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Original Research Paper

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STUDY OF DYSLIPIDEMIA IN ASSOCIATION WITH TOTAL ANTIOXIDANT STATUS IN PREECLAMPSIA.

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ABSTRACT

Introduction: Preeclampsia is a serious complication of the second half of pregnancy that occurs with a frequency of 5-15%. Preeclampsia is an endothelial disease with a major involvement of lipid mediated oxidative damage along with an imbalance between prooxidant production and antioxidant defenses. **Aims and objectives:** To study the association of dyslipidemia with total antioxidant status in the form of Ferric reducing antioxidant power (FRAP) in preeclampsia. **Materials and methods:** The present study was carried out for one year on pregnant women attending Obstetrics department as OP&IP at Narayana Medical College, Nellore.50 normal healthy pregnant women of > 20 weeks gestation were selected as controls.50 diagnosed preeclampsia cases > 20 weeks of gestation and with urine protein creatinine (P/C) ratio more than 0.3 were selected as cases. The cases were further divided into mild and severe. FBS, S. Creatinine, Urine protein and creatinine, Total cholesterol, Triacylglycerol, HDL-C, LDL-C, Uric acid, FRAP were measured. **Results:** In our study the decrease in (mean±S.D) values of TAS in PE was statistically significant when compared to controls(586.56 ±109.49 and 534.46 ±97.41,p Value=0.01). Total cholesterol, LDL-C and TAG levels were increased significantly in comparison to controls($p<0.001$). The decrease in HDL-C was not statistically significant($p=0.71$). FRAP correlated negatively with Total cholesterol in our study. **Discussion and conclusion:** The antioxidant levels are inversely proportional to dyslipidemia. Elevated LDL levels undergo oxidation to form oxidized LDL, which is involved in inflammation and free radical generation. In order to counteract the free radicals generated, antioxidant levels decrease. Hence decreased antioxidant status is associated with dyslipidemia, an important cardiovascular risk factor in preeclampsia.

KEYWORDS : PE: Preeclampsia, FRAP: Ferric reducing antioxidant power, TAS: Total Antioxidant status

INTRODUCTION

Preeclampsia is a serious complication of the second half of pregnancy that occurs with a frequency of 5-15% mechanisms.[1] Preeclampsia is characterized by an increased BP equal to or above 140/90 mmHg in the presence of proteinuria developed after 20 weeks of gestational age PE can result in eclampsia when convulsion develops or manifests as hemolysis, elevated liver enzymes and low platelet count (HELLP) syndrome. [2]

Oxidative stress has been implicated in the pathogenesis of several complication of human pregnancy including preeclampsia.[3] In preeclampsia dyslipidemia pattern of increased concentration of triglyceride, cholesterol and LDL and decreased concentration of HDL have been noticed.[4] Preeclampsia is associated with elevated lipid peroxidation and reduced antioxidant status.

The Ferric Reducing Antioxidant Power assay (FRAP) is a direct test of total antioxidant power, measures the ferric-to-ferrous iron reduction in the presence of antioxidants and is very simple and convenient in terms of its operation The FRAP assay measures the total reducing power of the antioxidant based on the fact that electron-donating antioxidants can be described as reductants. These reductants inactivate the oxidants in a redox reaction: one of the species is reduced while the other is oxidized, and it is this total reducing power that is referred to as total antioxidant power.[5]

AIMS AND OBJECTIVES

- To measure Total antioxidant status by FRAP method in preeclampsia
- To estimate lipid profile in preeclampsia
- To study the association of dyslipidemia with total antioxidant status in preeclampsia.

MATERIALS AND METHODS

The present study was carried out for one year on diagnosed patients of Preeclampsia attending the outpatient and inpatient departments of Narayana Medical College and Hospital, Nellore.

The study was undertaken on 50 Preeclampsia cases and 50 normal pregnant women. 50 normal healthy pregnant women of > 20 weeks of gestational age were selected as controls. 50 diagnosed preeclampsia cases > 20 weeks of gestational age ; SBP≥ 140 and DBP≥ 90 mm of Hg and with urine protein creatinine ratio more than o.3 were selected as cases for the study.

