Original Research Article

A Study of Serum Paraoxonase And Malondialdehyde in Pregnancy Induced Hypertension

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Abstract

Background: Pregnancy induced hypertension (PIH) is one of the leading cause of maternal and fetal mortality and morbidity. Treatment is symptomatic till date. Early identification and monitoring of disease progression could prevent adverse complications. Oxidative stress is considered as one of the etiological factor resulting in lipid peroxidation. Malondialdehyde (MDA) is formed as an end product of lipid peroxidation. It causes oxidation of LDL and eventually leads to membrane damage. This could be an indicator of oxidative stress. Paraoxonase (PON1) is a HDL associated esterase enzyme which exhibit antioxidative property by preventing lipoproteins from oxidative damage. **Aim& Objective:** The objective of the present study was to evaluate serum MDA and PON1 in normotensive pregnant women and in women with PIH and their role in predicting the severity of PIH. **Materials and methods:** A case control study was done, in which 50 women were normotensive pregnant women (Group 1) and 50 were women diagnosed with PIH (Group 2). Group 2 was further divided into mild (n=28) and severe PIH(n=22). Serum MDA levels and PON1 activity were estimated. Data was analysed using Graph pad prism version 7.0. Unpaired t-test was performed to test the significance of difference between the two groups and the subgroups.**Results:** serum MDA levels were significantly elevated in Group 2(5.087 ± 1.245nmol/ml) when compared to Group 1(2.812 ± 0.7395nmol/ml). In subgroups, serum MDA levels were significantly higher in severe PIH than in mild PIH ($P < 0.001$). Serum PON1 activity was significantly decreased in Group 2(225.3 ± 39.65IU/L) when compared to Group 1(335 ± 71.69IU/L). Also, PON1 levels were significantly decreased in severe PIH than in mild PIH with $P < 0.001$.**Conclusion:** Serum MDA was elevated in PIH indicating increased oxidative stress. PON1 activity was decreased resulting in oxidant and antioxidant imbalance. Thus, serum MDA and PON1 can play a significant role in the pathogenesis of PIH and they can aid in detecting the severity of the disease.

Keywords: pregnancy induced hypertension, serum malondialdehyde, serum paraoxonase, oxidative stress.

Introduction

Hypertensive disorders complicating pregnancy are one of the common and significant cause of maternal morbidity and mortality especially in developing countries [1]. Pregnancies complicated by hypertension are associated with increased risk of adverse fetal, neonatal and maternal outcomes, including preterm birth, intrauterine growth restriction (IUGR), perinatal death, acute renal, hepatic failure, antepartum haemorrhage, postpartum haemorrhage and maternal death[2].

Pregnancy induced hypertension (PIH) is defined as hypertension (blood pressure ≥ 140/90mmHg) with or without proteinuria (≥ 300 mg/24 hours) emerging after 20 weeks of gestation, but resolving up to 12 weeks postpartum[3]. The general classification of pregnancy-induced hypertension during pregnancy includes gestational hypertension (without proteinuria), preeclampsia (with proteinuria) and eclampsia (preeclampsia with convulsions) [4].

Approximately, 30% of hypertensive disorders of pregnancy were due to chronic hypertension while 70%

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of the cases were diagnosed as gestational hypertension/preeclampsia [2].

Epidemiology

Worldwide, 10% of all pregnancies are complicated by hypertension. It is estimated that pregnancy induced hypertension (PIH), affects about 5-8% of all pregnant women [5].

The incidence of preeclampsia in nulliparous (primigravida) population ranges from 3-10% worldwide. Incidence of eclampsia in the developed countries is about 1 in 2000 deliveries as compared to developing countries where it varies from 1 in 100 to 1 in 1700[6]. The incidence of PIH is 15.2% in India, while it is four times higher in primipara women than in multipara. 13% of the maternal deaths are in the women with pregnancy induced hypertension and eclampsia, the most severe form that accounts for major cause of death. The high incidence observed has pointed towards poverty, lack of education and unawareness regarding health care in this part of the world [6].

