Journal of Cardiovascular Disease Research

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 09, 2023

ORIGINAL RESEARCH

Study of Oxidative Stress in Pre-eclamptic Vs normotensive Pregnancy

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Abstract

Objectives: Pre-eclampsia (PE) is a significant public health problem globally, affecting both developed and developing countries and causing maternal and perinatal morbidity and mortality. Early detection and diagnosis of PE is very challenging. To gain insights into the pathophysiology of PE, we conducted a study to know oxidative stress.

Method: The study involved 60 subjects in their third trimester of gestation, comprising 30 pre-eclamptic (case) and 30 normotensive pregnancy (control). Samples were collected using inclusion and exclusion criteria from Obstetrics and Gynecology department in and outpatients at Jawahar Lal Nehru medical college and hospital (JNMCH) Aligarh Muslim University (AMU), Aligarh, Uttar Pradesh, India. Serum Malondialdehyde (MDA), was measured in micromoles of Thiobarbituric acid reactive substances (TBARS). Result was analyzed by using appropriate statistical tests and considered significant when $p<0.05$.

Results: The mean (± SD) value of serum malondialdehyde (MDA) in terms of micromolesof TBARS was 0.899 ± 0.287 micromoles/ml in PE, while it was 0.478 ± 0.201 micromoles/ml in controls. This increase in PE was highly significant (P= 0.0001).

The result indicated a significantly higher level of serum MDA in pre-eclamptic compared to normotensive.

Conclusion: In conclusion, the study sheds light on important factors associated with PE, including oxidative stress. Early identification and management of these risk factors could be critical in decreasing the incidence of PE and its adverse outcomes for both mothers and babies.However, further research is needed to understand these findings.

Keywords: oxidative stress, pre-eclampsia (PE), malondialdehyde (MDA), heart rate variability (HRV), body mass index (BMI)

Introduction

Worldwide. Pre-eclampsia (PE) is a leading cause of feto- maternal morbidity and mortality[1]. It affects 2–5% of all pregnancies [2], subdivided into early-onset forms less than 34 weeksof and late-onset more than 34 weeks of gestation [3]. As yet, no tool available for the early identification, only regular antenatal check-ups and pregnancy termination is key management but it can persist after delivery [4]. Social determinants of health, including race, age, comorbid conditions, and socioeconomic status are various risk factors associated [5]. In the developing countries, severe forms of PE and eclampsia are more common, ranging from a low of 4% ofall deliveries to as high as 18% [6]. A recent population-based study demonstrated approximately 15% experiences at least one hypertensive pregnancy during their reproductive life [7].

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In India, PE accounts for 11.71% of total pregnancies [8]. A national wise cross-sectional study found the highest incidence in Tripura state 87.5% and the lowest in Haryana 33% [9]. Prevalence of hypertensive disorders in Western UP was found at 4.1% [10]

The exact cause of pre-eclampsia is still not clearly understood. However, it is proposed that multiple factors are involved in initiation and progression, including maternal constitutional factors, inflammatory activation [11], endothelium malfunction[12],cardiovascular maladaptation[13], an antiangiogenic state [14] and lack of feto-maternal immune intolerance [15]. Presumably, the etiopathogenesis of pre-eclampsia revolves around placental oxidative stress which results from ischemia-reperfusion injury to the placenta [16]. Researchers have reported enhanced inflammatory response [17], and oxidative stress [18,19] in PE. Serum malondialdehyde (MDA) is an important biomarker for oxidative stress and lipid peroxidation.

Authors believe that some placental factors might be acting primarily on the vasomotor centre located on the medulla to modulate central parasympathetic outflow rather than exclusively acting peripherally on the blood vessel to alter vascular tone. PE is exaggerated state of the increased sympathetic activity of the normal pregnancy [20-22].

The study was conducted on 60 subjects divided into two groups, 30 cases, and 30 controls, recruited in third trimester of gestation. It was a cross-sectional hospital-based study. The objective was to gain more insight into pathophysiology of pre-eclampsia, we decided to explore the role of serum oxidative stress marker, malondialdehyde (MDA).

MATERIALS AND METHODS

The study was conducted on diagnosed cases of pre-eclampsia. A total of sixty subjects in the third trimester were selected from the Obstetrics and Gynecology out and inpatient Department of Jawahar Lal Nehru Medical College and Hospital. A.M.U., Aligarh between December 2014 and October 2016. Previously healthy, normotensive women were considered to have pre-eclampsia if their blood pressure after 20 weeks of gestation was raised to or more than 140/90 mm Hg. Pregnant who had systolic blood pressure (SBP) 140mmHg and/or diastolic blood pressure (DBP) 90mmHg and proteinuria [23] were classified as mild preeclampsia and those with SBP 160 and/or DBP 110mmHg and proteinuria [24] (Isler CM *et al* 1999) were classified as severe pre-eclampsia.

Informed and written consent was taken from the cases and controls for participation in the study with approval of the institutional Ethical Committee, J.N. Medical College Hospital, Aligarh.

Inclusion criteria

1. Diagnosed cases of pre-eclampsia in the third trimester were taken as cases.
2. Selected cases of pre-eclampsia were not suffering from any other disease.

Exclusion criteria

1. Maternal age less than 20 years and more than 30 years.
2. Suffering from such a disease in which oxidative stress was implicated in the pathophysiology, for example, diabetes, hypertension, etc.
3. Gestational Hypertension.
4. History of smoking and alcohol intake.
5. Duration of pregnancy less than 30 weeks.
6. Taking antioxidants.

