International Journal of Reproduction, Contraception, Obstetrics and Gynecology
Yanglem AS et al. Int J Reprod Contracept Obstet Gynecol. 2023 Nov;12(11):3294-3298
www.ijrcog.org
pISSN 2320-1770 | eISSN 2320-1789

DOI: https://dx.doi.org/10.18203/2320-1770.ijrcog20233297

Original Research Article

Serum malondialdehyde and serum glutathione peroxidase levels in pregnant women with and without preeclampsia

Ajitkumar S. Yanglem[1], Niren S. Koch[2], Sangeeta Naorem[3], Roshita D. Kshetrimayum[3]*, Guiphiuliu Kamei[3], Bidya Nongmaithem[3], Reshmi Okram[3]

[1]Department of Obstetrics and Gynecology, Regional Institute of Medical Sciences, Imphal, Manipur, India
[2]Department of Biochemistry, Zoram Medical College, Aizawl, Mizoram, India
[3]Department of Biochemistry, Regional Institute of Medical Sciences, Imphal, Manipur, India

Received: 28 August 2023
Accepted: 29 September 2023

***Correspondence:**
Dr. Roshita D. Kshetrimayum,
E-mail: kshetriroshita@gmail.com

ABSTRACT

Background: Preeclampsia is a pregnancy-specific disorder that affects 10% of all pregnancies which contributes heavily to maternal mortality and perinatal morbidity. Several studies have shown that oxidative stress plays an important role in the pathogenesis of preeclampsia. However, the association has not been proven indisputably. So, the study was done with the view to determine serum malondialdehyde and glutathione peroxidase levels in pregnant women with and without preeclampsia and to compare the levels between the two groups of participants.
Methods: This is a cross-sectional study conducted in the Department of Biochemistry and Department of Obstetrics and Gynaecology, RIMS. 55 preeclamptic patients and 55 pregnant women without preeclampsia were recruited as cases and controls respectively.
Results: Serum malondialdehyde was found to be significantly higher in cases (1280.02±619.55ng/ml) than the controls (826.51±599.84ng/ml) and glutathione peroxidase levels were found to be significantly decreased in the preeclamptic women (224.49±201.29pg/ml) when compared to the normal healthy pregnant women (448±350.54 pg/ml. Serum malondialdehyde levels were found to be positively correlated with blood pressure.
Conclusions: Serum malondialdehyde was increased in preeclampsia and serum glutathione levels was decreased in preeclamptic pregnant women when compared to the pregnant women without preeclampsia. Serum malondialdehyde levels were significantly correlated with high blood pressure. The oxidant-antioxidant system may be involved in the etiology of preeclampsia, however the cause and effect relation needs further evaluation.

Keywords: Antioxidants, Blood pressure, Pregnancy

INTRODUCTION

Preeclampsia (PE) is a pregnancy-specific disorder which can be defined as the new onset of hypertension and significant proteinuria in a previously normotensive women on or after 20th week of gestation with or without pathological edema.[1,2] Hypertension in preeclampsia is characterized by a systolic blood pressure of 140mmHg or more and diastolic pressure of 90mmHg or more, at least on two measurements within 6 hr or more.[3,4] It may be associated with complications like visual disturbances, oliguria, eclampsia, hemolysis, elevated liver enzymes, thrombocytopenia, pulmonary edema and fetal growth restriction.[5]

It is estimated that preeclampsia is a leading cause of death among all maternal deaths and contributes heavily to maternal and perinatal morbidity.[6] It affects approximately 5-10% of pregnancies worldwide.[7] Developing countries

are more adversely affected as 20-80% of increased maternal mortality is associated with preeclampsia while in developed countries it has contributed to 15% of preterm births.[8] In India, the incidence of preeclampsia is reported to be 15.2% of total pregnancies.[9]

The main treatment of preeclampsia is the termination of the pregnancy. So early diagnosis of women at high risk of preeclampsia are key issues in the management of preeclampsia. Despite several studies on preeclampsia, its exact etiology remains poorly understood. However, placental defects and oxidative stress have been implicated and was observed to develop early in pregnancies affected by the disease.[10,11] Oxidative stress, characterized by excessive production of reactive oxygen species, and an inadequate or overwhelmed antioxidant defense mechanisms have been proposed as an important mechanism in preeclampsia[12,13]

Malondialdehyde (MDA) is an important biomarker for cellular damage and lipid peroxidation of cell membranes.[14] Increased plasma malondialdehyde (MDA) has been reported to increase in preeclamptic women compared with healthy pregnant women.[15] Glutathione peroxidases (GPX) is an antioxidant enzyme that plays an important role in counteracting free radical disturbances and thereby protect cell membranes against free radical mediated lipid peroxidation.[16] Therefore, measurement of markers of oxidant stress may be useful in the prediction of preeclampsia. Many studies found significant increase in levels of malondialdehyde in pregnant women with preeclampsia.