The treatment of PE is symptomatic till date, as the etiopathogenesis is not yet fully understood. Numerous theories have been put forward emphasizing placental oxidative stress as the major mechanism involved in the pathogenesis of preeclampsia [7]. Recent reports suggest that free radical induced endothelial cell injury might be an etiologic factor. An imbalance of increased oxidant status and decreased antioxidant status in women with preeclampsia has also been noted [8].

Malondialdehyde

Malondialdehyde (MDA) is a three-carbon, low molecular weight aldehyde [9]. It is an end-product formed during lipid peroxidation [10].

From the sites of its formation, it permeates easily into remote tissues and exhibits high reactivity with proteins and nucleic acids [11]. Due to the ability to form covalent bonds with these compounds, it may modify their structure and properties and cause loss of integrity. This in turn leads to perturbation of their proper functioning and results in the dysfunction of individual organs. The concentration of MDA in serum is considered to be a measure of lipid peroxidation [11].

MDA is the most frequently used biomarker of oxidative stress in many health problems such as cancer, psychiatric disorders, chronic obstructive pulmonary disease, asthma, or cardiovascular diseases [12].

Paraoxonase (PON1)

Paraoxonase (PON1) is a serum esterase synthesized in the liver. The enzyme was originally found to be responsible for the hydrolysis of paraoxone, a toxin that irreversibly inhibits acetyl cholinesterase [13].

In the circulation, PON1 is bound to high density lipoprotein (HDL). Some of the anti-oxidative and anti-inflammatory actions of HDL are attributed to PON1 [14]. PON1 is strictly dependent on calcium for its enzymatic activity [13].

Recently, PON1 has been shown to inhibit the oxidative modification of LDL, and it is considered to be an antioxidant enzyme with a protective role in atherosclerosis [13].

Preeclampsia places great demand for maternity care because the onset and clinical course are unpredictable [14]. Imbalance between reactive oxygen species(ROS) and antioxidants appears to be an important contributing factor[15].Hence the present study was done to evaluate serum malondialdehyde levels and paraoxonase activity in pregnancy induced hypertension.

Aims and Objectives

1. To compare serumMalondialdehyde (MDA) levels in normal pregnant females and in woman with pregnancy induced hypertension(PIH)
2. To compare the serum Paraoxonase (PON1) activity in normal pregnant females and in woman with pregnancy induced hypertension
3. To study the possibility of serum MDA and PON1 as markers of severity in pregnancy induced hypertension.

Materials and Methods

Setting: A case control study was conducted in the Department of Biochemistry, Osmania General Hospital, Hyderabad.

Sources of samples and data

Department of Biochemistry, Osmania General Hospital/ Osmania medical college. Modern Maternity Hospital, Petlaburj, Hyderabad. A case-control study of 100 subjects divided equally into 2 groups with 50 each.

Table 1:Cases and controls

Group 1	Normotensive pregnant women[Controls]	50
Group 2	Women with pregnancy induced hypertension [cases]	50

Table 2:Subgroups

Subgroup 1	Mild PIH	28
Subgroup 2	Severe PIH	22

Informed consent was taken from all individuals who took part in the study. Ethical clearance was obtained for the study from the ethical committee of Osmania Medical College.

Inclusion Criteria

Age group: 18-35 years

Group 1: Normotensive pregnant women with gestational age >20weeks and BP< 140/90mmHg without proteinuria.

Group 2: Diagnosed cases of pregnancy induced hypertension with gestational age > 20weeks and BP >140/90mmHg with or without proteinuria.

Subgroups of group 2: Group 2 was further divided into

Mild PIH: Included women with Blood pressure ≥ 140/90 mmHg but < 160/110 mmHg after 20 weeks gestation, and proteinuria 3+ on dipstick

Severe PIH: Included women with Blood pressure ≥ 160/110 mmHg, and proteinuria 3+ on dipstick.

Exclusion Criteria

1. Gestational Diabetes
2. Chronic hypertension
3. Twin pregnancy
4. Liver failure
5. Renal failure
6. Thyroid disorders

Specimen Collection: 4 ml of fasting venous blood was collected under aseptic precautions into serum vacutainers. Collected blood was allowed to clot and then centrifuged. serum was separated. Hemolysed and lipemic samples were not included.

