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STUDY OF SERUM LIPID PROFILE, MALONDIALDEHYDE AND PARAOXONASE IN NORMAL PREGNANT WOMEN AND IN PREGNANT WOMEN WITH PRE-ECLAMPSIA

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ABSTRACT

Introduction: *Pre-eclampsia is one of the most serious complications of pregnancy and the pathophysiology of the disease is not fully understood. There is substantiated evidence that the diverse manifestations of pre-eclampsia and discrete pathology in many organ systems are derived from pathologic changes within vascular endothelium. The theme of endothelial cell dysfunction emphasized its focuses on role of oxidative stress in pathogenesis of pre-eclampsia.* ***Objective:*** *The aim of this study was to evaluate the serum levels of lipid profile (TC, LDL-C, HDL-C and TG), malondialdehyde (MDA) as an end product of lipid peroxidation and paraoxonase (PON) as an antioxidant enzyme and their relationship in normal pregnant women and pregnant women with pre-eclampsia.* ***Materials and methods:*** *50 pregnant women with pre-eclampsia as cases and 50 normal pregnant women as controls in the age group of 20-45 years were included in the study. Serum MDA and PON were determined spectrophotometrically, serum TC, LDL-C, HDL-C and TG by end point method in a semi autoanalyser.* ***Results:*** *Serum levels of TC, LDL-C, TG and MDA were significantly increased; HDL-C and PON levels were significantly decreased in cases as compared to controls. Pearson's correlation analysis showed a significant negative correlation between serum PON and MDA levels. A significant negative correlation was seen between serum PON and LDL-C levels and significant positive correlation between PON and HDL-cholesterol levels.* ***Conclusion:*** *The atherogenic lipid profile with increased lipid peroxidation and decreased PON activity may be a significant contributor to endothelial dysfunction causing pre-eclampsia.*

KEY WORDS

HDL-C, LDL-C, MDA, PON,Pre-eclampsia, TC, TG.

INTRODUCTION

Pre-eclampsia (PE) is one of the most important diseases of pregnancy and is a major cause of maternal and fetal morbidity and mortality. Although it occurs in 4-5% of all pregnancies, the pathophysiology of this syndrome is not fully understood. Clinically, pre-eclampsia is characterized by hypertension and proteinuria. Increasing clinical and biochemical evidences suggest that disturbance of normal endothelial cell function may be a primary cause in the pathogenesis of pre-eclampsia. In classic studies, vascular lesions in the placental bed of women with pre-eclampsia were reported to be similar to atherosclerotic plaques. It has been suggested that an abnormal lipid profile may have a role in pathogenesis of pre-eclampsia. The proposed mechanisms of lipid mediated cardiovascular pathology in adults resemble those suggested for pre-eclampsia and chronic abnormal endothelial hyperstimulation through lipid peroxidation have been suggested as precursors to dysfunction and damage. Oxidation of LDL-cholesterol seems to be an important step in this process. LDL gets readily oxidized by MDA to form oxidized LDL which is taken up by the scavenger receptors of macrophages to form foam cells which leads to the formation of

atherosclerotic plaque and vascular endothelial damage in pre-eclampsia. [1]

MATERIALS AND METHODS

A cross sectional study was carried out in the Department of Biochemistry of J.J.M medical college Davangere from May 2012 to April 2013. A total number of 100 subjects in the age group of 20-45 years and ≥20 weeks of gestation were selected from the department of OBG of Bapuji Hospital and Chigateri General Hospital, Davangere (both these hospitals are attached to teaching institute, J.J.M. Medical College, Davangere). Of the 100 women, 50 pregnant women with pre-eclampsia as cases and 50 normal pregnant women as controls were included in the study. Informed consent was taken and the study was approved by ethical and research committee of J.J.M. Medical college, Davangere.

Inclusion criteria: Fifty proven cases of PE in the age group of 20-45 years.