However, some studies showed no significant differences in the levels of serum malondialdehyde between healthy pregnant and preeclamptic women. Similarly, many studies found glutathione peroxidase levels to be either increased or decreased in preeclamptic women as compared to the healthy pregnant women.

This study will help determine a baseline level of biomarkers for oxidative stress among pregnant women with preeclampsia in the study area and thus, may contribute to the existing body of knowledge on the role of oxidative stress in the pathogenesis of preeclampsia. The aim of the study was to determine serum malondialdehyde (MDA) and serum glutathione peroxidase (GPX) levels in pregnant women with and without preeclampsia and compare the levels between them.

METHODS

This is a hospital-based comparative cross-sectional study conducted in the Department of Biochemistry and the Department of Obstetrics and Gynaecology, Regional Institute of Medical Sciences, Manipur, from February 2021 to October 2022. Ethical clearance was sought from the Research Ethical Board RIMS, Imphal. Altogether 110 pregnant women above 18 years of age participated in the study; 55 pregnant women with preeclampsia were taken as cases and 55 pregnant women without preeclampsia as controls. Convenient sampling was used in the study. Pregnant women with pre-existing hypertension, multiple pregnancy, gestational diabetes mellitus, renal disease, thyroid dysfunction, smokers, alcohol consumers and neoplastic disease were excluded from the study. Informed written consent was obtained from all the participants. serum MDA and serum GPX levels were measured by ELISA, Elabscience Biotechnology Inc., USA. All the data were analysed using SPSS Ver.21. Qualitative data was expressed as frequency and percentage and quantitative data was presented as mean and SD. Analysis was done using independent t test. Pearson correlation coefficient was used to find correlation between oxidative stress markers and blood pressure. P-value of less than 0.05 was taken statistically significant.

RESULTS

The difference in the mean ±SD of age for cases and controls was statistically insignificant (p-value =0.119). The mean ±SD of body mass index (BMI) in cases were found to be higher than the controls. The difference was found to be statistically significant (p-value =0.024). The mean ±SD of systolic blood pressure (SBP) and diastolic blood pressure (DBP) were higher in cases when compared to the controls. The difference were found to be statistically significant (p-value =0.000) (Table 1).

Table 1: Baseline characteristics of cases and controls (n=110).

Parameters	Cases (n=55)	Controls (n=55)	p-value
Age (years)	29.62±5.35	27.98±5.58	0.119
Body mass index (BMI) kg/m^2	27.48±2.53	26.48±2.04	0.024
SBP (mmHg)	162.02±15.32	117.64±8.78	0.000
DBP (mmHg)	104.69±10.51	75.89±5.74	0.000

Table 2: Comparison of serum malondialdehyde (MDA) levels, serum glutathione peroxidase (GPX) levels between cases and controls.

Parameter	Cases (Mean±SD)	Controls (Mean±SD)	p-values
Serum malondialdehyde (MDA) (ng/ml)	1280.02±619.55	826.51±599.84	0.000
Serum glutathione peroxidase (GPX) (pg/ml)	224.49±201.29	448.35±350.54	0.000

The mean ±SD of serum malondialdehyde (MDA) were significantly higher in cases when compared to the controls (p-value=0.000). The levels of glutathione peroxidase were significantly reduced in cases when compared to the controls (Table 2).

Serum malondialdehyde was found to be positively correlated with SBP and DBP and the findings were statistically significant with p- value <0 (Table 3).

Table 3: Correlation between serum malondialdehyde and blood pressure among cases.

Parameter	Pearson correlation (r)	p-value
SBP	0.323*	0.016
DBP	0.336*	0.012

*Correlation is significant at the 0.01 level (2-tailed)

Pearson correlation coefficient 'r' for serum glutathione peroxidase was found to be negatively correlated with the blood pressure (Table 4).

Table 4: Correlation between serum glutathione peroxidase and blood pressure parameters among cases.

