DOI: 10.14260/jemds/2015/593

ORIGINAL ARTICLE

STUDY OF OXIDATIVE STRESS IN PREGNENCY INDUCED HYPERTENSION (PIH)

B. Narayana Rao[1], M. Jayaprakash Babu[2]

HOW TO CITE THIS ARTICLE:
B. Narayana Rao, M. Jayaprakash Babu. "Study of Oxidative Stress in Pregnency Induced Hypertension (PIH)". Journal of Evolution of Medical and Dental Sciences 2015; Vol. 4, Issue 24, March 23; Page: 4115-4120, DOI: 10.14260/jemds/2015/593

ABSTRACT: Hypertensive disorders complicating pregnancy are common and form one of the deadly triad, along with hemorrhage and infection that contribute greatly to maternal morbidity and mortality. The present study was conducted in the Department of Biochemistry, Rangaraya Medical College, Kakinada, and Andhra Pradesh. The present study was undertaken to determine the changes in lipid peroxidation and lipoprotein concentrations in cord blood and maternal blood of pregnancy induced Hypertensive group consists of 50 pregnant women during delivery. In the present study the concentrations of Malondialdehyde (MDA) in Pregnancy induced hypertensive cases were significantly elevated in comparison with controls ($p < 0.001$) the same observation was reported in many studies. Fasting serum triglycerides correlate with serum malondialdehyde in women with preeclampsia. Plasma triglycerides in maternal blood in Pregnancy induced Hypertension were significantly higher than the control values ($p < 0.001$) Plasma Total Cholesterol in maternal blood shows a significant rise in Pregnancy induced hypertension cases against control ($p < 0.001$).
KEYWORDS: Oxidative stress, preeclampsia, Antioxidants, Dyslipidemia.

INTRODUCTION: Hypertensive disorders complicating pregnancy are common and form one of the deadly triad, along with hemorrhage and infection that contribute greatly to maternal morbidity and mortality. Hypertensive disorders are among the commonest medical disorders during pregnancy and complicate 7-10% of all pregnancies. According to the criteria of the International Society of the Study of Hypertension in Pregnancy, the preferred definition is a diagnosis of pregnancy-induced hypertension (blood pressure usually ≥140/90 mm Hg) occurring after week 20 of gestation. Preeclampsia is diagnosed by the new development of hypertension (usually ≥140/90 mm Hg), significant proteinuria (either ≥300 mg protein per day or a urinary protein/creatinine ratio ≥30 mg/mmol) and remission of these signs after delivery. Eclampsia is the occurrence of seizures in a preeclamptic patient that cannot be attributed to other causes.

The cause of preeclampsia remains largely unknown, but poor placentation is an important predisposing factor. The proposed "2-stage model"[1] in which reduced placental perfusion (stage 1) leads to the maternal syndrome (stage 2) is likely to provide a simplified, yet largely accurate, description of the origin of severe early-onset disease, but may be less relevant for later-onset milder disease.[2] The proposed role of the placenta in the pathology of preeclampsia is also strongly supported by the rapid resolution of symptoms after delivery. Although there is clearly a focal role for placental dysfunction in preeclampsia, a number of theories are proposed to explain how this may be associated with the maternal syndrome.[3]

A pivotal role of enhanced placental superoxide generation leading to oxidative stress is increasingly recognized.[4] Deleterious effects of free radicals include initiation of lipid peroxidation, oxidative damage of biomolecules, and cellular dysfunction, and it is proposed that these may initiate maternal vascular endothelial dysfunction and leukocyte activation, recognized features of this

DOI: 10.14260/jemds/2015/593

disorder. This study focuses on investigations into oxidative stress and its relevance to the cause and prevention of pre eclampsia.

RESEARCH DESIGN AND METHODS: The present study was conducted in the Department of Biochemistry, Rangaraya Medical College, Kakinada, Andhra Pradesh. The present study was undertaken to determine the changes in lipid peroxidation and lipoprotein concentrations in cord blood and maternal blood of pregnancy induced Hypertensive group consists of 50 pregnant women during delivery. The values were compared with the values of 20 healthy pregnant women. All of these subjects were from the Obstetrics and Gynecology wards of Govt. General Hospital, who were admitted for delivery. Demographic and clinical data were collected at routine obstetric visits. Blood samples were obtained by venous puncture from the antecubital vein of each women after delivery simultaneously the cord blood was also collected.

