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Lipid Peroxidation in the Patients of Pre-Eclampsia

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Abstract

Objective

To assess the level of lipid peroxidation by measuring the level of malondialdehyde in the patients of pre-eclampsia.

Introduction

Pre-eclampsia complicates 3-5% of pregnant women worldwide during their second half of pregnancy. It is a major cause of maternal and perinatal mortality and morbidity worldwide. In preeclampsia, oxidative stress is demonstrable both in the placenta and in the maternal circulation. Lipid peroxidation has been blamed to be the main causative factor for oxidative stress in preeclampsia. Lipid peroxidation refers to the oxidative degradation of lipids of the cell membranes. Malondialdehyde is a major breakdown product of lipid peroxides. We will assess the level of lipid peroxidation by measuring the level of serum malondialdehyde.

Material and Methods

Serum Malondialdehyde (MDA) was measured in terms of micromoles of TBARS formed/ml of blood with ohkawa et al 1979 method (with slight modification).

Results

Serum MDA was significantly increased in pre-eclamptic patients as compared to normal pregnants (P value < 0.01). We do not found any significant change in serum MDA levels with increasing maternal age; neither in pre-eclamptics nor in normal pregnant. Serum MDA levels were significantly increased in pre-eclamptic group having DBP > 100 mmHg as compared to pre-eclamptic group having DBP = 90-100 mmHg (P value < 0.01). There was no significant change in MDA levels in nulliparous and multiparous; neither among pre-eclamptics nor among normal pregnant (P value > 0.05).

Conclusion

Increased lipid peroxidation is an important factor in the pathogenesis of pre-eclampsia.

Keywords : Lipid Peroxidation, Pre-eclampsia, Hypertension

Introduction

Pre-eclampsia is defined by the International Society for the Study of Hypertension in Pregnancy as "*Gestational hypertension of at least 140/90 mmHg on two separate occasions ≥4 hours apart accompanied by significant proteinuria of at least 300 mg in a 24-hour collection of urine, arising de novo after the 20th week of gestation in a previously normotensive woman and resolving completely by the 6th postpartum week*".[1] Pre-eclampsia complicates 3-5% of pregnant women worldwide during their second half of pregnancy.[2] It is a major cause of maternal and perinatal mortality and morbidity worldwide.

Preeclampsia is the third leading cause of maternal mortality in the United States and accounts for 20% of maternal deaths.[3] In developing countries, it is a leading cause of maternal mortality, causing an estimated >60,000 maternal deaths worldwide per year.[2] Delivery of the placenta remains the only known treatment for this clinical disease, suggesting that the placenta is the principal contributor to the pathogenesis of pre-eclampsia.[2]

In preeclampsia, oxidative stress is demonstrable both in the placenta and in the maternal circulation.[4,5] Lipid peroxidation has been blamed to be the main causative factor for oxidative stress in preeclampsia. Lipid peroxidation refers to the oxidative degradation of lipids. It is the process in which free radicals steal electrons from the lipids in cell membranes, resulting in cell damage. Free radicals initiate lipid peroxidation by attacking polyunsaturated fatty acids in cell membranes.[6]

Uncontrolled peroxidation of fatty acids and cholesterol alter membrane fluidity and permeability as lipid peroxides are toxic compounds that damage endothelial cells, increase peripheral vasoconstriction, increase thromboxane synthesis and decrease prostacyclin synthesis.[7] Once steady state levels of lipid peroxides begin to rise, the stage would be set for self perpetuating chain-reaction processes to take place. Endothelial contact with lipid peroxides would allow peroxidative damage of endothelial cell membrane lipids. This ultimately reduce the ability of the endothelium to act as permeability barrier to plasma components. Exposure of vascular endothelium to lipid peroxides would begin to shut off production of prostacyclin, increasing the propensity for vasoconstriction and platelet aggregation.[8] Tissue hypoxia stimulates lipid peroxidation[9] and if this occurred in the ischaemic placenta, lipid peroxides could be released or circulating fatty acids could be oxidised such that plasma levels of peroxidised lipid increase. Lipid peroxidation products are injurious to endothelial cells *in vitro.*[10] It is attractive, therefore, to implicate these moieties in the pathogenesis of pre-eclampsia. Measures of lipid peroxidation assayed in pre-eclamptic subjects include malondialdehyde, lipid hydroperoxides and conjugated dienes.