Parameters	Pearson correlation (r)	p-value
SBP	-0.055	0.692
DBP	-0.038	0.786

DISCUSSION

In the present study a total of 110 pregnant women, 55 preeclamptic cases and 55 normal pregnant women admitted in Antenatal Ward, RIMS were recruited. It is observed from Table 1 that the mean±SD of age in preeclamptic women and non-preeclamptic women were 29.62±5.35 years and 27.98±5.58 years respectively. The difference was statistically insignificant (p-value =0.119) which showed that the study groups were comparable with respect to age. BMI, SBP and DBP were found to be significantly higher in the cases than the controls. The mean BMI of cases was found to be 27.48±2.53 kg/m^2 whereas mean BMI of the controls was 26.48±2.04 kg/m^2 and the difference was statistically significant (p<0.05). The mean±SD of systolic blood pressure in cases and control were found to be 162.02±15.32 mmHg and 117.64±8.78 mmHg respectively. The mean±SD of diastolic blood pressure in cases and control were found to be 104.69±10.51 mmHg and 75.89±5.74 mmHg respectively. A study by Tabassum et al among Riyadh population had shown that BMI, SBP and DBP were higher in preeclamptic women when compared to controls group and the mean values were 167.0mmHg, 98.51mmHg and 35.12kg/m^2 respectively in the case group.[17]

The mean±SD of serum malondialdehyde level among cases was 1280.02±619.55ng/ml whereas it was found to be 826.51 ±599.84ng/ml among the controls, as shown in Table 2. The findings were supported by the results of the study by Siddiqui et al who found out in their study that the mean value of serum malondialdehyde in preeclamptic women was 1531±663ng/ml which was significantly higher than the normotensive women i.e. 1067.45±346.2ng/ml.[18] The exact pathophysiology of preeclampsia is not known, but it has been established that placenta plays a major role, contributing to abnormal placentation and reduction in placental perfusion. Abnormal invasion of cytotrophoblast cells into the spiral arteries is the main pathophysiology in preeclampsia.[19,20] Shallow trophoblastic invasion of the decidual arteries result in a high resistance, low-flow uteroplacental circulation pattern, and subsequent placental ischaemia and hypoxia.[21] Poor placental perfusion may lead to placental ischaemia which in turn will initiate a cascade of events culminating in loss of placental cellular function and integrity, and synthesis of humoral stimuli which provoke maternal inflammatory response and vascular endothelial cell activation, characteristic of preeclampsia.[22] The ischaemic placenta releases free radicals which lead to increased lipid peroxidation resulting in excessive increase in MDA levels. According to Hubal et al, free radicals initiate lipid peroxidation by attacking polyunsaturated fatty acids in cell membranes.[23] Peroxidation of fatty acids and cholesterol associated with the cell membrane can alter the fluidity and permeability and consequently, damage the membrane. MDA is the product of lipid peroxidation of cell membrane during increased oxidative stress condition.[24,25] MDA can be formed either as a product of lipid peroxidation or as by-product of platelet cyclooxygenase turnover, resulting in production of vasoconstrictive eicosanoid thromboxane.[26] MDA level might be a causative factor for pathogenesis of preeclampsia.

It is evident from Table 2 that the levels of glutathione peroxidase were found to be significantly decreased in the preeclamptic women (224.49±201.29pg/ml) when compared to the normal healthy pregnant women (448±350.54 pg/ml). Similar findings were observed in a study conducted by Chamy et al where they found a marked reduction in antioxidant enzyme glutathione peroxidase and it was associated with increased risk and severity of preeclampsia.[27] Glutathione and glutathione-related enzymes, are one of the major defense systems and free radical scavenger which play an important role in controlling oxidative stress.[28] The increase in oxidative stress might not be so important if there was a compensatory increase in antioxidant protection but the opposite occurred. Glutathione peroxidase is one of the primary antioxidants that is present in tissues and helps in combatting the lipid peroxides.[29,30] Glutathione peroxidase uses glutathione as its co-factor to convert lipid peroxidation into relatively harmless hydroxylated fatty acids, water and glutathione disulphide.[31] Disturbances that cause excess free-radical production are typically accompanied by increased consumption of antioxidants, which leads to decreased antioxidant concentrations in blood.[32]

Several studies have suggested that lipid peroxides and increased oxidative stress due to reactive oxygen species play a significant role in the pathogenesis of preeclampsia. It is evident from Table 3 that MDA levels in preeclamptic women were positively correlated with both SBP and DBP and the findings were significant with $p<0.05$. A study by Omar et al also found a positive correlation between MDA level and SBP ($r=0.693$, $p<0.001$) and DBP ($r=0.467$, $p<0.001$).[33] Valko et al opined that oxidative stress have been implicated to play a major role in pathogenesis of several vascular disorders, such as hypertension, diabetes and atherosclerosis.[34]

The endogenous antioxidant glutathione peroxidase showed negative correlation with SBP and DBP although the findings were not statistically significant (Table 4). A study conducted by Madazli et al found that GPX decreased significantly with increments in diastolic pressure.[19] Therefore, vascular endothelial cell dysfunction in preeclampsia may be caused by uncontrolled lipid peroxidation which overwhelms the protective mechanisms of the antioxidants.

