent was obtained from all individual participants included in the study.

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