Serum Malondialdehyde (MDA): - It was measured in terms of micromoles of TBARS formed/ml of blood.

Statistical analysis

Results were analysed using appropriate statistical tests with the help of Graph Pad Prism software. All normally distributed data are reported as mean ± SD

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1. Mean
2. Standard Deviation (S.D,)
3. Unpaired t-test
4. P value- Statistical significance was assumed at $P < 0.05$.

Observations and results

The present study was done to know the level of serum oxidative stress in terms of Thiobarbituric acid reactive substance (TBARS) in pre-eclamptic and normal pregnant women and then these values were compared between two groups.

Serum malondialdehyde (MDA)

The comparison for serum malondialdehyde was done in normal pregnancy and pre-eclampsia (Table 1). The mean value of serum malondialdehyde (MDA) in terms of micromoles of TBARS formed was 0.899 ± 0.287micromoles/ml in pre-eclampsia patients, while it was 0.478
± 0.205 micromoles/ml of TBARS in normal pregnant women. This increase in pre-eclampsia patients was highly significant (P value = 0.0001).

Table 1: Mean values of serum malondialdehyde in normal pregnantand pre-eclampsia patients.

	Controls	**Pre-eclampsia**	**P value**
Mean value of serum MDA (µmoles of TBARS formed/ml of serum) ±SD	0.478 ± 0.205	0.899 ± 0.287	0.0001

P value < 0.01 which is significant, MND -Malondialdehyde, TBARS-Thiobarbituric reactive substance ,

SD= standard deviation

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Demographic parameters

No significant variation was found for gestational age, maternal age, and parity between both study groups (Table 2). As expected, the values of systolic and diastolic blood pressure were significantly higher in PE group compared to normotensive pregnant.

Maternal age: The mean maternal age in pre-eclampsia patients was 26.2 ± 3.5 years and in normal pregnant women was 25.4 ± 3.3 years. (P value > 0.05)

Gestational age: The mean gestational age in pre-eclampsia was 34.8 ± 2.5 weeks and in normal pregnant controls was 35.17 ± 2.35 weeks. (P value > 0.05)

Table 4: Mean maternal age, mean parity, mean gestational age, mean systolic BP, and mean diastolic BP of all subjects.

Parameters	Pre-eclampsia (N=30)	Normal Pregnant (N=30)	P value
Mean maternal age (years) ±SD	26.23 ± 3.47	25.40 ± 3.26	>0.05
Mean gestational age (weeks) ±SD	34.8 ± 2.46	35.17 ± 2.34	>0.05
Mean parity ±SD	1.17± 1.02(range 0-3)	1.06±0.98 (range 0-2)	>0.05
Mean SBP (mmHg) ±SD	150.53 ± 10.22	117.8 ± 6.65	0.0001
Mean DBP (mmHg) ±SD	92.73 ± 7.75	75.73 ± 4.03.0	0.0001

*P value < 0.05 which is significant. SBP: Systolic blood pressure, DBP: Diastolic blood pressure, SD= standard deviation

Parity: Mean parity in pre-eclampsia patients was 1.17 ± 1.02 and in normal pregnant women was 1.06 ± 0.98. P value was > 0.05.

DISCUSSION:

In the present study, we found that the level of malondialdehyde (MDA) was increased significantly in pre-eclampsia patients as compared to normal pregnant females (Table-1). This result is similar to other studies [25-27]. It is suggested that two factors play important in the pathophysiology of PE: lipid peroxidation [28,29]. and increased systemic inflammatory response [30-32] which, in turn, promotes a high release of free radicals [33]. In PE, the ischemic placentamay be a potential source of the increase in products of lipid peroxidation [34].

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We also compared the maternal age, gestational age, blood pressure and parity (Table-4), and we did not see any association with PE in contrast to other studies [35,36]. The variation in our study and others might be due to the differences in the type of study and different population distributions.

Thus, we could expect that if is there any direct relation between oxidative stress and inflammatory response occurring in preeclampsia, these parameters must be correlated witheach other, but we did not do so in this study.

Summary

The present study was done on the Uttar Pradesh population in J.N. Medical College, A.M.U. Aligarh. Thirty cases of pre-eclampsia in their third trimester were compared with thirty normotensive pregnancies, taken as controls. Informed and written consent was taken from all the subjects. Intra-cubital venous blood sample was collected from cases and controls and serum was obtained after centrifugation and stored in a deep freezer in the Physiology PG lab. Sera of cases and controls were analysed for malondialdehyde. Cases and controls were matched for age, parity, gestational age and MDA.

The findings of our study are as given below:

1. The mean level of serum malondialdehyde is increased significantly in pre-eclamptic as compared to controls.
2. Maternal age and Parity did not show any relation between the two groups.
3. Maternal height has no relation between the two groups.

CONCLUSION

We concluded from this study that increased lipid peroxidation of plasma membrane due to oxidative stress is an important factor in the pathogenesis of pre-eclampsia in this population because lipid peroxides damage endothelial cells, and produce vasoconstriction and inflammation. Thus, oxidative stress and other inflammatory process may be involved in the pathogenesis of pre-eclampsia.

LIMITATIONS

The present study was conducted with certain limitations. We have taken both study groups in their third trimester, aged between 20 to 30 years. Subjects were from a specific region and the sample size was small. To know the role of these parameters in early pregnancy and their implementation to control the incidence of pre-eclampsia, is required further studies.

Conflicts of Interest: The authors declare that they have no conflicts of interest.

Financial support and sponsorship: Nil.

Acknowledge: The authors gratefully acknowledge the supports of all faculty and staff members.

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