ORIGINAL RESEARCH PAPER
Volume - 13 | Issue - 10 | October - 2024 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

PRO-OXIDANT AND ANTIOXIDANT STATUS AS A DIAGNOSTIC INDEX OF PREECLAMPSIA RISK

Biochemistry

Mr. Jacob Joel Bunga — Final Year MBBS, Santhiram Medical College, Nandyal.
Dr. Havilah Polur — Assistant Professor, Department Of Biochemistry, Government Medical College, Ananthapur.
Dr. Naveen Kumar Sambu — Senior Laboratory Specialist, Mohammed Bin Khalifa Bin Salman, Al Khalifa, Specialist Cardiac Centre, Bahrain.
Dr. Putta Suman — Senior Resident, Department of Biochemistry, Government Medical College, Nandyal.
Dr. Durga Prasad Kedam — Professor & Head, Department Of Biochemistry, Santhiram Medical College, Nandyal.
Dr. Indumathi Bobbala* — Assistant Professor, Department Of Biochemistry, Santhiram Medical College, Nandyal. *Corresponding Author

ABSTRACT

Background: Preeclampsia still causes maternal death and morbidity. This condition pathogenesis involves oxidative stress. This study hypothesizes that decreased antioxidant defense mechanisms may increase lipid peroxidation, notably malondialdehyde (MDA), and preeclampsia risk. **Aim:** Biochemical changes in lipid peroxidation (MDA) and enzymatic antioxidants like Superoxide Dismutase(SOD) and Glutathione peroxidase (GPx) were investigated in normal and preeclampsia pregnant women. **Materials and Methods:** Of the 100 cases, 50 were healthy pregnant women and 50 were preeclampsia women who met the inclusion and exclusion criteria. Fasting venous blood samples were taken during antepartum to evaluate serum MDA, plasma SOD, and GPx levels. **Result:** The findings revealed a significant elevation in MDA levels 326.13 ± 101.54 and 195.07 ± 20.06 , p< 0. 001 and decreased antioxidant enzymes SOD levels 84.65 (±) 11.72 and 7,691 (±) 1,046 and GPX levels 133.60 (±) 10.03 and 10,310 (±) 1,592 (p<0.0001) respectively in the preeclampsia women compared to normal pregnant women. **Conclusion:** In preeclampsia, increased MDA and reduced antioxidant activity indicate oxidative stress. The insufficient neutralisation of reactive oxygen species by antioxidants causes preeclampsia-related oxidative damage and tissue destruction.

KEYWORDS

Superoxide dismutase, Glutathione peroxidase, Malondialdehyde, Oxidative Stress, Anti-oxidants, Pre-eclampsia, Pregnancy Induced hypertension.

INTRODUCTION

In 5%-15% of instances, late-term pregnancy-induced hypertension (PIH) is a significant consequence. Edema, increased blood pressure, protein loss through urine, and haemostatic mechanisms are symptoms. This condition causes foetal development restriction, infant sickness, death, and maternal mortality, according to the WHO [1]. The reasons of pregnancy-induced hypertension (PIH) were always unknown. However, emerging evidence suggests that oxygen free radicals and lipid peroxidation contribute to preeclampsia pathophysiology. Uncontrolled lipid peroxidation impairs vascular endothelial cell dysfunction, contributing to preeclampsia [1- 4]. Lipid peroxides and oxidative imbalance may cause endothelial cell injury through cytotoxic mechanisms. In non-pregnant people and normal pregnancies, antioxidants or free radical scavengers combat lipid peroxidation or free radical damage. PIH may result from increased free radical generation, low antioxidant levels, peroxidation imbalance, or cellular malfunction [Fig 1]. Numerous investigations have shown that PIH increases oxygen-free radical generation and decreases antioxidant levels (SOD and GPX). Several studies found that pregnancy-induced hypertension (PIH) increases oxygen-free radical generation and decreases antioxidant levels, particularly SOD and GPX. In preeclampsia patients, plasma lipid peroxides rise and catalase, SOD, and Glutathione Peroxidase fall [3- 8]. This study examined serum MDA and erythrocyte antioxidant levels of SOD and GPx in normal pregnant women and PIH women.