Storage: Serum was stored in Eppendorf tubes at -80ºC.

Parameters Estimated

Serum: 1) Malondialdehyde (MDA)
2) Paraoxonase (PON-1)

Methods

Serum Malondialdehyde

METHOD: Thiobarbituric acid method by Nadigeret.al (TBA method)[16-18].

Serum Paraoxonase (PON1)

Method: Usingp-Nitrophenylacetateby Aldridge W.N[19,20].

Observations and Results

The present study was undertaken in the Department of Biochemistry, Osmania Medical College, Osmania General Hospital, and Modern maternity hospital, Petlaburj, Hyderabad.

A total of 100 subjects were included in the study, of which 50 subjects were normotensive pregnant women(Group1), 50 were women diagnosed with pregnancy induced hypertension (Group 2).

Group 2 was further divided into 2 subgroups based on blood pressure and proteinuria as: mild PIH and severe PIH

Table 3: Sub groups

Subgroup 1	Mild PIH	28
Subgroup 2	Severe PIH	22

The following parameters were analysed for all the samples:

1. Serum Malondialdehyde (MDA)
2. Serum Paraoxonase (PON)

The data was analysed using Graph Pad Prism software version 7.0 and the results were expressed as Mean and Standard deviation of various parameters in different groups.

The results were expressed in nmol/ml for malondialdehyde and IU/L for paraoxonase.

Table 4: Study parameters in the two groups

Parameter	Group 1			Group 2		
	Mean	±S.D	SEM	Mean	±S.D	SEM
MDA(nmol/ml)	2.812	0.7395	0.1046	5.087	1.245	0.1761
PON-1(IU/L)	335	71.69	10.14	225.3	39.65	5.607

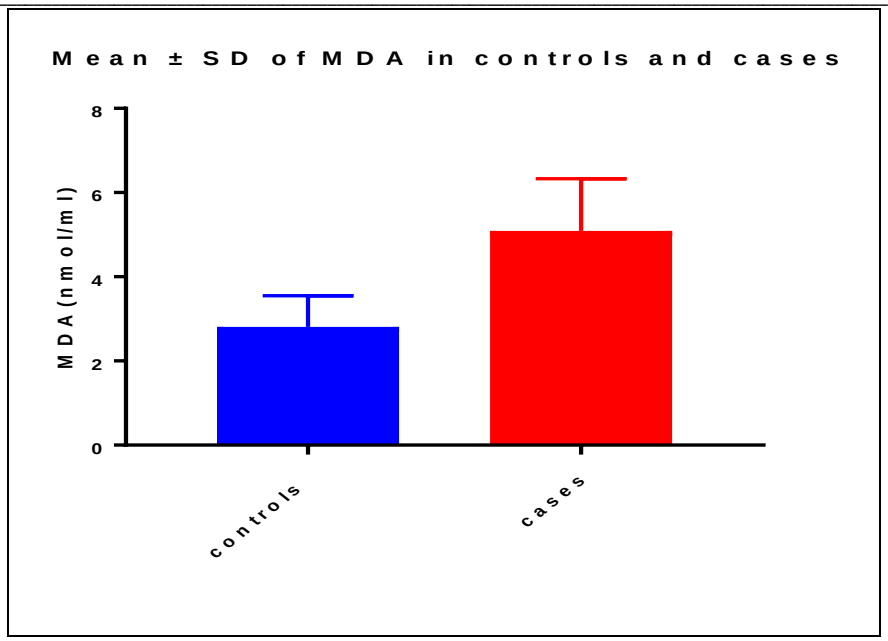

Fig. 1: Graphical representation of Mean ± SD of Serum MDA in Group 1 and Group 2

Serum MDA levels were elevated in PIH group when compared to the control group. The mean ± S.D of Serum MDA for control group was 2.812 ± 0.7395. The mean ± S.D of Serum MDA for PIH cases was 5.087 ± 1.245.

