

## Appraisal of Oxidative Stress Markers, Vitamin E and their Correlation with Blood Pressure in Preeclampsia: A Case Control Study

N. Asha Rani<sup>1,\*</sup>, J N Naidu<sup>2</sup>

<sup>1</sup>Assistant Professor, Adichunchanagiri Institute of Medical Sciences, B. G. Nagara, Karnataka

<sup>2</sup>Professor and HOD, Dept. of Biochemistry, Narayana Medical College, Andhra Pradesh.

**\*Corresponding Author:**

E-mail: ashanellore@gmail.com

### Abstract

**Background and Objectives:** Preeclampsia (PE), a hypertensive disorder unique to pregnancy and contributes to majority of maternal and perinatal morbidity and mortality. The triggering event in preeclampsia is postulated to be placental ischemia and endothelial dysfunction. In this context the present study was undertaken to investigate serum levels of nitric oxide, thiobarbituric acid reacting substances (TBARS) and Vitamin E (Vit E) and their correlation with blood pressure in preeclamptic pregnant women.

**Methods:** Fifty clinically diagnosed preeclampsia patient and fifty age and trimester matched normotensive pregnant women were included in the study. Fasting venous sample were collected and nitric oxide, TBARS and vitamin E levels were measured.

**Results and Interpretation:** The mean values of serum nitric oxide, TBARS were significantly higher ( $< 0.001$ ) in women with preeclampsia when compared to normotensive group whereas vitamin E levels were significantly lower among cases than the control group. Also observed that nitric oxide levels and TBARS positively correlated and vitamin E negatively correlated with the blood pressure and correlations were statistically significant.

**Conclusions:** The findings of present study points increased oxidative stress and decreased antioxidant levels may result in endothelial cell dysfunction. The levels of nitric oxide, TBARS and vitamin E could be used to assess the severity of preeclampsia in addition to other clinical and laboratory parameters.

**Key words:** Preeclampsia, oxidative stress, nitric oxide, vitamin E, blood pressure

| Access this article online  |   |
|---|---|
| Quick Response Code:  | Website:<br>www.innovativepublication.com |
|  | DOI:<br>10.5958/2394-6377.2016.00003.4    |

### Introduction

Preeclampsia (PE), a multifactorial hypertensive disorder unique to pregnancy and is the major contributor of maternal and perinatal morbidity and mortality. It is characterized by hypertension and proteinuria with or without edema seen after 20 weeks of gestation. The exact pathophysiology of maternal changes seen during preeclampsia is not clear. But many research observations point that there is increased oxidative stress with imbalance in antioxidant status<sup>1</sup> and endothelial cell dysfunction<sup>2</sup>.

Nitric oxide (NO) is a potent vasodilator and a free radical synthesized from L- arginine by the action of endothelial nitric oxide synthase (eNOS) enzyme. Placental ischemia seen in preeclampsia initiates generation of free radicals and NO being highly susceptible to oxidative damage reacts with free radicals and results in wide spread endothelial damage<sup>3</sup>. Antioxidant vitamins act as free radical scavengers and protect tissues/ cells from lipid peroxidation. Many studies have reported that regulation of blood pressure

as one of the important functions of antioxidant vitamins<sup>3</sup>.

Evidences pertaining to NO production in preeclampsia has been in conflicts with observations of reduced<sup>4</sup>, increased<sup>5,6</sup> and or no change<sup>7</sup> in NO metabolites in circulation and also there is sparse information regarding role of antioxidant vitamins in preeclampsia.

To address these controversies, the present study was undertaken which aimed to investigate serum concentrations of NO, thiobarbituric acid reacting substances (TBARS) and Vitamin E (Vit E) and their correlation with blood pressure in preeclamptic pregnant women.

