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LIPID PEROXIDATION AND LIPOPROTEIN CONCENTRATIONS IN CORD BLOOD OF PREGNANCY INDUCED HYPERTENSION

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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 undertaken to determine the changes in lipid peroxidation and lipoprotein concentrations in cord blood of pregnancy induced Hypertensive patients. The MDA levels in cord 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. Hydrolysis of Tgs compared with normal gestation, resulting in impaired Generation of LDL particles from Tg rich lipoproteins. Plasma Uric acid in Pregnancy induced Hypertension cases were raised significantly in comparison with controls ($p < 0.001$).

KEYWORDS: lipid peroxidation, pregnancy induced hypertension, lipoprotiens.

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. 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.[1]. 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 disorder.[5] This study focuses on investigations into oxidative stress and its relevance to the cause and prevention of pre eclampsia.

Aim of the study: The present study was undertaken to determine the changes in lipid peroxidation and lipoprotein concentrations in cord blood of pregnancy induced Hypertensive patients.

MATERIALS AND METHODS

Research design:

Inclusion criteria: Case control study of 50 Pregnancy induced Hypertensive group women (15-45 years) during delivery. For control group age match, denied any history of chronic disease as test group (without PIH) deliveries were taken. All of these subjects were from the Obstetrics and Gynecology wards of Govt. General Hospital, who were admitted.

Exclusion criteria: Complications other than pregnancy induced hypertension**.**

Ethical approval and inform consent: The study was approved by the Institutional ethics committee of our college, and informed consent was obtained from both the cases and control groups.

Sample size: Seventy (Test group 50 and control group 20). Distribution of age and Gravida mentioned in Table 1 & 2.

Methodology:

Demographic and clinical data were collected at routine obstetric visits. Blood samples were obtained from the cord blood of each woman during delivery. Plasma was separated and analyzed by using standard methods.

Biochemical parameters like fasting lipid profile, glucose, urea, creatinine, albumin and uric acid done in ERBA semi automated analyzer by using standard kits.[6]

Malondialdehyde (MDA) estimation done with thiobarbituric acid (TBA) reaction method by spectrophotometer at 530 nm. Mahalouz et al 1986.

Table 1. Age distribution of the controls and PIH cases

Age in yrs	Control	PIH
15 – 20	4	13
21 – 25	10	29
26 - 30	6	08

Table 2. Distribution of Gravida

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

STATISTICAL ANALYSIS

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.

RESULTS

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 prooxidants 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. 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. 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. Biochemical parameters are showed in Table 3.

Table 3. Showing the Biochemical parameters in Cord **blood** of Control and PIH cases

Parameter	Control	PIH	t	P value
Plasma Glucose in mgs%	65 ± 5.2	67 ± 7	1.168	NS
Urea in mgs%	22 ± 2.6	24 ± 3.4	2.888	<0.005
Creatinine in mgs%	0.87 ± 0.13	0.98 ± 0.2	2.292	<0.01
Uric Acid in mgs%	4.1 ± 0.5	4.4 ± 0.4	2.556	<0.01
Triglycerides in mgs%	64 ± 8	59 ± 4	3.166	<0.001
Total Cholesterol in mgs%	171 ± 8	170 ± 4	0.664	NS
HDL Cholesterol in mgs%	41 ± 4.4	39 ± 2	2.806	<0.005
LDL cholesterol in mgs%	118 ± 9	120 ± 3	1.369	NS
VLDL Cholesterol mgs%	13 ± 2	12 ± 0.8	3.691	<0.001
Total Protein in gm%	6.9 ± 0.4	6.3 ± 0.3	6.867	<0.001
Globulins in gm%	3.3 ± 0.3	3.1 ± 0.3	2.907	<0.001
Albumin in gm%	3.5 ± 0.3	3.2 ± 0.2	5.075	<0.001
MDA in nmol/dl	397 ± 36	660 ± 31	30.58	<0.001

DISCUSSION

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 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.[7] 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.[8] Hypertriglyceridemia has been proposed to be a potential risk factor for preeclampsia. 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 prothrombic activity.

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.[9] The mechanism for hyperurcemia 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 cord 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.In the present study serum protein fractions were decreased in PIH in comparison with controls serum total proteins ($p < 0.001$), Globulins ($p < 0.001$), Albumin ($p < 0.001$).[9] 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.[10] The loss of serum protein and the increase in capillary endothelial permeability lead to a decrease in intravascular volume and increased tissue edema.

CONCLUSION

The concentrations of Malondialdehyde (MDA) in Pregnancy induced hypertensive cases were significantly elevated in comparison with controls ($p < 0.001$) in cord blood due to increased placental production of lipid peroxides.[11] 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 cord blood in Pregnancy induced Hypertension were significantly higher than the control values ($p < 0.001$ 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. Plasma Uric acid in Pregnancy induced Hypertension cases were raised significantly in comparison with controls ($p < 0.001$).

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CONFLICT OF INTEREST

No Conflict of interest.

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