The Control group denied any history of chronic disease and of same age group as test group. Consent was obtained from both the cases and control groups. Plasma was separated and analyzed by using standard methods. The observed values were compared with control group for statistical analysis. All data were expressed as Mean ± standard deviation. One way analysis of variance followed by student 't' test was used to compare the values. Differences with a P value of less than 0.05 were considered to be statistically significant. Biochemical parameters fasting lipid profile, glucose, urea, creatinine, albumin and uric acid done in ERBA semi automated analyzer by using standard kits. Malondialdehyde (MDA) estimation done with thiobarbituric acid (TBA) reaction method by spectrophotometer at 530 nm.

Age in yrs.	Control (n = 20)	PIH (n = 50)
15 – 20	4	13
21 – 25	10	29
26 - 30	6	08

Table 1: Age distribution of the controls and PIH cases

Gravida	Control (n = 20)	PIH (n =50)
Primi gravida (G1)	15	27
Second Gravida (G2)	5	16
Third gravida (G3)	--	07

Table 2: Distribution of Gravida

Parameter	Control (n=20)	PIH (n=50)	Controls (n=20) VS PIH (n = 50)	
			't'	P value
B.P (Systolic) mm Hg	114 ± 8	156 ± 14	12.576	<0.001
B.P (Diastolic) mm Hg	74 ± 6.5	96 ± 8.5	10.833	<0.001
Plasma Glucose in mgs%	69 ± 6.6	84 ± 14	4.720	<0.001
Urea in mgs%	20 ± 2.7	23 ± 3.7	1.010	NS
Creatinine in mgs%	0.87± 0.12	0.99 ± 0.1	4.286	<0.001

DOI: 10.14260/jemds/2015/593

Uric Acid in mgs%	4.2 ± 0.6	6.1 ± 0.6	12.453	<0.001
Triglycerides in mgs%	153 ± 11	259 ± 32	14.393	<0.001
Total Cholesterol in mgs%	212 ± 19	247 ± 13	8.935	<0.001
HDL Cholesterol mgs%	47 ± 3.4	47 ± 5	0.345	NS
LDL cholesterol mgs%	134 ± 20	148 ± 11	3.667	<0.001
VLDL Cholesterol mgs%	30 ± 2.3	52 ± 6.4	14.325	<0.001
Total Protein gm%	7.2 ± 0.4	5.9 ± 0.3	14.84	<0.001
Globulins gm%	3.2 ± 0.5	3.4 ± 0.21	2.099	<0.025
Albumin gm%	3.95 ± 0.4	2.5 ± 0.3	18.354	<0.001
MDA in nmol/dl	385 ± 31	755 ± 30	46.18	<0.001

Table 3: Showing the statistical values of Biochemical parameters in maternal blood of controls and PIH cases

RESULTS AND DISCUSSION: In the present study all Pregnancy induced hypertensive cases were having systolic blood pressure 156 ± 14 mmHg and Diastolic blood pressure 94 ± 9 mmHg., when compared to normal pregnant women as controls the blood pressure was significantly elevated SBP was $p < 0.001$ and DBP was $p < 0.001$. Endothelial dysfunction is considered a central component of the pathophysiology of preeclampsia and known to contribute to the pathogenesis of cardio vascular disease. Pregnancy is characterized by increased generation of pro oxidants from the placenta. Poor oxidant reserves can also tilt the balance in favor of prooxidation. Lipid Peroxidation results in primary lipid Peroxidation products such as lipid Hydro peroxides and secondary products such as malondialdehyde (MDA) and lipid peroxides.[5]

Lipid Hydro peroxides are formed and bind to lipoproteins. They are then carried to distant sites where the hydroperoxides can cause ongoing lipid peroxidation and result in systemic oxidative stress. Increased ROS leads to increased lipid Peroxidation. Increased placental production of lipid peroxides and thromboxane was demonstrated from both the trophoblast and the villous core components of placentas in patients with preeclampsia.[6] In the present study the concentrations of Malondialdehyde (MDA) in Pregnancy induced hypertensive cases were significantly elevated in comparison with controls ($p < 0.001$) the same observation was reported in many studies.[7] (Kato et.al. Bowen et al., Braekke et. al. Isabel Sanchez et al.,).

