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Original Article

Study of Serum Malondialdehyde Level in Pre-eclampsia

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ABSTRACT

The current theory suggests that in preeclampsia there is an increase in the lipid peroxidation products and leads to a decrease in the plasma antioxidants except uric acid and changes in the lipid profile levels, contributing to the pathogenesis of preeclampsia. In this context, this study was undertaken to determine the changes in plasma levels of lipid peroxide, in women with preeclampsia. Objectives:.To measure the levels of serum malondialdehyde in pre-eclampsia in comparison with normal pregnancy. Materials and Methods: Study consisting of 30 preeclamptic and 30 healthy pregnant women. Fasting venous blood samples were collected during antepartum period and plasma level of malondialdehyde is estimated.Results: In the preeclamptic group malondialdehyde, a lipid peroxidation product was significantly increased. Conclusion:The findings of the present study are consistent with previous studies, suggesting that lipid peroxidation is important factors in the pathogenesis of preeclampsia.

1. Introduction

Pregnancy is a physiological stress in which many changes occur in the milieu interior of the body, more and more stress is being laid on the biochemical changes, which occur in the blood during the normal pregnancy and becomes exaggerated in complications of pregnancy like pre-eclampsia[1]. Pre-eclampsia is defined as a pregnancy-specific syndrome observed after the 20th week of pregnancy with systolic blood pressure of 140 mm of Hg or diastolic blood pressure of 90 mm of Hg accompanied by significant proteinuria (i.e., urinary excretion of 0.3 g protein in a 24-h specimen).In women with pre-eclampsia, blood pressure usually returns to baseline within days to weeks after delivery[2].

Pre-eclampsia is a complex multisystem disorder seen exclusively in the human species. Worldwide, it is a leading cause of maternal and fetal morbidity and mortality [3]. Pre-eclampsia is a hypertensive disorder which develops in late pregnancy and is usually associated with placental hypoxia and dysfunction[6].

Various factors are implicated in the pathogenesis of pre-eclampsia, including genetic, immune, vascular and oxidative stress [7]. Pre-eclampsia occurs during second and third trimester of pregnancy and is more common in nulliparous women .Proteinuria is an important sign of pre-eclampsia and Chesley (1985) rightfully concluded that the diagnosis is questionable in its absence[1].

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It is well known that oxidative stress increases during normal pregnancy. In healthy pregnancy, it has been reported that plasma lipid hydro peroxides levels are increased.More oxidative stress in pre-eclampsia results in lipid peroxides, reactive oxygen species and super oxide anion radicals to cause endothelial injury and dysfunction, platelet and neutrophil activation, increased cytokines, superoxide radical production and endothelial damage in a vicious cycle[4]

An increase in resistance to angiotensin, a predominance of lipid metabolism over glucose utilization and an increased synthesis by the liver of thyroid and steroid-binding proteins, fibrinogen and other proteins are characteristic of pregnancy. Plasma lipids and lipoproteins undergo both quantitative and qualitative changes during pregnancy[5]

The present study has been undertaken to determine the serum level of peroxidation product i.e. Malondialdehyde (MDA) in women with pre-eclampsia.

MATERIALS AND METHODS

The study was carried out in 30 pre-eclampsia primi patient and 30 normotensive primi pregnant controls who attended the outpatient and inpatient departments of Kempegowda Institute of Medical Sciences, Bangalore during the year 2011-12. The institutional ethical committee approved the study protocol. Inclusion criteria: Cases of pre-eclampsia primi patients in the age group of 18 to 30 years and with gestation age more than 20 weeks.Controls of normotensive primi pregnant women in the age

group of 18 to 30 years and more than 20 weeks of gestation.Exclusion criteria: Elderly primi gravida subjects, gestational diabetes, chronic hypertension, multiple gestation, those with family history of pre-eclampsia, acute and chronic infections, renal diseases, liver diseases, endocrine disorders, smokers, alcoholics and with history of multivitamin intake.Method of collection of data Informed consent was taken from patients and controls. A pre-structured and pre-tested proforma was used to collect the data. Baseline data including age and BMI, detailed medical history, clinical examinations and relevant investigations were included as part of the methodology. Specimen collection: Blood: 5 ml plain venous blood sample after overnight fasting was obtained by venepuncture from both cases and controls. This was followed by centrifugation and then sample was processed immediately. Estimations of serum Malondialdehyde were performed using the serum.