### Material and Methods

The present study was carried out in the tertiary care hospital, Nellore. Informed consent was taken from all the participants after getting ethical clearance from the Institutional Ethical Committee. A non-probability convenient sampling technique was done. A total of 100 pregnant women were recruited for the study, who attended the antenatal OPD or admitted at the tertiary care hospital, Nellore. The study group included controls = normotensive pregnant women (n=50) and cases = pregnant women with preeclampsia (n=50). The control group had systolic / diastolic blood pressure below 120/80 mm of Hg and no history of proteinuria or hypertension. The case group had blood pressure of  $\geq 140/90$  mm of Hg measured on at least

two occasions 6hour apart during 24 hour period and proteinuria of  $\geq 0.3$  g/day. Pregnant women with previous history of hypertension, diabetes, renal disorder, smoking, cardiovascular diseases, pregnant women not willing and on antioxidant vitamin therapy were excluded from the study. After recruiting into the study, 5ml venous blood was drawn from all the participants for estimation of TBARS by TBA method<sup>8</sup> as a marker of lipid peroxidation, serum Vit E, an antioxidant vitamin measured by HPLC method and serum nitrate and nitrite levels as NO is an unstable molecule by Griess method<sup>9</sup> as an index of endothelial damage.

### Statistical analysis

The data are expressed as mean  $\pm$  SD. Student 't' was employed for mean comparison of the groups. Pearson's correlation analysis was used to observe correlation between NO, TBARS and vitamin E with systolic and diastolic blood pressure in women with preeclampsia. The results were accepted to be statistically significant when p value was less than 0.05.

### Results

Of the 100 women participated, 50 were in normotensive group and 50 were in preeclampsia group. The groups were comparable with regard to maternal age and gestational week.

Mean maternal age, systolic and diastolic blood pressure, serum levels of nitric oxide, TBARS and vitamin E of all the participants are demonstrated in Table 1.

The mean values of serum NO, TBARS were significantly higher in women with preeclampsia when compared to normotensive group whereas vitamin E levels were significantly lower among cases than the control group.

Both nitric oxide and TBARS showed statistically significant positive correlation with systolic and diastolic blood pressure. The scatter plot (fig. 1 to 3) shows the correlation of vitamin E with systolic, diastolic blood pressure and TBARS respectively. There exists a negative correlation between Vitamin E and systolic blood pressure ( $r = -0.01$ ,  $p > 0.05$ ), diastolic blood pressure ( $r = -0.11$ ,  $p > 0.05$ ) and TBARS ( $r = -0.27$ ,  $p < 0.05$ ) but the relationship between the variables is only weak, which may be due to the small sample size.

**Table 1: Showing Clinical data of study groups**

|                      | <b>Cases (n= 50)<br/>Mean <math>\pm</math> SD</b> | <b>Controls (n= 50)<br/>Mean <math>\pm</math> SD</b> | <b>p value</b>   |
|----------------------|---|--|------------------|
| Maternal Age (Yr)    | 22.98 $\pm$ 3.46                                  | 22.12 $\pm$ 2.71                                     | = <b>0.1656</b>  |
| SBP (mmHg)           | 156.6 $\pm$ 20.36                                 | 113 $\pm$ 6.46                                       | < <b>0.0001*</b> |
| DBP (mmHg)           | 102.6 $\pm$ 10.06                                 | 73.8 $\pm$ 6.66                                      | < <b>0.0001*</b> |
| TBARS ( $\mu$ mol/L) | 6.68 $\pm$ 2.90                                   | 2.97 $\pm$ 0.98                                      | < <b>0.001*</b>  |
| NO ( $\mu$ mol/L)    | 160 $\pm$ 74.2                                    | 69 $\pm$ 31.76                                       | < <b>0.001*</b>  |
| Vit E (mg/dL)        | 1.20 $\pm$ 0.41                                   | 1.96 $\pm$ 0.24                                      | < <b>0.001</b>   |

\*statistically significant

**Table 2: Showing correlation analysis of Blood Pressure with NO and TBARS in Preeclampsia group**

| <b>Correlation parameter</b> | <b>r value</b> | <b>p value</b> |
|------------------------------|----------------|----------------|
| Systolic BP and NO           | 0.68           | 0.000*         |
| Systolic BP and TBARS        | 0.57           | 0.000*         |
| Diastolic BP and NO          | 0.51           | 0.000*         |
| Diastolic BP and TBARS       | 0.35           | 0.006*         |