Pregnant women with conditions that may affect the oxidative parameters, such as anaemia, diabetes mellitus and other chronic illnesses were excluded from the study. Patients with family H/O hypertension and diabetes, patients taking vitamin A, E and C supplements and other drugs, which are known to affect antioxidant concentrations were excluded.

Pregnant women with a known kidney disease, heavy exercise (more than 1 hour of vigorous exercise on the day of urine collection) and bacteriuria were also excluded .The study was approved by Institutional ethical committee of Narayana Medical College and Hospital, Nellore, Andhra Pradesh and a written informed consent was obtained from the patients.

The Pre eclamptic women were further categorized into mild and severe based on the diagnostic criteria. Accordingly in the present study the Pre eclamptic women with SBP ≥ 140 & < 160 mm of Hg, DBP ≥90 & < 110 mm of Hg, and with no symptoms of headache, epigastric or right upper quadrant pain, visual disturbances were categorized as mild preeclampsia.

Women with SBP ≥ 160 mm of Hg, DBP ≥ 110 mm of Hg, and those who presented with history of headache, visual disturbances or epigastric / right upper quadrant pain were categorized as severe preeclampsia.

Among 50 cases 27 were mild preeclamptic and 23 were severe preeclamptic. The biochemical parameters estimated were Fasting blood sugar, Serum Creatinine, Urine protein, Urine creatinine, Total cholesterol, Triglycerides, HDL cholesterol, LDL cholesterol, Uric acid, FRAP using commercially available kits.The **mean and standard deviation** were calculated for all the Biochemical parameters. The significance between the groups were determined using **Student t- test** for Equality of means. The **p-value of < 0.05**

was considered significant

RESULTS AND DISCUSSION

The present study was conducted on fifty normal healthy pregnant women as controls and fifty preeclamptic women as cases. The cases were further divided into twenty seven women with mild preeclampsia and twenty three with severe preeclampsia.

Hypertension is the most common medical problem encountered in pregnancy and remains an important cause of maternal, and fetal, morbidity and mortality.[6] The pathophysiology of preeclampsia remains uncertain despite many research efforts.[7]

The association of alteration of serum lipid profile with PIH is well documented. An abnormal lipid profile is known to be strongly associated with atherosclerotic cardiovascular diseases. Some previous studies showed that the most dramatic damage that occurs in the lipid profile in normal pregnancy is serum hypertriglyceridemia.The principle modulator of this hypertriglyceridemia is oestrogen, as pregnancy is associated with hyperoestrogenaemia. Oestrogen induces hepatic biosynthesis of endogenous triglycerides, which is carried by VLDL .[8]

This process may be modulated by hyperinsulinism found in pregnancy.[9] Increased TG, found in pregnancy induced hypertension, is likely to be deposited in predisposed vessels, such as uterine spiral arteries and contributes to the endothelial dysfunction, both directly and indirectly through generation of small, dense LDL.[10]

The Preeclampsia is a state of hypoestrogenemia. The principal source of oestrogen in pregnancy is from DHEA formed in fetal adrenal glands. In preeclampsia, due to uteroplacental insufficiency, the lipids do not reach the fetal adrenal glands leading to impaired formation of DHEA. The state of hypoestrogenemia leads to decreased expression of VLDL / apo E receptors in the placenta that are essential for the lipid transport to the fetus. This results in reduced transport of VLDL to fetal compartment, which may be the reason for maternal hypertriglyceridemia.[12]

In the presence of increased triacylglycerol-rich lipoproteins, CETP activity is increased so that all circulating lipoproteins become enriched in triacylglycerol, in particular HDL and LDL particles. Triacylglycerol-rich HDL particles are converted by the triglyceride lipase activity of hepatic lipase into smaller particles which are better substrates for catabolic pathways.[13]Low level of HDL in pre-eclampsia is however not only because of hypooestrogenaemia but also due to insulin resistance .[14]

In our present study total cholesterol, triacylglycerol and LDL values were elevated in total cases when compared to controls(P-value<0.05,table.no.1). The decrease in HDL cholesterol was not significant when compared to controls(Table No.1). Among cases severe preeclamptic patients showed elevated values in total cholesterol and triacylglycerol levels when compared to mild preeclamptic patients(table.no.2,P value<0.05) This was in accordance with the study done by J.T.Gohil etal,[1] I. Cuneyt Evruke etal,[15] Pradnya Phalak[3] .

