Original Article

Biomarkers of Oxidative Stress in Normal and Pre-eclamptic Women

Ara S[1], Nigar T[2], Habib MA[3],

Abstract

Preeclampsia is a serious pregnancy complication. Little is known about which clinical risk factors are associated with the progression from normal to preeclampsia. Recent evidence suggests that the oxidative stress is one of the important factor associated with preeclampsia. High uric acid and MDA levels are indicative of oxidative stress. The purpose of this study was to evaluate the possible relationship between the biochemical markers (Uric acid & MDA) of oxidative stress in preeclamptic & normal pregnant women. In our study we investigated total number of 40 healthy pregnant and clinically diagnosed preeclamtic women. Among them 20 healthy (third trimester) normal pregnant women were taken as control group and another 20 clinically diagnosed PET women (at pre labour state) were taken as observational group. MDA and uric acid level were within normal range (2.63 ± 0.66 & 337.88 ± 16.52 µmol/l) respectively in normal pregnant women but significantly higher (3.74 ± 1.45 & 428.50 ± 23.65 µmol/l) in the group of preeclamptic women. This study review our current understanding of oxidative stress biomarkers (Uric acid & MDA) in preeclampsia and highlights that increased MDA and Uric acid levels are associated with preeclampsia.

Key words: *Oxidative stress, Malondialdehyde (MDA), Uric acid, Preeclampsia.*

Introduction

Preeclampsia is a medical condition characterized by high blood pressure and significant amounts of protein in the urine of a pregnant woman. If left untreated, it can develop into eclampsia, the life-threatening occurrence of seizures during pregnancy. It is a leading cause of maternal mortality in developed countries and increases perinatal mortality five-fold[1]. Preeclampsia affects approximately 6-8% of all pregnancies worldwide,[2] with onset of symptoms in the late second or third trimester, most commonly after the 2nd week[3]. Some women will experience preeclampsia as early as 20 weeks, though this is rare. It is much more common in women who are pregnant for the first timed,[3] and its frequency drops significantly in subsequent pregnancies. In the United Kingdom fewer than ten women will die each year from pre-eclampsia[4] but this remains a relatively common cause of death in pregnancy in the developed world. Only about one in two thousand women will have an eclamptic convulsion but the associated maternal mortality is 2%[5]. There are many different causes for the development of preeclampsia. It appears likely that there are substances from the placenta that can cause endothelial dysfunction in the maternal blood vessels of susceptible women[6]. Endothelial cell dysfunction may account for the altered vascular reactivity, activation of coagulation cascade and loss of vascular integrity that accompany the disease[7]. Several investigators have reported that maternal blood level of lipid peroxides are significantly elevated in preeclampsia[8]. These uncontrolled lipid peroxidation is a key contributing factor to pathophysiologic condition of preeclampsia[9].

1. Shahin Ara, Associate professor, Department of Pharmacology, Rajshahi Medical College, Rajshahi.
2. Taslima Nigar, Medical officer, National Cancer Research Institute, Mohakhali, Dhaka. (Formerly a student of MS course, Rajshahi Medical College, Rajshahi).
3. Md. Anwar Habib, Professor & Head, Department of Pharmacology, Rajshahi Medical College, Rajshahi.

Although eclampsia is potentially fatal (2% of cases), pre-eclampsia is often asymptomatic. So its detection depends on signs or investigations. Pre-eclampsia is associated with the elevated uric acid level which is a component of the preeclampsia syndrome that was recognized many years ago[10]. It is one of the most consistent and earliest detectable changes and has been cited as a better indicator of fetal risk in preeclampsia[11,12]. Malondialdehyde (MDA) is the organic compound. Reactive oxygen species (ROS) degrade polyunsaturated lipids, forming malondialdehyde[13]. The production of this aldehyde is used as a biomarker to measure the level of oxidative stress in an organism[14,15]. In the current study, we investigated oxidative stress biomarkers (MDA & Uric acid) in normal and preeclapmtic women to revalidate the earlier findings[10,11,12,15,17,18].

Materials And Methods

This is a cross sectional comparative study that was carried out on total number of 40 women, of them 20 healthy (third trimester) pregnant women were taken as control and 20 clinically diagnosed preeclamptic women (in pre-labour state) were taken as observational group. Study population were selected from department of Obstetrics & Gynecology, outdoor and indoor, Rajshahi Medical College Hospital, Rajshahi. Oxidative stress was observed by estimating plasma MDA and uric acid level.

Estimation of MDA

MDA level was estimated following the method of Das et al (1990)[16], as described bellow. Techniques:0.5 ml plasma was mixed with 2.5 ml of 20% trichloroacetic acid (TCA) and after 10 minute, the sample was centrifuged (3500 rpm for 10 min). The precipitate was washed with sulfuric acid (0.05 mol/liter) and treated in a test tube with 2.5 ml of sulfuric acid and 3 ml of thiobarbituric acid (TBA) reagent (2.0 gm TBA/L in 2 mol sodium sulfate/l). The test tube was placed in boiling water bath for 30 min and cooled in a running tap water. The TBA reactive material was mixed with 4 ml n-butanol and centrifuged (3500 rpm for 10 min). A standard (0.5ml) of MDA was treated similarly. The optical density (O.D) of n-butanol extract of plasma and MDA standard was measured at 532 nm against a butanol blank. The result was expressed as µmol MDA/l of plasma. Estimation of Uric acid Plasma uric acid was measured by a diagnostic kit provided by LABKIT.

Result

Plasma MDA and Uric acid levels were shown in Table-1.