\*statistically significant

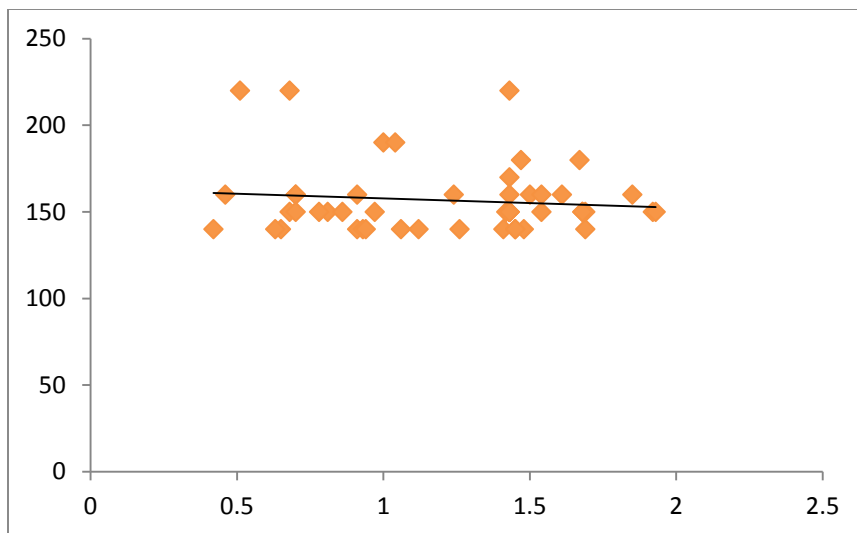


Fig. 1: Scatter plot of vitamin E vs Systolic BP

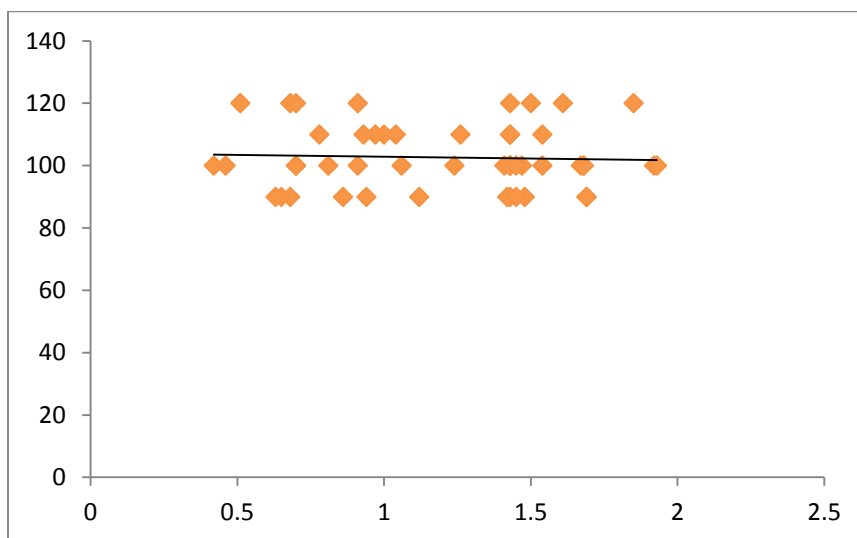


Fig. 2: Scatter plot of Vitamin E vs Diastolic BP

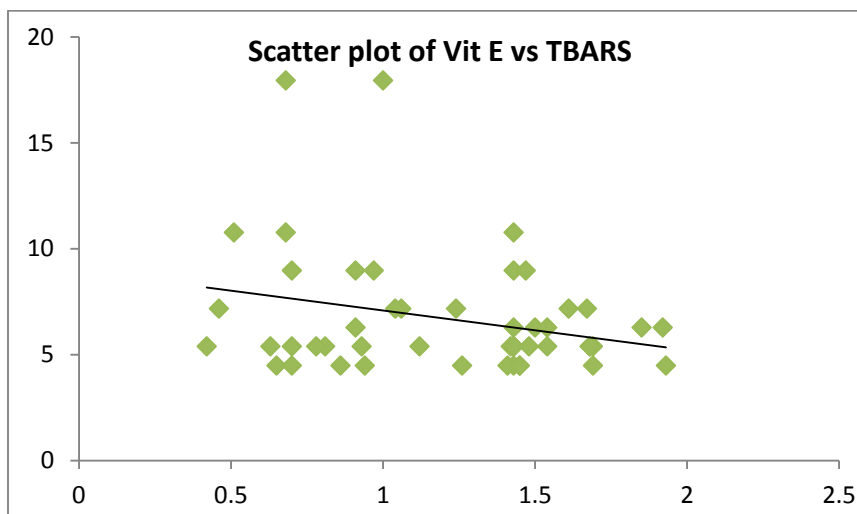


Fig. 3: Scatter plot of Vitamin E vs TBARS

## Discussion

Preeclampsia is a multi-organ disorder unique to pregnancy with a prevalence of 55.6% nationwide<sup>10</sup> with similar prevalence in rural and urban population.

It is been postulated that, in PE endothelial dysfunction is the key component<sup>11</sup> with inadequate trophoblastic invasion of the decidual vessels causing placental ischemia. To overcome these adverse placental effects there will be altered production of NO levels<sup>5,12</sup>. Some study<sup>7</sup> have showed no difference in means of total NO levels but significantly higher level of nitrites in preeclampsia when compared to normotensive pregnant women but failed to demonstrate correlation between total NO, nitrate and nitrite values with severity of preeclampsia. Another study<sup>4</sup> demonstrated increased nitrate levels in second trimester of pregnancy but decreased in third trimester of pregnancy in PE as compared to normal pregnancy.

The findings of current study shows increased NO levels in PE group as compared to normotensive pregnant women, which may be an adaptive mechanism to overcome the placental changes seen during preeclampsia. There is also a positive correlation with blood pressure signifying that NO production increases with severity of the disease.

Many authors have reported increase in lipid peroxidation products in Preeclampsia<sup>12,13</sup>. The results of the present study also revealed increased formation of lipid peroxidation product, MDA commonly measured by thiobarbituric acid reaction in cases when compared to controls. The above findings support the notion that lipid peroxidation plays an important role in the pathogenesis of preeclampsia.