Preeclampsia remains a potentially dangerous complication of pregnancy. The cause remains largely unknown, but oxidative stress and a generalized inflammatory state are features of the maternal syndrome.

Table.No.1: Mean and SD values of Biochemical parameters in cases and controls

		controls		cases			
	units	Mean	S.D	Mean	S.D	P value	t value
SBP	mm/Hg	110.8	8	159.2	16.8	<0.0001	18.33
DBP	mm/Hg	73.6	5.6	103.6	8.9	<0.0001	20.04
FBS	mg/dl	82.88	7.31	84.64	16.4	0.49	0.69
S. Creat	mg/dl	1.04	0.23	1.24	0.42	<0.003	2.95
P/CRatio		0.13	0.02	0.64	0.26	<0.0001	13.82
TC	mg/dl	156.3	32.0	183.2	40.3	0.0004	3.695
TGL	mg/dl	107.28	37.2	142.38	32.4	<0.0001	5.02
HDL	mg/dl	46.92	12.2	44.4	10.3	0.27	1.10
LDL	mg/dl	85.6	18.8	112.6	27.2	<0.0001	5.77
Uric Acid	mg/dl	4.25	0.94	4.33	1.21	0.36	0.712
FRAP	µmol/l	586.56	109	534.46	97.4	0.01	2.51

Table. No.2 : Mean and SD values of Biochemical parameters in mild PE and severe PE

		Mild PE		Severe PE			
	units	Mean	S.D	Mean	S.D	P value	t value
SBP	mm/Hg	144.8	5.09	176.08	7.17	<0.0001	17.97
DBP	mm/Hg	97.03	4.65	111.21	6.28	<0.0001	9.15
S. Creat	mg/dl	0.92	0.15	1.61	0.33	<0.001	9.75
P/C Ratio		0.44	0.05	0.876	0.20	<0.001	20.90
TC	mg/dl	172.3	38.57	196.04	39.4	0.03	2.14
TGL	mg/dl	131.41	32.29	153.04	28.6	0.01	2.48
HDL	mg/dl	44.2	10.04	44.65	11.0	0.88	0.14
LDL	mg/dl	106.8	28.4	119.47	24.6	0.10	1.66
Uric Acid	mg/dl	4.03	1.04	4.69	1.32	0.05	1.97
FRAP	µmol/l	565.86	80.06	497.56	104	<0.001	2.61

Md.Zakir H etal[5] reported that PE is associated with increased **oxidative stress,** low **antioxidant activity** and increased **lipid peroxidation.** Shaarawy et al. [16] observed that serum total antioxidant status in mild and severe preeclampsia and eclampsia were significantly lower than that of healthy pregnant women. The increase in P/C ratio was in accordance with study conducted by Nahid shahbazian etal. We found that there is a significant correlation between the spot urine P/C ratio and 24-hour urine protein excretion in women with preeclampsia.[4]

The measurement of total antioxidant power in plasma provides information on global antioxidant status that may include antioxidants that are not yet recognized or easily measured individually.[12]

Several methods have been developed to assess the total antioxidant capacity of human serum or plasma because of the difficulty in measuring each antioxidant component separately and the interactions among different antioxidant components in the serum or plasma.[17]

In our present study FRAP levels were significantly decreased in cases when compared to control subjects(Table.no.1, P-value =0.01). Among cases, severe preclamptic patients showed significantly decreased levels when compared to mild preeclamptic patients. (Table.No.2,P-value<0.001). This was in accordance with the study conducted by Bosco etal [18]and Zusterzeel etal. [19]