Pregnant women of ≥20 weeks of gestation with blood pressure of ≥140/90mmHg noted for the first time during pregnancy on ≥2 occasions at least 6 or more hours apart and with proteinuria of ≥1+ (≥30mg/dl) by dipstick method in a random urine sample were included in the study as cases.

Fifty age matched normal pregnant women with ≥20 weeks of gestation diagnosed based on clinical, biochemical and ultrasound findings and without any major illness and who were not on any medications were included as controls in the study.

Exclusion criteria: Pregnant women with chronic hypertension that was present before pregnancy, diabetic and on insulin therapy or on antihypertensive or any hypolipidemic drugs or on antioxidant medication, proven liver or cardiac or renal diseases or any other major illness with gestational diabetes, multiple pregnancy, abruptio placenta/hydatidiform mole/molar pregnancy were excluded from the study.

Methods: After 12 hours of overnight fasting about 5 ml of venous blood was drawn from the subjects including both cases and controls under aseptic precautions in a sterile plain bulb and allowed to clot. The serum was separated by centrifugation and used for estimation of levels of TC by CHOD-PAP method, HDL-C by phosphotungstic acid method, TG by GPO-Trider end point method, with the commercially available kit method for ERBA CHEM-5 v2 plus semiautoanalyser.[2] Serum LDL-Clevel was calculated from the measured parameters by Friedwald formula [2] and serum MDA level was estimated by Nadiger et al method [3]and serum PON level by Mackness and Mackness method. [4]

RESULTS

Results are expressed as mean±SD and range values. Student's unpaired t-test is used for comparing the means of two groups. Relationship between parameters is assessed by Pearson's correlation coefficient. For all the tests, the probability value (p-value) of <0.05 is considered statistically significant.

A significant elevation in serum levels of TC, LDL-C and TG ($p<0.001$) and significantly decreased serum level of HDL-C ($p<0.05$) was seen in pre-eclampsia as compared to controls (**Table 1**). The mean MDA levels in cases and controls is 7.22±1.53 and 2.53±0.90 respectively. MDA is increased significantly ($p<0.001$) in pre-eclampsia as compared to controls. The mean PON levels in cases and controls is 58.52±9.25 and 91.98±12.88. PON levels were significantly decreased ($p<0.001$) in cases as compared to controls (**Table 2**). A statistically significant ($p<0.001$) negative correlation was seen between PON and MDA with r value of -0.64 and between PON and LDL-C with r value of -0.29 which is statistically significant ($p<0.05$). A statistically significant ($p<0.05$) positive correlation was found between PON and HDL-C with r value of +0.41 (**Table 3**).

Table 1: The serum levels of TC, LDL-C, HDL-C, TG in normal pregnant women and pregnant women with PE.

		Controls (n=50)	PE (n=50)	Controls V/s PE		
				Mean diff	t value	p value
TC mg/dl	Mean±SD	189.7±20.3	229.2±22.4	39.5	9.25	<0.001**
	Range	127.3-225.0	199.0-290.0			
LDL-C	Mean±SD	123.5±17.8	156.5±23.2	33.0	8.00	<0.001**

mg/dl	Range	68.0-157.0	124.0-217.9			
HDL-C	Mean±SD	36.36±5.20	32.43±5.76	3.93	3.58	<0.05*
mg/dl	Range	28.0-53.0	23.5-53.0			
TG	Mean±SD	160.7±26	202.1±22.3	41.4	8.54	<0.001**
mg/dl	Range	99.0-213	135.0-266.8			