Vitamin E, a naturally occurring lipid soluble chain breaking antioxidant helps in buffering the deleterious effects of free radicals there by reducing the oxidative stress and damage. Many studies have examined the association of vitamin E levels with pregnancy and its outcome such as fetal growth<sup>14</sup> and also blood pressure<sup>15</sup> and have shown that vitamins are important for fetal growth and to control blood pressure. Vitamin E prevents oxidation of nitric oxide by eliminating free radicals from circulation and thus helps in maintaining the vasodilator status of the blood vessel<sup>16</sup>. One more study<sup>15</sup> reported decreased Vitamin E levels in severe PE but unaltered in mild PE. The present study reports decreased serum Vit E levels in PE and also showed negative correlation with lipid peroxidation products which supports the evidence that increased oxidative stress and decreased antioxidant levels favor the risk for the development of preeclampsia. The decreased serum vitamin E levels in preeclampsia could be attributed to the increased blood pressure seen in preeclampsia which demands an increased amount of vitamin E to neutralize the deleterious effects of oxidative stress caused by the oxidation of nitric oxide.

In conclusion, the findings of the present study suggest that an abnormal lipid peroxides and nitric

oxide along with decreased vitamin E levels, promotes oxidative stress and gives an immense value in understanding the pathogenesis of preeclampsia. Evaluating for the above parameters in early pregnancy would help in early detection and prevention of both maternal and fetal complications seen in preeclampsia.