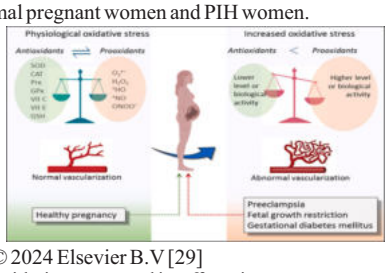

Figure 1: Oxidative stress and its effects in pregnancy.

MATERIALS AND METHODS

100 subjects were enrolled, 50 of whom had Pregnancy Induced Hypertension (PIH) and 50 of whom were normal on the outpatient and inpatient units of Santhiram Medical College & General Hospital, Nandyal. Patients with diabetes, high blood pressure, renal diseases, hepatitis, and a history of multivitamin use that affects antioxidant concentrations were excluded from the study. Clinical history and physical examinations of both cases and control histories and examinations were recorded 5 ml of venipuncture blood sample was taken in a heparinised tube (5units/ml) and plain tube. Thiobarbituric acid assay was used to measure malondialdehyde [9]. Assay kits were used to assess antioxidant enzymes like SOD and GPx in hemolysate of erythrocytes [10-11].

Statistical Analysis

Data analysis was done using licensed SPSS software, quantitative variables represented as mean ± SD and significance assessed using a Student t-test. A p value<0.05 was considered statistically significant.

RESULTS

Table 1 shows case and control blood pressure and gestational age. The mean Systolic blood pressure in patients is 149.3±5.5 while in controls it is 117.1±5.1, a significant P value <0.001. Diastolic Blood Pressure has a substantial difference (P < 0.001) between patients and controls, with a mean of 97.2 ±4.8 and 75.3±5.2 respectively.

This study compares lipid peroxidation and main antioxidants SOD and GPx in PIH patients and normal pregnant women. PIH patients have significantly higher malondialdehyde levels than normal pregnant women 326.13 ± 101.54 and 195.07 ± 20.06, p< 0. 001 respectively. Table 2 and Figure 2.

Superoxide Dismutase (SOD) Experiment

PIH and normal pregnancy had Mean and standard deviation SOD values of 84.65 + 11.72(U/mL) and 133.6 + 10.03 (U/mL) Table 2 and Figure 3 demonstrate a significant (p < 0.0001) decrease in SOD in PIH

compared to controls.

Glutathione Peroxidase (GPx) Experiment

Glutathione Peroxidase levels were measured in erythrocytes. The mean GPx values and their standard deviations were 7691±1046 (U/L) and 10310 ± 1592 (U/L) respectively in PIH and normal pregnancy, shown in Table 2 and Figure 4. Glutathione peroxidase levels were statistically significant lower in PIH cases than in normal pregnancy ($p < 0.0001$)

Table 1: Age (in years), gestational age (in weeks) and Systolic and Diastolic Blood Pressure (BP) in normal pregnant women and PIH pregnant women.

	(Group I) PIH pregnant women (n=50)	(Group II) Normal pregnant women (n=50)
Age in years	30.28±3.12	29.14±3.31
Gestational Age in weeks	28.32±3.43	28.29±2.22
Blood Pressure (BP) (mmHg)		
Mean Systolic BP	149.3±5.5	117.1±5.1
Mean Diastolic BP	97.2±4.8	75.3±5.2

*All values are mean ± SD

Table 2: Mean ± SD of MDA, SOD & GPx in the PIH (Group I), and Normal pregnancy (Group II)

	PIH (Group I) (n=50) Mean ± SD	Normal pregnancy (Group II) (n=50) Mean ± SD	p-Value
Malondialdehyde (MDA) nmol/L	326.13 ± 101.54	195.07 ± 20.06	< 0. 001
Superoxide Dismutase (SOD) (U/mL)	84.65±11.72	133.60+10.03	<0.0001
Glutathione Peroxidase (GPx) (U/L)	7,691±1,046	10,310±1,592	<0.0001