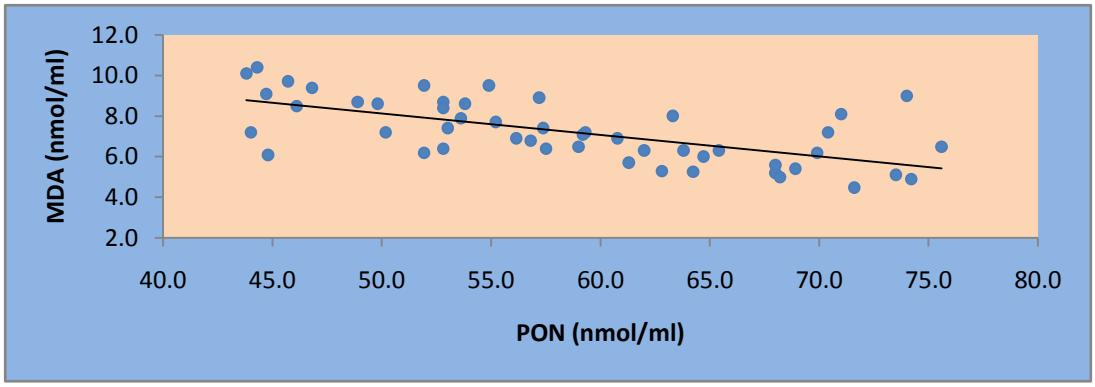
Table 2: The serum levels of MDA and PON in normal pregnant women and in pregnant women with PE.

		Controls (n=50)	PE (n=50)	Controls v/s PE		
				Mean Diff	t value	p value
MDA nmol/ml	Mean±SD	2.53±0.90	7.22±1.53	4.69	18.66	<0.001**
	Range	1.20-4.50	4.47-10.40			
PON nmol/ml	Mean±SD	91.98±12.88	58.52±9.25	33.47	14.92	<0.001**
	Range	65.4 -113.52	43.8-75.6			

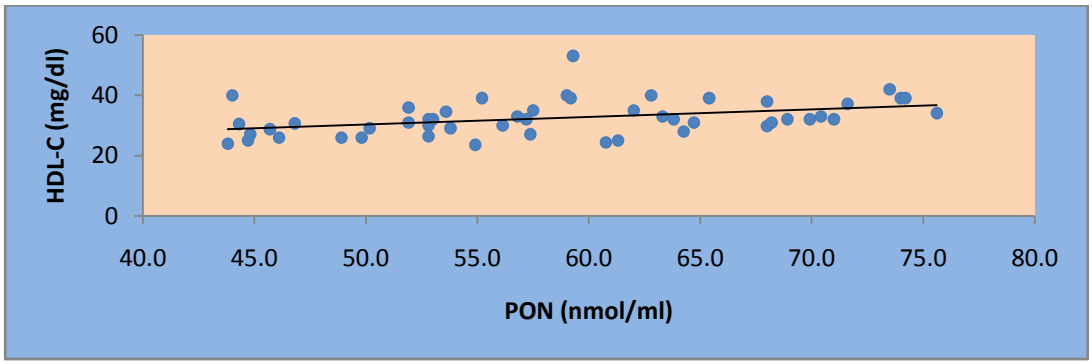
Table 3: correlation between serum MDA and PON and between serum PON and HDL-C and between serum PON and LDL-C in PE cases

Correlation	r value	p value
PON vs MDA	-0.64	< 0.001**
PON vs LDL	-0.29	<0.05*
PON vs HDL	+0.41	<0.05*

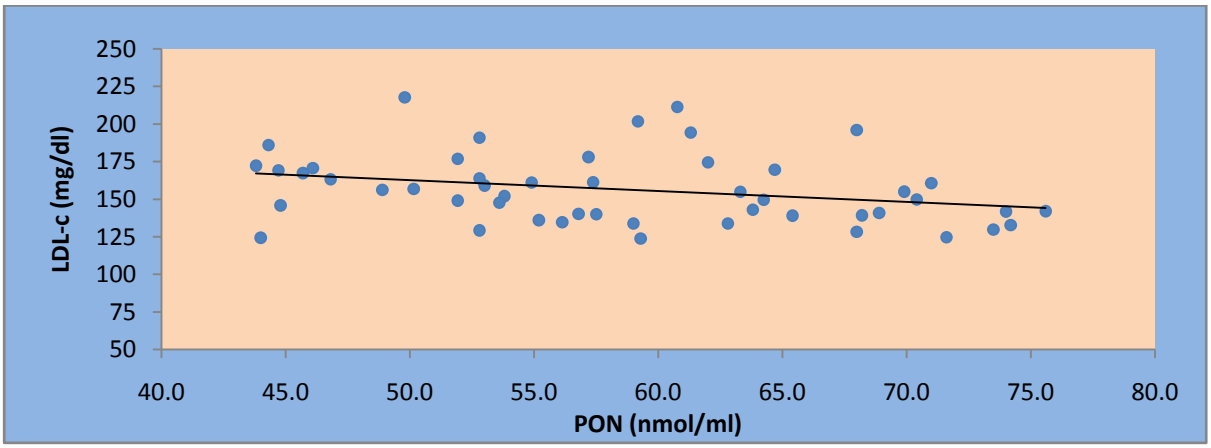
Graph 1: Correlation between serum MDA levels and serum PON levels in pregnant women with PE.