**Limitation of the study:** Small sample size and no categorization of preeclampsia depending on blood pressure were done and also the study participants included pregnant women of all parity.

## Acknowledgment

I am thankful to all the pregnant women who participated in the study and laboratory in-charge Dr Ramalingam, who helped in conduction of this study.

**Conflict of Interest: None**

**Source of Support: Nil**

## References

1. P Phalak, J Kulkarni, M Tilak, A.P. Thorat. Role of lipid peroxidation and antioxidant status in pathogenesis of Pre-eclampsia. *Indian Journal of Basic & Applied Medical Research*.2013;6(2):536-9.
2. LM Dusse et al. Is there a link between endothelial dysfunction, coagulation activation and nitric oxide synthesis in preeclampsia? *Clinica Chimica Acta*.2013;415:226–9.
3. K Dakshinamurti and S Dakshinamurti. Blood pressure regulation and micronutrients. *Nutrition Research Reviews*. 2001;14:3–43.
4. R Gupta, K. N. Maruthy, A M. Mhaskar, LD Padmanabhan. Serum Nitrate Levels as an Index of Endothelial Function in Pre-Eclampsia and Normal Pregnancy. *Indian J Physiol Pharmacol*.2003;47(2):185–190.
5. U. von Mandach, D. Lauth and R. Huch. Maternal and fetal nitric oxide production in normal and abnormal pregnancy. *The Journal of Maternal–Fetal and Neonatal Medicine*.2003;13:22–7.
6. Hatice P, Gulsen B, Elmas O, Aysel P, Gogsen O. Nitric Oxide, Lipid Peroxide, and Uric Acid Levels in Pre-Eclampsia and Eclampsia. *Tohoku J Exp Med* 2004;202:87-92.
7. Ebru Erdemoğlu, Mustafa Uğur, Evrim Erdemoğlu. Plasma homocysteine and nitric oxide levels in preeclampsia. *J Turkish-German Gynecol Assoc* 2009;10:26-9.
8. Satoh KE. Lipid peroxide in cerebrovascular disorder determined by a new colorimetric method. *Clin Chem Acta*.1978;90:37-43.
9. Curtis NE, Gudi NM, King RG, Marriott PJ, Rook TJ, Brennecke SP. Nitric oxide metabolites in normal human pregnancy and preeclampsia. *Hypertens Pregnancy*.1995;14:339-49.
10. International Institute for Population Sciences, Macro International (2007) National Family Health Survey (NFHS-3), 2005–06: India: Vol. I. Mumbai, IIPS.
11. Roberts JM, Roberts NT, Musci JT, Rodgers GM, Hubel CA, Mc Langhlin MK. Preeclampsia: an endothelial cell disorder. *AM J Obstet Gynecol* 1989;161:1200-04.

12. Trivedi DJ, Trivedi CD, Sagre A. Oxidant and antioxidant imbalance as root cause in preeclampsia. *Transworld Medical Journal*. 1(2):33-6.
13. Khatri M. Circulating biomarkers of oxidative stress in normal pregnancy and preeclampsia and efficacy of antioxidant supplementation. *Int J Reprod Contracept Obstet Gynecol*. 2013;2(3):304-10.
14. Theresa O Scholl, Xinhua Chen, Melissa Sims, and T Peter Stein. Vitamin E: maternal concentrations are associated with fetal growth<sup>1-3</sup>. *Am J Clin Nutr*.2006;84:1442– 8.
15. F.F. Yanik et al. Pre-eclampsia and eclampsia associated with increased lipid peroxidation and decreased serum vitamin E levels. *International Journal of Gynecology & Obstetrics*. 1999;(64):27-33.
16. S N Islam, T Ahsan, S Khatun, Md N I Khan & M Ahsan. Serum Vitamin E, C and A Status in Pre-Eclampsia and Eclampsia Patients, and Their Correlation with Blood Pressure: a Study in Dhaka, Bangladesh. *Mal J Nutr*.2004;10(2):207-14.