CONCLUSION

The study shows that the levels of lipid peroxidation product serum malondialdehyde was found to be significantly higher in preeclamptic women compared to pregnant women without preeclampsia. Serum glutathione peroxidase levels were found to be significantly decreased in preeclamptic women when compared to the pregnant women without preeclampsia. Serum malondialdehyde was found to be positively correlated with SBP, DBP, and the correlation were found to be significant. However, serum glutathione peroxidase was found to be negatively correlated with blood pressure but the findings were not significant.

Our study thas some limitations that should be acknowledged. Being a cross-sectional study, the causal and effect relationship between serum malondialdehyde, serum glutathione peroxidase and preeclampsia could not be determined. Secondly, being a hospital-based study with small sample size, the findings may not be representative of the true burden of the disease in the community. More robust prospective cohort studies could shed light on the role of oxidative stress markers in the pathophysiology, prevention and treatment of preeclampsia. It may be concluded that detection of oxidative markers in time and supplementation with antioxidants may be protective against the development of preeclampsia in pregnant women.

ACKNOWLEDGMENTS

Authors would like to thank the Department of Biochemistry and Department of Obstetrics and Gynaecology, Regional Institute of Medical Sciences, Imphal, India for their support. The authors would like to thank all participants for their active participation in the study.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Research Ethical Board, RIMS, Imphal

REFERENCES

1. Adiga U, D'souza V, Kamath A, Mangalore N. Antioxidant activity and lipid peroxidation in preeclampsia. J Chin Med Assoc. 2007;70(10):435
2. Genc H, Uzun H, Benian A, Simsek G, Gelisgen R, Madazli R, et al. Evaluation of oxidative stress markers in first trimester for assessment of preeclampsia risk. Arch Gynecol Obstet. 2011;284(6):1367-73.
3. Jia RZ, Liu XM, Wang X, Wu HQ. Relationship between cardiovascular function and fetal growth restriction in women with pre-eclampsia. Int J Gynaecol Obstet. 2010 ;110(1):61-3.
4. Melchiorre K, Sutherland GR, Liberati M, Thilaganathan B. Preeclampsia is associated with persistent postpartum cardiovascular impairment. Hypertension. 2011;58(4):709-15.
5. Cunningham FG, Leveno KJ, Bloom SL, Hauth JC, Gilstrap LC III, Westrom KD. Williams Obstetrics. 22nd ed. New York: McGraw-Hill;2005:761-808.
6. Poston L. Endothelial dysfunction in pre-eclampsia. Pharmacological reports. 2006;58:69.
7. Sarsam DS, Shamden M, Al Wazan R. Expectant versus aggressive management in severe preeclampsia remote from term. Singapore Med J. 2008;49(9):698.
8. Roberts JM, Lain KY. Recent insights into the pathogenesis of pre-eclampsia. Placenta. 2002;23(5):359-72.
9. Dutta DC. Text book of obstetrics. 3rd ed. New Central Book Agency (P) Ltd.Calcutta; 1995:230-6.
10. Hansson SR, Naav A, Erlandsson L. Oxidative stress in preeclampsia and the role of free fetal hemoglobin. Front Physiol. 2015;5:516.
11. Redman CW, Sargent IL. The pathogenesis of Preeclampsia. Gynecol Obstet Fertil. 2001;29:518-22.
12. Roberts JM, Hubel CA. Is oxidative stress the link in the two-stage model of pre-eclampsia?. The Lancet. 1999;354(9181):788-9.
13. Mistry HD, Kurlak LO, Williams PJ, Ramsay MM, Symonds ME, Pipkin FB. Differential expression and distribution of placental glutathione peroxidases 1, 3 and 4 in normal and preeclamptic pregnancy. Placenta. 2010;31(5):401-8.
14. Silva DM, Marreiro DD, Moita Neto JM, Brito JA, Neta EA, Matias JP et al. Oxidative stress and immunological alteration in women with preeclampsia. Hypert Pregn. 2013;32(3):304-11.
15. Jain SK, Wise R. Relationship between elevated lipid peroxides, vitamin E deficiency and hypertension in preeclampsia. Mol Cel Biochem. 1995;151(1):33-8.