Graph 2: Correlation between serum HDL-cholesterol levels and serum PON levels in pregnant women with PE.



Graph 3: Correlation between serum LDL-cholesterol levels and serum PON levels in pregnant women with PE.



DISCUSSION

The pathophysiology of pre-eclampsia is poorly understood. Free radicals and other damaging reactive oxygen species predominantly supueroxide anions are increased in oxidative stress and their activation is thought to increase during pre-eclampsia.[5] It has been postulated that defective placentation leads to placental hypoxemia which initiates cascade of events including excessive lipid peroxidation in placental tissue. In pre-eclamptic women, increased placental production and elevated circulating levels of lipid peroxides have been well documented.[6] It is suggested that imbalance between lipid peroxidation products and antioxidant activity are an important factor in the pathogenesis of pre-eclampsia.[1] Recent studies suggested that endothelial cell injury may be the initiator of the pathophysiological events of pre-eclampsia. Either placental overproduction of lipid peroxides or decreased placental antioxidant enzyme activity can lead to endothelial dysfunction. Increased production of lipid peroxidation products and insufficient antioxidant capacity leads to oxidative stress and subsequently oxidative injury may occur in both the maternal and placental compartments. A number of reports indicate that blood levels of lipid peroxidation products are elevated in women with pre-eclampsia relative to normal pregnancy. Furthermore; the placental production of lipid peroxides have been demonstrated to be abnormally increased in pre-eclampsia.[5] In the present study there is increase in serum levels of MDA, the lipid peroxidation product in the pre-eclamptic women, which is consistent with the earlier reports.[7.8] In the present study we observed significantly elevated serum levels of TC, LDL-C and TG and significantly decreased serum levels of HDL-C in pre-eclamptic women compared to the normal pregnant women due to the hormonal changes seen in PE, this significant rise in lipid levels is in agreement with the previous published reports.[9,10,11] This raised lipid levels might have a causal role in the pathogenesis of pre-eclampsia. It is reported that in pre-eclampsia; LDL-cholesterol gets readily oxidized by lipid peroxides and this oxidized lipid contributes to vascular endothelial damage.[12] Pre-eclampsia is associated with increased utilization of antioxidants. Several studies have demonstrated decreased serum levels of antioxidant enzyme PON in pre-eclamptic women compared to normal pregnant women [1, 13, 14]; similarly in the present study we have observed a significant decrease in serum levels of PON in the pre-eclamptic women. PON which is bound to HDL acts as an antioxidant that protects the LDL from the oxidative modifications. The reduction in the activitiy of PON may be related to liver damage as damaged liver cells are not able to express PON or may be a consequence of decrease in HDL levels.[1] Hence prevention of LDL oxidation by PON may play an important role in preventing the development of pre-eclampsia.

CONCLUSION

The results of the present study suggests that an abnormal lipid profile, increased lipid peroxidation (MDA) and decrease in the activity of antioxidant enzyme PON may play a role in the pathogenesis of pre-eclampsia. However further studies are needed in large scale to understand the pathogenic mechanism of pre-eclampsia.

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