Estimation of Serum Malondialdehyde by TBA method. [14,15,16]

Principle: Malondialdehyde (MDA), a reactive aldehyde is a product of lipid peroxidation. It reacts with thiobarbituric acid (TBA) to form pink colored complex of TBA-MDA adduct and this color is measured at 532 nm. The formation of the MDA-TBA adduct is initiated by a nucleophilic attack involving carbon-5 of TBA onto carbon-1 of MDA, followed by dehydration and a similar reaction of the intermediate MDA-TBA adduct with a second molecule of TBA.

Reagents: TBA (0.67%w/v) was prepared by dissolving 335 mg TBA in 50 ml of water. TCA (40%w/v) was prepared by dissolving 20g TCA in 50 ml of water.

Procedure: One ml of serum was mixed with each 1 ml of TCA and TBA. For blank, 1 ml of distilled water was mixed with 1 ml of TCA and TBA. Both the test tubes were kept in boiling water bath and cooled with ice-cold water and centrifuged at 3000 rpm for 10 minutes. The upper clear supernatant fluid was transferred to a cuvette and the absorbance was measured at 530 nm with a spectrophotometer after adjusting to zero with blank.

Calculation: The MDA level (nmol/l) of serum was calculated based on the molar absorption coefficient of MDA. The molar absorption coefficient for 1 mol/L of MDA is 1.56×10^5.

RESULTS

The present study is undertaken to evaluate the significance of serum malondialdehyde levels in pre-eclampsia.30 pre-eclampsia cases were considered for the study. 30 ages matched normotensive primi pregnant were chosen as controls.

Statistical test used: arithmetic mean, standard deviation, student paired t test

Distribution of study sample according to age group

Table No 1: Age distribution of cases and controls

Age in years	Cases		Controls	
	Number	%	Number	%
≤ 20	4	13.33	2	6.67
21-24	10	33.33	19	63.33
≥25	16	53.34	9	30.00
Total	30	100.00	30	100

Table No 2: Distribution of gestational age in cases and controls

Gestational age in weeks	Cases		Controls	
	Number	%	Number	%
22 - 28	13	43.33	16	53.33
29 - 34	17	56.67	14	46.67
Total	30	100	30	100

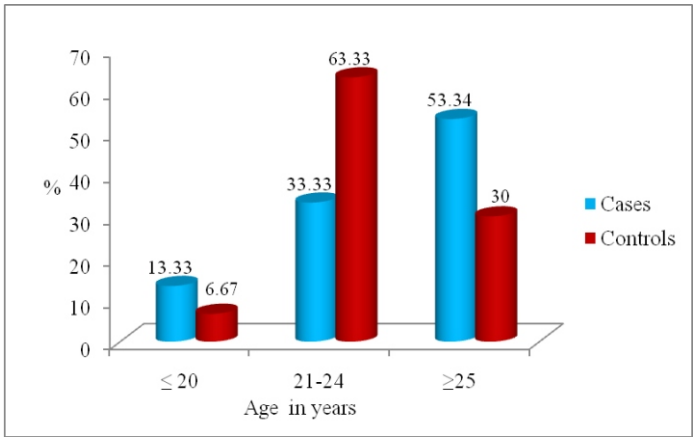
Table No 3: Blood Pressure Levels in cases and controls

		Cases	Controls	t test values	P values
BP (mm Hg)	SBP	167.07 ± 12.82	123.93 ± 5.32	17.02	0.001
	DBP	98.67 ± 2.43	78.4 ± 3.08	28.31	0.001