16. Madazli RI, Benian A, Aydin S, Uzun H, Tolun N. The plasma and placental levels of malondialdehyde, glutathione and superoxide dismutase in pre-eclampsia. J Obstet Gynaecol. 2002;22(5):477-80.
17. Tabassum H, Al-Jameil N, Ali MN, Khan FA, Al-Rashed M. Status of serum electrolytes in preeclamptic pregnant women of Riyadh, Saudi Arabia. Biomed Res. 2015;26(2):219-24.
18. Siddiqui IA, Jaleel A, Al'Kadri HM, Akram S, Tamimi W. Biomarkers of oxidative stress in women with pre-eclampsia. Biomark Med. 2013;7(2):229-34
19. Genbacev O, DiFederico E, McMaster M, Fisher SJ. Invasive cytotrophoblast apoptosis in pre-eclampsia. Human Reproduction. 1999;14(suppl_2):59-66.
20. Fisher SJ, McMaster M, Roberts JM. The placenta in normal pregnancy and preeclampsia. InChesley's hypertensive disorders in pregnancy. Academic Press; 2015:81-112.
21. Roberts JM, Redman CW. Pre-eclampsia: more than pregnancy-induced hypertension. Lancet. 1993;341(8858):1447-51.
22. Dumollard R, Carroll J, Duchen MR, Campbell K, Swann K. Mitochondrial function and redox state in mammalian embryos. InSeminars in cell & developmental biology. 2009;20(3):346-53.
23. Hubel CA, Roberts JM, Taylor RN, Musci TJ, Rogers GM, McLaughlin MK. Lipid peroxidation in pregnancy: new perspectives on preeclampsia. Am J Obstet Gynecol. 1989;161(4):1025-34.
24. Schrier RW, Shapiro JI, Chan L, Harris DC. Increased nephron oxygen consumption: potential role in progression of chronic renal disease. Ame J Kidn Di. 1994;23(2):176-82.
25. Balal M, Canacankatan N, Paydas S, Seyrek N, Karayaylali I, Kayrın L. Oxidative-antioxidative system in peripartum acute renal failure and preeclampsia-eclampsia. Renal Failure. 2004;26(6):625-32.
26. Raijmakers MT, Zusterzeel PL, Roes EM, Steegers EA, Mulder TP, Peters WH. Oxidized and free whole blood thiols in preeclampsia. Obstet Gynecol. 2001;97(2):272-6.
27. Chamy VM, Lepe J, Catalán Á, Retamal D, Escobar JA, Madrid EM. Oxidative stress is closely related to clinical severity of pre-eclampsia. Biolog Res. 2006;39(2):229-36.
28. Dewantiningrum J, Hafiz A. The role of glutathione peroxidase maternal serum level in late onset of severe preeclampsia. Hypert Pregn. 2016;35(4):483-9.
29. Levander OA. Selenium and sulfur in antioxidant protective systems: relationships with vitamin E and malaria. Proceedings Soci Experim Biol Med. 1992;200(2):255-9.
30. Krinsky NI. Mechanism of action of biological antioxidants. Proceedings Soci Experim Biol Medi. 1992;2002(2):248-54.
31. Walsh SW, Wang Y. Deficient glutathione peroxidase activity in preeclampsia is associated with increased placental production of thromboxane and lipid peroxides. Am J Obstet Gynecol. 1993;169(6):1456-61.
32. Frei B, England L, Ames BN. Ascorbate is an outstanding antioxidant in human blood plasma. Proceed National Acad Sci. 1989;86(16):6377-81.
33. Omar M, Borg HM. Assessment of oxidative stress markers and level of antioxidant in preeclampsia. Ind J Obstet Gynecol Res. 2019;6:268-75.
34. Valko M, Leibfritz D, Moncol J, Cronin MT, Mazur M, Telser J. Free radicals and antioxidants in normal physiological functions and human disease. Int J Biochem Cell Biol. 2007;39(1):44-84.

Cite this article as: Yanglem AS, Koch NS, Naorem S, Kshetrimayum RD, Kamei G, Nongmaithem B, et al. Serum malondialdehyde and serum glutathione peroxidase levels in pregnant women with and without preeclampsia. Int J Reprod Contracept Obstet Gynecol 2023;12:3294-8.