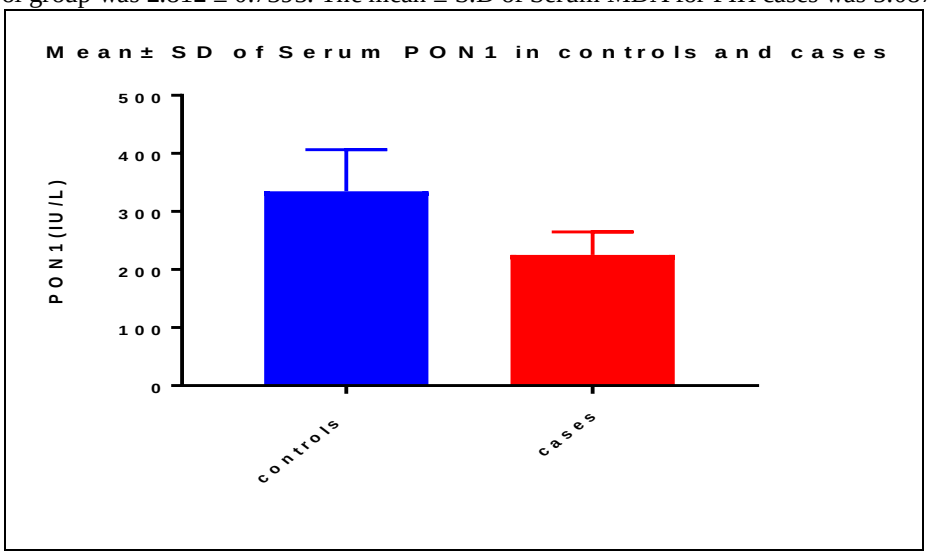

Fig. 2: Graphical representation of Mean ± SD of Serum PON1 in Group 1 and Group 2

Serum PON1 levels were decreased in PIH group when compared to the control group. The mean ± S.D of Serum PON1 for control group was 335 ± 71.69. The mean ± S.D of Serum PON1 for PIH cases was 225.3 ± 39.65.

In order to assess the significance of the differences observed in the mean values of MDA and PON1 parameters in different groups studied, the data was subjected to unpaired t test. The significance of difference of mean values of different groups was represented by P values and P value <0.05 was considered as significant.

Table 5: Unpaired T-Test between Group 1 and Group 2

Parameters	t-value	P-value	Degreeof freedom
MDA	11.11	<0.0001	98
PON1	9.468	<0.0001	98

The unpaired 't' test has shown that the difference in mean values of serum MDA and PON1 in two groups was statisticallysignificant with a P value <0.0001.

MDA and PON-1 activity were analysed in the case subgroups

Table 6: Study parameters in the sub groups

GROUP 2						
SUBGROUPS	**MILD PIH**			**SEVERE PIH**		
	Mean	**±SD**	**SEM**	**Mean**	**±SD**	**SEM**
MDA(nmol/ml)	4.357	0.9257	0.1749	6.016	0.9484	0.2022
PON1(IU/L)	248.4	35.28	6.668	195.8	21.10	4.498