Malondialdehyde is a major breakdown product of lipid peroxides. Most authors have found elevated circulating malondialdehyde levels in pre-eclampsia compared with normal pregnancies.[11,12] S.V. Kashinakunti et al (2010) has done a case control study with 30 preeclamptic patients and 30 healthy pregnant controls.[13] They found that MDA was significantly increased in preeclamptic patients as compared to healthy controls. We compared serum malondialdehyde levels of pre-eclampsia patients with those of normal pregnant women.

Material and Methods

Selection of Cases

In this study the work was conducted on the newly diagnosed cases of pre-eclampsia. Thirty pre-eclamptic women in third trimester of pregnancy were selected from Obstetrics and Gynaecology Inpatient Department of J.N. Medical College Hospital. A.M.U., Aligarh between October 2013 and March 2014.

Selection of Controls

Thirty women with normal pregnancy in their third trimester and apparently good health were selected as controls. They were selected from Antenatal Clinic of Obstetrics and Gynaecology Department, J.N. Medical College Hospital, Aligarh.

Informed consent (in accordance with the Helinski Declaration of 1975, revised in 1983) was taken from the cases and controls for participation in the study with approval of institutional Ethical Committee, J.N. Medical College Hospital, Aligarh.

Exclusion Criteria

1. Maternal age less than 20 years and more than 30 years.
2. Pre-eclamptic patients who were suffering from such a disease in which oxidative stress was implicated in the pathophysiology, for e.g, diabetes, hypertension etc.
3. Patients of Gestational Hypertension.
4. Patients with history of smoking and alcohol intake.
5. Duration of pregnancy less than 30 weeks.
6. Patients taking antioxidants.

Biochemical Analysis

The blood samples were collected in EDTA vials for serum Malondialdehyde estimation. All the samples were centrifuged in the lab and serum was separated for study. Following biochemical parameter was estimated:

Serum Malondialdehyde (MDA)

It was measured in terms of micromoles of TBARS formed/ml of blood with ohkawa et al 1979 method (with slight modification).

Study Design

In the present study the subjects were grouped into cases and controls. They were further divided into groups on the basis of gestational age, parity, diastolic blood pressure, and maternal age. The values of various parameters under study were compared with that of matched controls.

Statistical Analysis of Data

Results were analysed using appropriate statistical tests with the help of GraphPad Prism-5.0 software.

1. Mean
2. Standard deviation (S.D.)
3. T- test
4. **Observations and Results**

Table 1: Mean Values of Serum Malondialdehyde in Normal Pregnant and Pre-eclampsia Patients.

Mean value of serum MDA (µmoles of TBARS formed/ml of serum)	Controls	Pre-eclampsia
	0.460 ± 0.201	0.780 ± 0.334 *

* P value < 0.01 which is significant

Table 2: Mean Values of Serum MDA in < 25years and > 25 Years Age Groups in Normal Pregnant Women and Pre-Eclampsia Patients

Mean value of MDA (µmoles of TBARS formed/ml of blood)	Controls		Pre-eclampsia	
	< 25 yrs	>25 yrs	<25 yrs	>25yrs
	0.434 ± 0.116	0.496 ± 0.288 *	0.783 ± 0.416	0.776 ± 0.161 *

*P value > 0.05 which is insignificant

Table 3: Mean Levels of Serum MDA in Pre-Eclamptics Divided Into Two Groups According To Diastolic Blood Pressure.