The studies by Bowen et.al. Found significantly higher values of MDA in cord blood in patients with PIH. Same finding was observed in the present study, there was significant rise in the MDA levels in cord and maternal blood of Pregnancy induced Hypertension patients. MDA levels were significantly elevated ($p < 0.001$). Supporting a concept of elevated oxidative stress in fetal circulation in pregnancy induced hypertension. In the less severe forms of the disease, the antioxidants and the placenta may be able to scavenge prooxidants.[8]

This may explain why lipid peroxides were not elevated in some of the studies. Normal pregnancy is associated with physiological hyperlipidemia. physiological alterations are manifested by increased levels of triglycerides and cholesterol in pregnancy, which decrease after delivery. In Pregnancy induced hypertension which induces preeclampsia state is further characterized by further elevation of serum triglycerides. Hypertriglyceridemia has been proposed to be a potential risk factor for preeclampsia.[9]

DOI: 10.14260/jemds/2015/593

A large cohort nested control study found that hypertriglyceridemia, if demonstrated before twenty weeks gestation, may serve as a marker for early onset of preeclampsia. In the present study, the serum triglycerides were significantly elevated in Pregnancy induced hypertension ($p < 0.001$). Fasting serum triglycerides correlate with serum malondialdehyde in women with preeclampsia. Elevated triglycerides may compromise vascular function in several ways. For example, triglycerides – rich lipoproteins have prothrombotic activity.[10]

Serum total cholesterol levels were significantly raised in Pregnancy induced hypertensive cases in comparison with controls ($p < 0.001$) in both cord and maternal blood. Whereas the HDL cholesterol change was not significant. Same was observed by Hubel CA et.al., Sattar N et al., the hypertriglycedemia is also accompanied by increased prevalence of smaller, denser LDL particles and decreased HDL cholesterol. The mechanisms underlying the dyslipidemia in preeclampsia are poorly understood. Urinary excretion of uric acid is a complex process, with complete filtration at the glomerulus, proximal tubule reabsorption, distal tubule reabsorption, distal tubule secretion, post secretion reabsorption. Elevated serum uric acid levels have been associated with preeclampsia.[11]

The mechanism for hyperuricemia with preeclampsia has not yet been elucidated, but has been postulated to result from decreased glomerular filtration or increased net tubular reabsorption, as well as increased fetal production as a result of fetal hypoxia.

In the present study serum uric acid levels in maternal blood of Pregnancy induced hypertension was significantly elevated in comparison with controls ($p <0.001$). As uric acid is a water soluble antioxidant presenting in the body. Same observations were seen in many studies Halvorsen BL et.al. Benzie IF et.al.[12] In the present study serum protein fractions were decreased in PIH in comparison with controls serum total proteins ($p < 0.001$), Globulins ($p < 0.025$), Albumin ($p < 0.001$). In pre eclampsia, the urine protein excretion rises above a threshold of 0.3 g per 24h. This finding is generally associated with the classic pathological finding of glomeruloendotheliosis. The loss of serum protein and the increase in capillary endothelial permeability lead to a decrease in intravascular volume and increased tissue edema. In the present study plasma glucose, Urea and plasma Creatinine was estimated in maternal blood of Pregnancy induced Hypertension and compared with control cases. There were no significant changes observed.

CONCLUSIONS: Pre-eclampsia is associated with significant morbidity and mortality for mother and baby, but it resolves completely postpartum. Pre eclampsia is a major contributor to premature births and intrauterine growth restriction.[13] The concentrations of Malondialdehyde (MDA) in Pregnancy induced hypertensive cases were significantly elevated in comparison with controls ($p < 0.001$) in maternal blood due to increased placental production of lipid peroxides. Lipid Peroxidation results in primary lipid Peroxidation products such as lipid hydro peroxides and secondary products such as malondialdehyde and lipid peroxides Plasma triglycerides in maternal blood in Pregnancy induced Hypertension were significantly higher than the control values ($p < 0.001$) Plasma Total Cholesterol in maternal blood shows a significant rise in Pregnancy induced hypertension cases against control ($p < 0.001$). LDL and VLDL cholesterol in PIH were raised significantly.[14] ($p < 0.001$) and ($p < 0.001$).