*All values are mean ± SD

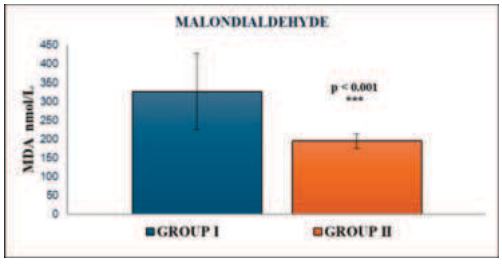

Figure 2: Malondialdehyde Levels in PIH (Group I) and Normal Pregnancy (Group II).

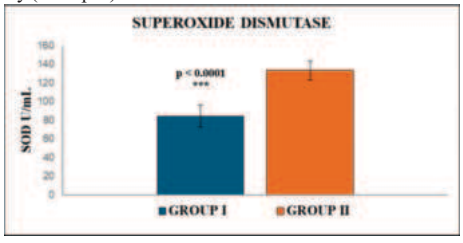

Figure 3: Super Oxide Dismutase Levels in PIH (Group I) and Normal Pregnancy (Group II).

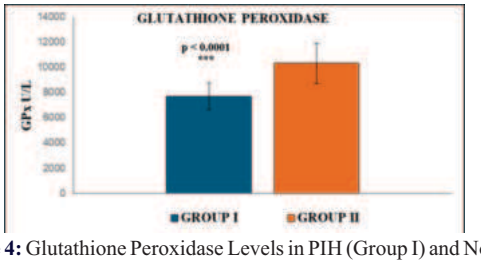

Figure 4: Glutathione Peroxidase Levels in PIH (Group I) and Normal Pregnancy (Group II).

DISCUSSION

PIH leading cause of maternal and infant mortality and morbidity, preeclampsia is among the most dangerous pregnancy disorders. A possible imbalance between oxidants and antioxidants is a suspected etiology in preeclampsia, although the exact cause is unclear. Patients with preeclampsia suffer increased oxidative stress, similar to those with hypertension and diabetes [12]. Endothelial dysfunction can result from increased placental lipid peroxide production or impaired antioxidant enzyme activity. Lack of antioxidant capability causes oxidative stress, which can damage maternal and fetal organs organs. In preeclampsia, placental anomalies and metabolic alterations promote oxidative stress [13]. Thus, this study examined lipid peroxidation and erythrocyte SOD and GPx levels in healthy pregnant women and PIH women.

PIH patients had 84.65 ± 11.72 (U/mL) erythrocyte superoxide dismutase (SOD) levels, while the normal pregnancy control group had 133.60 ± 10.03 (U/ml). The PIH group showed a substantial drop in SOD levels in comparison with the normal pregnancy group ($p < 0.001$). These findings are consistent with Saja M et al., [14]. Taravati A et al., [15], and Sonal Sogani et al [16] who found lower SOD levels in PIH patients than in normal pregnancies. Significant reduction in SOD levels in PIH patients may be attributed to free radical damage. Superoxide anions are constantly created by haemoglobin auto-oxidation in erythrocytes, which can block nitric oxide (NO) and cause relaxation and vasoconstriction, according to Lalthenglian et al. [17]. Comparatively, reduced erythrocyte superoxide dismutase (SOD) activity was observed in PIH when compared to the control groups was a common finding in the majority of investigations [17,18]. Glutathione peroxidase causes reduction of hydrogen and lipid peroxides, is inconsistently active during pregnancy and PIH. Our study reported mean GPx levels of 7,691 ± 1,046 in the PIH group and 10.310 ± 1.592 in the normal pregnant group, found a substantial decrease in Glutathione peroxidase levels in PIH group than in control P<0.0001).

Our findings are comparable with Alexa et al. [19] and Jendryzco et al. [20] who found lower Glutathione peroxidase levels in pregnancy-induced hypertension (PIH) than in normal pregnancies. In contrast, Kumar and Das[21], Wang and Walsh[22], Hubel[23], and Orzan [24] found increased Glutathione peroxidase levels in PIH patients. Our data suggests that normal gestation increases lipid peroxidation products while antioxidant activity remains steady or decreases, lowering GPx levels. Hypertension-complicated pregnancies, the oxidative system balance deficiency worsens in the course of second and third trimesters, advocating a collapse in the protective mechanism.