Mean value of serum MDA in micromoles	Normal Pregnant; DBP ≤ 90 mm Hg	Pre-eclampsia DBP - 90-100 mm Hg	Pre-eclampsia DBP > 100 mm Hg
	0.460 ± 0.201	0.525 ± 0.216	0.950 ± 0.289*

*P value < 0.01 which is significant

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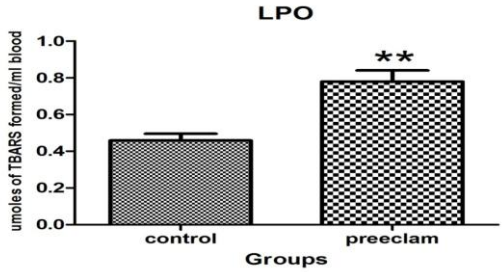
Table 4: Mean Value of Serum MDA in Nulliparous and Multiparous Groups in Normal Pregnant and Pre-Eclampsia

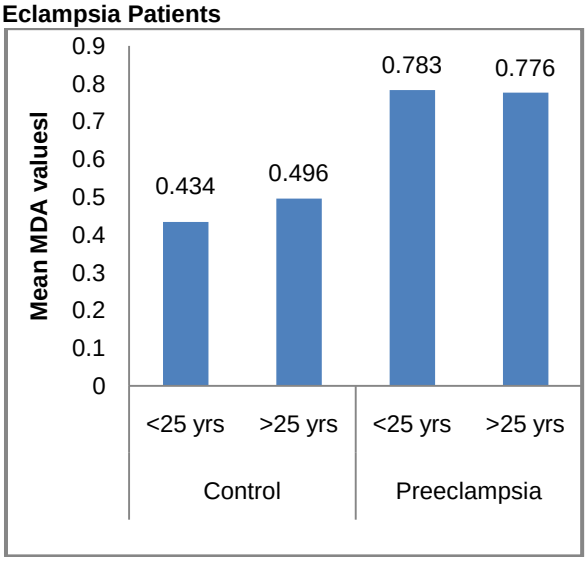
Mean value of serum MDA(µmoles of TBARS/ml blood)	Normal pregnant women		Pre-eclampsia patients	
	Nullipara (N= 15)	Multipara (N= 15)	Nullipara (N=18)	Multipara (N= 12)
	0.073 ± 0.021*	0.070 ± 0.017	0.111 ± 0.038	0.125 ± 0.052*

*P value > 0.05 which is insignificant

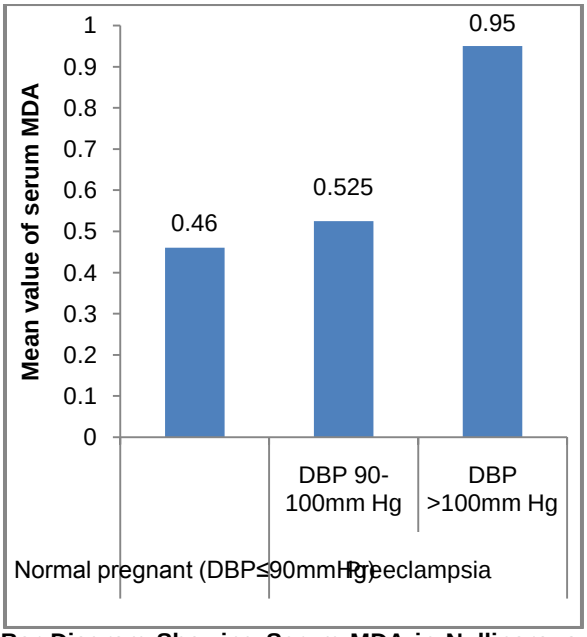
Bar Diagram Showing Serum Malondialdehyde in Pre-Eclampsia and Normal Controls



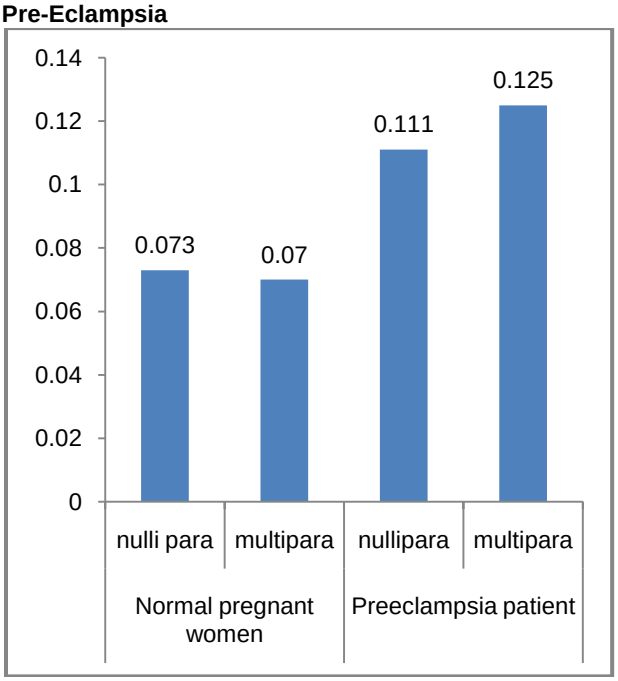
Bar diagram Showing Serum MDA Levels in Two Age Groups in Normal Pregnant Women and Pre-Eclampsia Patients