Table. No : 3 Chisquare analysis of mean values of controls, mild PE and severe PE

	P value
TC	0.05
HDL-C	0.04
LDL-C	0.05
TAG	0.04
S. Creatinine	0.13
Uric acid	0.09
FRAP	0.03

Chisquare analysis on controls, mild PE and severe PE biochemical parameters showed a significant elevation of triacylglycerol (P-value<0.05, Table no.3). There was a decrease in HDL-C and FRAP values among controls, mild PE and Severe PE cases (P-value<0.05, Table no.3)

Table. No : 4 Correlation analysis in Mild PE

		r- value	P value
SBP Vs	TC	0.81	<0.05
	HDL-C	-0.42	<0.05
	P/C ratio	0.51	<0.05
DBP Vs			
	TAG	0.62	<0.05
	P/C ratio	0.72	<0.05
FRAP Vs	HDL	0.31	<0.05

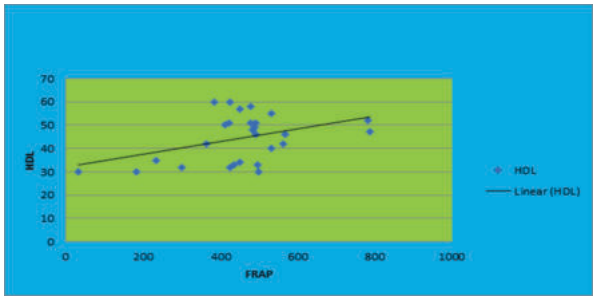

Figure. No : 1 Correlation graph of HDL with FRAP

Table. No : 5 Correlation analysis in severe PE

		r- value	P value
SBP Vs	TC	0.73	<0.05
	LDL-C	0.55	<0.05
	P/C ratio	0.84	<0.05
DBP Vs	TAG	0.43	<0.05
	P/C ratio	0.71	<0.05
	FRAP	-0.63	<0.05
FRAP Vs	TC	-0.33	<0.05
	LDL-C	-0.46	<0.05
	P/C ratio	-0.58	<0.05

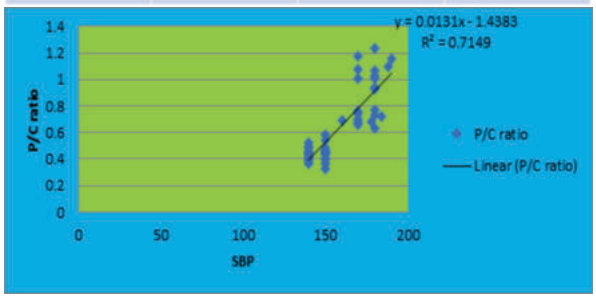

Figure. No : 2 Correlation graph of SBP Vs P/C ratio in severe PE

Correlation analysis on biochemical parameters was done in our study and a p value <0.05 was considered significant. Among mild PE cases (Table no.4) SBP (Systolic blood pressure) correlated positively with TC and urine P/C ratio, negatively correlated with HDL- C. DBP (Diastolic blood pressure) correlated positively with TAG and urine P/C ratio. FRAP correlated positively with HDL(Figure no.1)

Among Severe PE cases (Table no.5) SBP (Systolic blood pressure) correlated positively with TC, LDL-C and urine P/C ratio (Figure no.2). DBP (Diastolic blood pressure) correlated positively with TAG , urine P/C ratio and negatively with FRAP. FRAP correlated negatively with TC, LDL-C and urine P/C ratio.

CONCLUSION:

Preeclampsia is one of the most serious complications of pregnancy and free radical damage has been implicated in the pathophysiology of this condition. The antioxidant levels are inversely proportional to dyslipidemia. Elevated LDL levels undergo oxidation to form oxidized LDL, which is involved in inflammation and free radical generation.

In order to counteract the free radicals generated, antioxidant levels decrease. Total antioxidant activity is not a simple sum of individual antioxidants, but the dynamic equilibrium & cooperation between them. In our study, decreased antioxidant status was associated with dyslipidemia, an important cardiovascular risk factor in preeclampsia.

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