Table No 4: Biochemical parameters to assess MDA levels in cases and controls

Biochemical parameters	Cases	Controls	t test value	p values
MDA (nmol/L)	223.68 ± 25.59	79.90 ± 7.84	29.43	0.001

Fig No 1: Bar diagram showing age distribution of cases and controls



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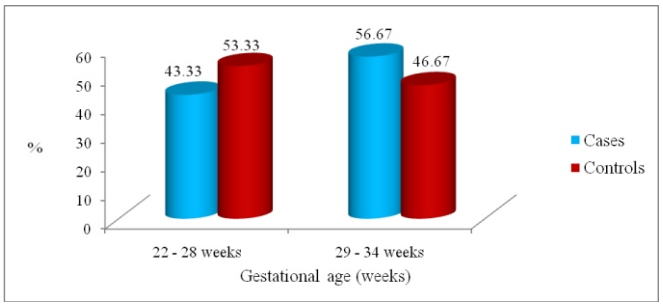
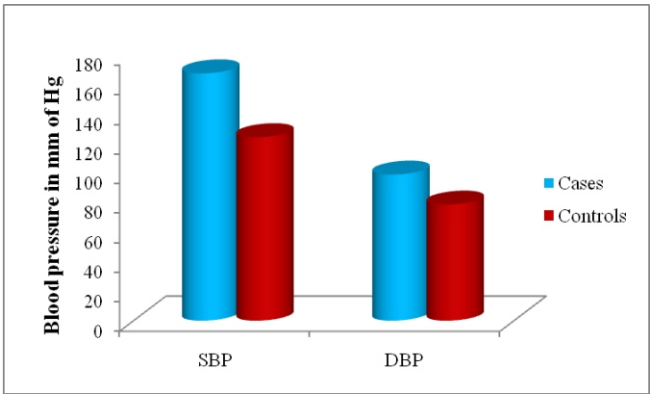
Distribution of study sample according to age group

Fig No 2: Bar diagram showing distribution of gestational age in cases and controls



The distribution of the study samples according to the gestational age is given in Table 2 and graphically represented in fig.2. The cases and controls are divided into 2 groups (22-28 weeks and 29-34 weeks). Maximum numbers of cases are in the gestational age group of 29-34 weeks (56.67%) and maximum numbers of controls are in the gestational age group of 22-28 weeks (53.33%). **Comparison of Blood Pressure between cases and controls**

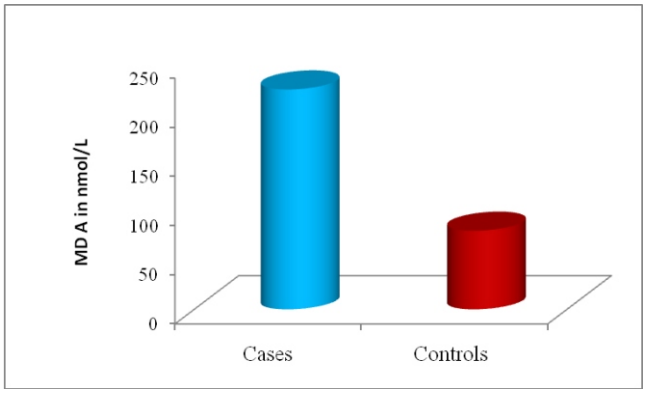
Fig No 3: Bar diagram showing Blood pressure ranges in cases and Controls



Comparison of Blood Pressure between cases and controls are shown in the Table 3 and graphically represented in fig.3, respectively. The mean value of systolic blood pressure among cases as compared to controls was statistically significant, (p value < 0.001,t test value 17.02) and mean value of diastolic blood pressure among cases as compared to controls was statistically significant,(p value < 0.001,t test value 28.31).

Biochemical parameters to assess MDA Levels in cases and controls

Fig No 4: Bar diagram showing MDA level in cases and controls



Comparison of Biochemical parameters to assess lipid peroxidation between cases and controls are shown in the Table 4. The mean serum malondialdehyde levels is higher among cases as compared to controls was statistically significant (p value <0.01, t test value 29.43). Distribution of controls and cases according to serum malondialdehyde level is graphically represented in Fig. 4.