Bar Diagram Showing Serum MDA in pre-Eclamptics Divided into Two Groups According to Diastolic Blood Pressure



Bar Diagram Showing Serum MDA in Nulliparous and Multiparous Groups in Normal Pregnant and Pre-Eclampsia



Discussion

Pre-eclampsia has many effects on the body. Some of these effects manifest clinically and some become evident only on hematological investigations. One such hematological effect in pre-eclampsia patients is increase in oxidative stress. The main cause of oxidative stress found in pre-eclampsia is lipid peroxidation. Lipid peroxidation refers to oxidative degradation of lipids present in the cell membranes. It is a well established mechanism of

cellular injury, and is used as an indicator of oxidative stress in cells and tissues. Most important marker of lipid peroxidation is Malondialdehyde (MDA) which is a byproduct of lipid peroxidation.

Many studies have found that lipid peroxidation is increased in normal pregnancy. Main aim of our study is to find out the level of lipid peroxidation in preeclampsia. In our study we found that the levels of malondialdehyde (MDA) were increased significantly in pre-eclampsia patients as compared to normal pregnant females (P value<0.0001) as shown in table1. This increase signifies that lipid peroxidation is increased in pre-eclampsia patients as compared to normal pregnant. Our result is in accordance with results of S.V. Kashinakunti et al (2010).[13] They has done a case-control study with thirty cases of pre-eclampsia and thirty normal pregnant women as controls. They found increased serum malondialdehyde levels in pre-eclampsia patients as compared to normal pregnant controls.

We divided Pre-eclamptic patients into two groups according to maternal age; (i) age ≤ 25 yrs (ii) age > 25 yrs. We do not found any significant change in serum MDA levels with maternal age (P value > 0.05). Mohanty S and Nayak N (2006) concluded in their study that in their geographical area (South India) younger maternal age contributes to increased risk of pregnancy induced hypertension.[14] In their study 26% of PIH patients were < 20 years of age and only 15% of controls were > 20 years of age. In our study no significant change was found in preeclamptics of less than 25 years age group. Reason may be change in geographical distribution of pre-eclamptic patients as compared to above studies.
Pre-eclamptic patients were divided into two groups according to diastolic blood pressure (DBP). (i) DBP = 90-100 mmHg (ii) DBP > 100 mmHg Mean levels of serum malondialdehyde (MDA) were significantly increased in pre-eclamptic group having DBP > 100 mmHg as compared to pre-eclamptic group having DBP = 90-100 mmHg (P value < 0.01). In our study, all the subjects were also grouped into nulliparous and multiparous and MDA levels were calculated. In pre-eclamptic group 60% subjects were nulliparous (N=18) and 40% subjects were multiparous (N=12). We do not found any significant change in MDA levels in nulliparous and multiparous pre-eclamptics (P value > 0.05). In normal pregnant group 50% subjects were nulliparous (N=15) and 50% subjects were multiparous (N=15). We also don't found any significant change in MDA levels in nulliparous and multiparous normal pregnant women (P value > 0.05). We found only one study in support of our finding. Rajasingham and Seed et al (2009) found in a prospective study that high incidence of pre-eclampsia was unrelated to oxidative stress markers in nulliparous women.[15] Further studies are required to find the status of oxidative stress.

Conclusion

We conclude from our study that increased lipid peroxiation is an important factor in the pathogenesis of pre-eclampsia because lipid peroxides damage endothelial cells and produce vasoconstriction

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