Multiple factors complicate protective antioxidant pathways, which may explain the differences in reporting between normal gestation and PIH [25]. Maria Isabel Covas et al. [26] found more biological variability in SOD in erythrocytes and GPx in whole blood, which limits its diagnostic and screening capability. SOD, however, has lesser biological variation and is less impacted by environmental and physiological changes as well, making it the best scavenger enzyme for pathological antioxidant status diagnostics and population screening.

Walsh et al. [27] found that placental tissue has increased lipid peroxidation and reduced SOD and GPx enzymes. They believe that in a healthy placenta, GPx lowers peroxide concentrations, which inhibits prostaglandin H synthase. In PIH, lower placental GPx activity raises peroxide levels, which stimulates PGH synthase and increases thromboxane and lipid peroxide synthesis. According to Covas et al. [26], erythrocyte SOD levels were positively correlated with whole blood GPx levels. Individual physiological antioxidant defense mechanisms are expected to vary. Thus, evaluating antioxidant levels may help predict oxidative stress vulnerability [28].

CONCLUSION

This study found that Pregnancy-Induced Hypertension (PIH) patients have increased lipid peroxidation, reduced antioxidant levels, and decreased enzyme activity, indicating indirect oxidative stress. Consequently, the assessment of lipid peroxidation and antioxidant status may hold significant diagnostic, pathophysiological, and therapeutic relevance in the PIH.

Acknowledgment

The corresponding authors deeply acknowledge the support and

funding by ICMR-STS. The reference number was 2020-07110.