This suggests that there might be an even more profound decrease in the Hydrolysis of Tgs compared with normal gestation, resulting in impaired Generation of LDL particles from Tg rich lipoproteins.[15] Plasma Uric acid in Pregnancy induced Hypertension cases were raised significantly in

comparison with controls ($p < 0.001$). The elevated levels have been associated with pregnancy induced hypertension may be due to an increase in fetal uric acid production or a decrease in uric acid clearance. Serum protein fractions were decreased in PIH in comparison with controls. The loss of serum protein and the increase in capillary endothelial permeability lead to a decrease in intravascular volume.

BIBLIOGRAPHY:

1. Hubel CA. Oxidative stress in the pathogenesis of preeclampsia. Proc Soc Exp Biol Med. 1999; 222: 222–235.
2. Redman CWG, Sargent IL. Pre-eclampsia, the placenta and the maternal systemic inflammatory response -a review. Placenta. 2003; 24: S21–S27.
3. Brosens IA, Robertson WB, Dixon HG. The role of the spiral arteries in the pathogenesis of preeclampsia. Obstetric Gynecology Annul. 1972; 1: 177–191.
4. Roberts JM, Hubel CA. Is oxidative stress the link in the two-stage model of pre eclampsia? Lancet. 1999; 354: 788–789.
5. Roberts J. Pregnancy-related hypertension. In: Creasy R, Resnik R, Eds. Maternal Fetal Medicine. Philadelphia: W. B. Saunders, pp804–843, 1994.
6. Friedman SA, Taylor RN, Roberts JM. Pathophysiology of preeclampsia. Clin Perinatol 18:661–682, 1991
7. Lindheimer M, Roberts J, Cunningham F, Eds. Chesley's Hypertensive Disorders in Pregnancy (2nd ed). Stamford, CT: Appleton & Lange, 1999.
8. Roberts JM, Taylor RN, Musci TJ, Rodgers GM, Hubel CA, McLaughlin MK. Preeclampsia: An endothelial cell disorder. Am J Obstet Gynecol 163:1365–1366, 1990
9. Taylor RN, Roberts JM. Endothelial cell dysfunction. In: Lindheimer MD, Roberts JM, Cunningham FG, Eds. Chesley's Hypertensive Disorders in Pregnancy (2nd ed). Stamford, CT: Appleton & Lange, pp395–429, 1999.
10. Roberts JM. Endothelial dysfunction in preeclampsia. Sem Reprod Endocrinol 16:5–15, 1998
11. Redman CW. Current topic: Preeclampsia and the placenta. Placenta 12:301–308, 1991
12. Cross JC. Trophoblast functions in normal and preeclamptic pregnancy. Fetal Matern Med Rev 8:57–66, 1996.
13. Sagol S, Ozkinay E, Ozsener S. Impaired antioxidant activity in women with pre-eclampsia. Int J Gynaecol Obstet. 1999; 64: 121–127.
14. Kharb S. Vitamin E and C in preeclampsia. Eur J Obstet Gynecologic Reprod Biol. 2000; 93: 37–39.
15. Valsecchi L, Cairone R, Castiglioni MT, Almirante GM, Ferrari A. Serum levels of alpha-tocopherol in hypertensive pregnancies. Hypertens Pregnancy. 1999; 18: 189–195.

DOI: 10.14260/jemds/2015/593

ORIGINAL ARTICLE

AUTHORS:

1. B. Narayana Rao
2. M. Jayaprakash Babu

PARTICULARS OF CONTRIBUTORS:

1. Assistant Professor, Department of Biochemistry, Homibhabha Cancer Hospital and Research center, Vishakhapatnam.
2. Professor, Department of Biochemistry, Gitam Institute of Medical Sciences, Vishakhapatnam.

FINANCIAL OR OTHER COMPETING INTERESTS: None

NAME ADDRESS EMAIL ID OF THE CORRESPONDING AUTHOR:
Dr. B. Narayana Rao,
Assistant Professor,
Department of Biochemistry,
Homibhabha Cancer Hospital &
Research Center, Vishakhapatnam-530053.
E-mail: bankuru36@gmail.com

Date of Submission: 27/02/2015.
Date of Peer Review: 28/02/2015.
Date of Acceptance: 10/03/2015.
Date of Publishing: 20/03/2015.