Table-1 MDA & Uric Acid levels in Normal pregnant and Pre-eclamptic women

Parameters	Normal Pregnant (n=20)	Preeclamptic (n=20)	P value
Mean MDA (µmol/l ± SE)	2.63 ± 0.66	3.74 ± 1.45	P<0.001
Mean Uric Acid (µmol/l ± SE)	337.88 ± 16.52	428.50 ± 23.65	P<0.001

Plasma MDA and uric acid levels were within normal physiological limit in all the control subjects but were signifiantly ($p<0.001$) higher in preeclamptic women.

Discussion

Biomarkers of oxidative stress (MDA and Uric acid) were studied in normal and preeclamptic women. From the findings of present study it was evident that there was a significant increased in mean plasma MDA level in preeclamptic women. This finding was consistant with the observations of others[15]. They however did not estimate the serum uric acid level. In our study we estimate the serum uric acid level which was also significantly higher in preeclamptic women. This finding was in agreement with others[10,11,12,17,18,] but they did not investigate plasma MDA level. Some investigator[17] claimed increased plasma uric acid level as a predictor of preeclampsia. Our studies showed that both increased plasma MDA & increased uric acid level were associated with preeclampsia. But among these two parameters, plasma MDA level is usually measured in experimental' laboratory for research purpose and not done in usual clinical diagnostic laboratory. Therefore the measurement of plasma uric acid level should be considered worthwhile during the antenatal check-up.

Conclusions

Both plasma MDA as well as uric acid levels were increased in preeclampsia. Increased plasma uric acid level may be considered as a predictor of preeclampsia. So that serial measurement of plasma uric acid level should be included during antenatal check-up.

Acknowledgement

We are grateful to Prof. Nazimuddin Ahmed Ex. Principal and Head, Dept. of Pharmacology, Rajshahi Medical College, Rajshahi for his kind co-operation and valuable suggestions in conducting this work.

Reference

1. Roberts JM. Pregnancy related hypertension. In: Creasy RK, Resnik R, editors. Maternal Fetal Medicine, pp. 833-872. Philadelphia, PA: WB Saunders; 1998.

2. World Health Organization (WHO). World health report 2005: make every mother and child count. Geneva: WHO; 2005, page 63 .

3. Robbins and Cotran, Pathological Basis of Disease, 7th ed.

4. Department of Health (2001) Why mothers Die, 1197-1999. Report on confidential Enquiries into maternal Deaths in the United Kingdom. London: ROCG Press

5. Douglas KA, Redman CW (November 1994). "Eclampsia in the United Kingdom". BMJ 309 (6966): 1395-400. doi:10.1136/bmj.309.6966.1395. PMC 2541348. PMID 7819845.

6. a b c Drife JO, Magowan (eds). Clinical Obstetrics and Gynaecology, chapter 39, pp 367-370. ISBN 0-7020-1775-2.

7. Roberts JM. Endothelial dysfunction in preeclampsia. Semin Reprod Endocrinol, 1998; 16:5-15.

8. Ishihara M. Studies on lipoperoxide of normal pregnant women and of patient with toxemia of pregnancy. Clin Chim Acta.1978;18:158-62.

9. Hubel CA, Roberts JM, Taylor RN. Lipid peroxidation in pregnancy: new perspectives on pre-eclampsia. AM J Obstet Gynecol 1989;161:1025-1034.

10. Chesley Leon C. PhD. Diagnosis of preeclampsia. Hypertensive disorders of pregnancy. New York: Appleton-Century-Crofts; 1978.

11. Redman CW, Beilin LJ, Bonnar J, Wilkinson RH. Plasma-urate measurements in predicting fetal death in hypertensive pregnancy. Lancet. 1976; 1: 1370-1373.Medline

12. Chesley LC. Diagnosis of preeclampsia. Obstet Gynecol 65: 423-425,1985

13. Pryor WA, Stanley JP (1975). "Letter: A suggested mechanism for the production of malondialdehyde during the autoxidation of polyunsaturated fatty acids. Nonenzymatic production of prostaglandin endoperoxides during autoxidation". J. Org. Chem. 40 (24): 3615-7. doi:10.1021/jo00912a038. PMID 1185332.

14. Moore K, Roberts LJ (1998). "Measurement of lipid peroxidation". Free Radic. Res. 28 (6): 659-71. doi:10.3109/10715769809065821. PMID 9736317.

15. Del Rio D, Stewart AJ, Pellegrini N (2005). "A review of recent studies on malondialdehyde as toxic molecule and biological marker of oxidative stress". Nutr Metab Cardiovasc Dis 15 (4): 316-28. doi:10.1016/j.numecd.2005.05.003.PMID 16054557.

16. Das, B.S. Thurnham, D.I, Patnaik, J.K, Das, D.B., Satpathy, R. Bose, T.K, 1990 . Increased plasma lipid peroxidation in riboflavin- deficient, malaria infected children. Am J Clin Nutr, vol.51, pp. 859-63.

17. F Saleh S Shukar-ud-Din N Soomro,To determine that serum uric acid as a predictor in pre-eclampsia during pregnancy. Pak J Surg 2010; 26(3):246-251.

18. Koopmans, CM; Van Pampus, MG; Groen, H; Aarnoudse, JG; Van Den Berg, PP; Mol, BW (2009). "Accuracy of serum uric acid as a predictive test for maternal complications in pre-eclampsia: bivariate meta-analysis and decision analysis". European journal of obstetrics, gynecology, and reproductive biology146 (1): 8-14. doi:10.1016/j.ejogrb.2009.05.014. PMID 19540647.