REFERENCES

1. Kintiraki E, Papakatsika S, Kotronis G, et al.: Pregnancy-Induced hypertension. Hormones (Athens). 2015, 14 (2): 211-23.10.14310/horm.2002.1582.
2. Uzan J, Carbonnel M, Piconne O, et al.: Pre-eclampsia: pathophysiology, diagnosis, and management. Vasc Health Risk Manag.2011, 7:467-74. 10.2147/VHRM.S20181.
3. Aouache R, Biquard L, Vaiman D, et al.: Oxidative Stress in Preeclampsia and Placental Diseases.Int J Mol Sci. 2018, 19(5):1496. 10.3390/ijms19051496.
4. Braunthal S, Brateanu A. Hypertension in pregnancy: Pathophysiology and treatment. SAGE Open Med.2019, 7:2050312119843700. 10.1177/2050312119843700.
5. Mammaro A, Carrara S, Cavaliere A, et al.: Hypertensive disorders of pregnancy. J Prenat Med. 2009, 3(1):1-5.
6. Kattah AG, Garovic VD. The management of hypertension in pregnancy. Adv Chronic Kidney Dis. 2013 May; 20(3):229-39. 10.1053/j.ackd.2013.01.014.
7. Hansson SR, Nääv Å, Erlandsson L. Oxidative stress in preeclampsia and the role of free fetal hemoglobin. Front Physiol. 2015, 13;5:516. 10.3389/fphys.2014.00516.
8. Watanabe K, Mori T, Iwasaki A, Kimura C, Matsushita H, Shinohara K, Wakatsuki A. Increased oxygen free radical production during pregnancy may impair vascular reactivity in preeclamptic women. Hypertens Res. 2013, 36(4):356-60. 10.1038/hr .2012.208.
9. Yagi K.: "Assay for lipid peroxide level and its clinical significance". In: Yagi K. (ed.). Lipid Peroxide Level in Biology Medi- cine. New York, Academic Press, 1982, 223.
10. McCord JM, Fridovich I. Superoxide dismutase. An enzymic function for erythrocuprein (hemocuprein). J Biol Chem. 1969, 25; 244(22):6049-55.
11. Paglia DE, Valentine WN. Studies on the quantitative and qualitative characterization of erythrocyte glutathione peroxidase. J Lab Clin Med. 1967, 70(1):158-69.
12. Duhig K, Chappell LC, Shennan AH. Oxidative stress in pregnancy and reproduction. Obstet Med. 2016, 9(3):113-6.10.1177/1753495X16648495.
13. Raijmakers MT, Dechend R, Poston L. Oxidative stress and preeclampsia: rationale for antioxidant clinical trials. Hypertension. 2004, 44(4):374-80. 10.1161/01.HYP.000014 1085.98320.01.
14. Saja MB, Lina AS, Samia AE. Hydrogen peroxide levels correlate with superoxide dismutase in Iraqi women with pregnancy-induced hypertension. Asia J Pharm Clin Res. 2018, 11(11): 430-433.
15. Taravati A, Tohidi F. Comprehensive analysis of oxidative stress markers and antioxidants status in preeclampsia. Taiwan J Obstet Gynecol. 2018, 57(6):779-790. 10.1016/j.tjog.2018.10.002.
16. Sonal Sogani. Comparison of levels of lipid peroxidative marker and antioxidants between preeclamptic and normotensive pregnant women. Int J Clin Biochem Res. 2021, 87-91.
17. Lalthleglian T, Rajen S, M. Amula Singh, et.al.: Oxidative stress in PIH induced hypertension. Ind J Med Biochem; 2003; 7(1): 31-35.
18. Madazli R, 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):477-80.10.1080/0144361021000003573.
19. Alexa ID, Jerca L. Rolul stresului. The role of oxidative stress in the etiology of pre-eclampsia: changes at the GSH and GSH-Px levels in normal pregnancy and pre-eclampsia. Rev Med Chir Soc Med Nat Iasi. 1996, 100(1-2):131-5.
20. Jen DA, Tomala J. Decreased activity of oxido-reductases in erythrocytes and blood platelets from venous and umbilical blood of women with PIH. Ginekol Pol. 1995 66(12): 656-9.
21. Kumar CA, Das UN. Lipid peroxides, anti-oxidants and nitric oxide in patients with pre-eclampsia and essential hypertension. Med Sci Monit. 2000, 6(5):901-7.
22. SW Walsh, Yuping wang. Deficient glutathione peroxidase activity in preeclampsia is associated with increased placental production of Thromboxane A2 and lipid peroxides. Am J Obstet Gynecol. 1993, 169: 1456-61
23. Carl A Hubel. Oxidative stress in the pathogenesis of preeclampsia; Proc Soc for exp biol and Med. 1999, 21: 222-235
24. Orzan H, Flcol y, Kimya Y, Congiz C, Ediz B. Plasma antioxidant status and lipid profile in non-gravida women with a H/O preeclampsia. J Obstet Gynecol Res. 2002, 28(5): 274-9.
25. Nakai A, Oya A, Kobe H, Asakura H, Yokota A, Koshino T, Araki T. Changes in maternal lipid peroxidation levels and antioxidant enzymatic activities before and after delivery. J Nippon Med Sch. 2000, 67(6):434-9. 10.1272/jnms.67.434.
26. Maria isabel covas, luis coca, Carmen ricos. Biological variation of superoxide dismutase in erythrocytes and GPx in whole blood. Clin Chem. 1997, 43(10): 1991-1993.
27. SW Walsh, Yuping wang. Deficient glutathione peroxidase activity in preeclampsia is associated with increased placental production of Thromboxane A2 and lipid peroxides. Am J Obstet Gynecol. 1993, 169: 1456-61.
28. Chandan K Sen. Oxidants and antioxidants in exercise a brief review. J Applied Physiology. 1995; 79(3): 675-685.
29. Prins JR, Schoots MH, Wessels JI, Campmans-Kuijpers MJE, Navis GJ, van Goor H, Robertson SA, van der Beek EM, Sobrevia L, Gordijn SJ. The influence of the dietary exposome on oxidative stress in pregnancy complications. Mol Aspects Med. 2022 Oct;87:101098. doi: 10.1016/j.mam.2022.101098.