DISCUSSION

Preeclampsia remains one of the most serious complications of pregnancy. The pathophysiology of the disease remains poorly understood. The exact cause of preeclampsia remains elusive; placental ischemia, immune maladaptation, genetic factors are probably all involved to some extent. In normal pregnancy the diameter of the spiral arteries increases greatly due to trophoblastic invasion of the spiral arteries in the decidual and myometrial segments of the placental bed, whereas in preeclampsia such physiological adaptation does not occur[18]. Abundant evidence indicates reduced placental perfusion in preeclampsia [19]. Implantation is superficial in preeclampsia. In particular, cytotrophoblasts fail to invade the spiral arterioles. As a result, these vessels do not enlarge, severely compromising their ability to deliver maternal blood to the intervillous space. Predisposing to the medical condition[20]. Recent investigations suggest that endothelial cell injury may be the initiator of the pathophysiological events of preeclampsia[12].

. Feto-placental unit may be the origin of oxygen free radicals and lipid peroxides [21,22]. Reactive oxygen species can cause cellular damage by oxidizing nucleic acids, proteins and membrane lipids[17]. They may also influence vascular tonicity, either indirectly by inactivating the endothelium derived relaxing factor, which is nitric oxide, and reducing the release of prostacyclin or directly by contracting smooth muscles [23]. Such events establish a cycle ultimately leading to manifestations of preeclampsia [11]. Thus uncontrolled lipid peroxidation may play an important role in the pathophysiology of preeclampsia.

Preeclampsia is associated with an imbalance between the oxidant and antioxidant status. Preeclamptic patients are exposed to increased oxidative stress. Either placental hyper secretion of lipid peroxides or decreased placental antioxidant enzyme activity

can lead to endothelial dysfunction. Insufficient antioxidant capacity leads to oxidative stress, and subsequently, oxidative injury may occur in both the maternal and placental compartment[13].

Uncontrolled lipid peroxidation may contribute to various disease processes via disruption of membrane lipids and cell components [11]. Lipid peroxidation of membrane associated fatty acids and cholesterol may alter cell membrane fluidity and permeability, causing cell membrane damage [9]. The byproducts of tissue lipid peroxidation propagate further lipid peroxidation in the same tissue and at sites distal to areas of initial damage [23]. A number of reports indicate that blood levels of lipid peroxidation products are elevated in women with preeclampsia relative to normal pregnancy [8,24]. Further more placental production of lipid peroxides has been demonstrated to be abnormally increased in preeclampsia [21]. Consistent with previous reports, in the present study there is significant increase in plasma levels ($P < 0.001$) of malondialdehyde in preeclamptic pregnancies.

The present study suggested that vascular endothelial cell dysfunction in preeclampsia may be caused by uncontrolled lipid peroxidation which overwhelms the protective mechanisms of the antioxidants. Vascular contact with placenta originated circulating peroxidation products may cause dysfunction of the vascular endothelium by promoting peroxidative damage of endothelial cell membranes. Since antioxidant deficiency is a cause of lipid peroxide accumulation, vitamin C therapy may alter the disease process if initiated in early gestation to patients at risk. Further studies are needed to clarify the effectiveness of prophylactic antioxidant therapy in preeclampsia [11]. Thus, in preeclampsia, placental abnormality and the associated metabolic changes cause increased oxidative stress [13].

The interaction of plasma lipids, free radicals, and endothelial cells is hypothesized to be of major importance in the early development of vascular dysfunction in diabetes [10]. Whether such interactions contribute to the pathophysiological mechanisms of preeclampsia warrants further analysis.

CONCLUSION

Serum malondialdehyde levels in pre-eclampsia cases have been evaluated with age and BMI matched controls.

The serum malondialdehyde levels are significantly higher in pre-eclampsia patients compared with controls.

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