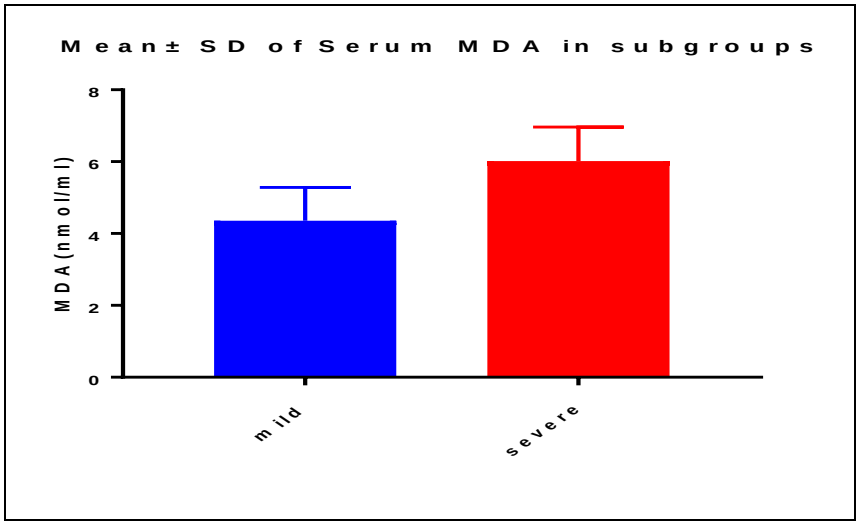

Fig. 3: Graphical representation of Mean ± SD of Serum MDA in the subgroups

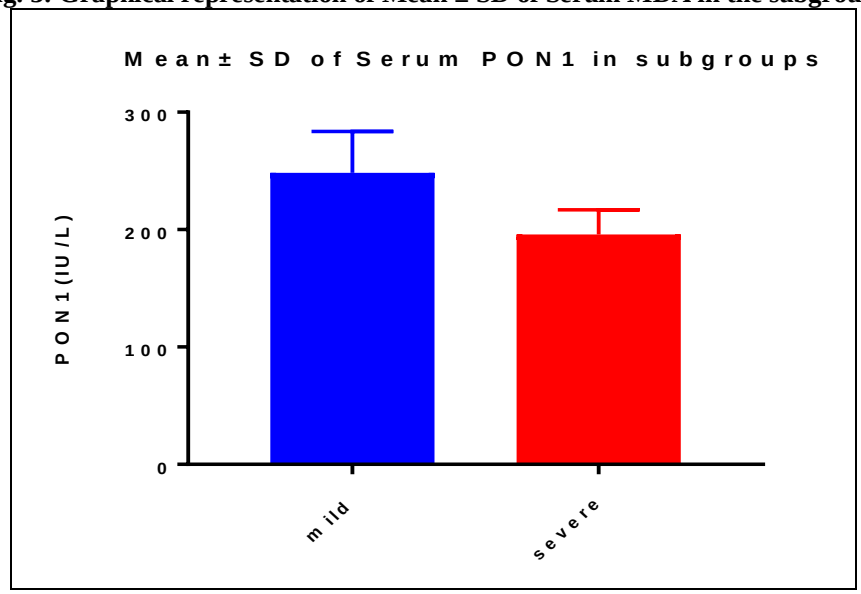

Fig. 4: Graphical representation of Mean ± SD of Serum PON1 in the subgroups

The Mean ± SD of Serum MDA levels differed in the two sub groups; the levels of Serum MDA being high in severe PIH (6.016 ± 0.9484) and less in mild PIH (4.357± 0.9257).

The Mean ± SD of Serum PON1 levels also differed in the two sub groups; the levels of Serum PON1 being high in mild PIH (248.4 ± 35.28) and less in severe PIH (195.8 ± 21.10).

In order to assess the significance of the differences observed in the mean values of MDA and PON1 in the two subgroups, the data was subjected to unpaired t-test. The significance of difference of mean values within the subgroups was represented by P values and P value <0.05 was considered significant.

Table 7: Unpaired T-Test Between subgroups

Parameter	t- value	P-value	Degree of freedom
MDA	6.225	<0.0001	48
PON1	6.169	<0.0001	48

Unpaired t-test has shown that the differences in mean values of serum MDA and PON1 in the two sub groups was statistically significant with a P value of <0.0001.

Discussion

Hypertensive disorders are one of the most common complications of pregnancy, with a reported incidence ranging from 5% to 10%[21]. They are responsible for 8-9% of maternal deaths in India and 15 -20% of maternal deaths in western world[1].

There are four major categories of hypertension in pregnancy–gestational hypertension (GH), preeclampsia/eclampsia, chronic hypertension and chronic hypertension with superimposed preeclampsia [22].Milder form of disease is gestational hypertension and its severe form is eclampsia[1].

Oxidative stress occurs when the production of ROS overwhelms the antioxidant capacity resulting in overall damage to cells and has been implicated in the pathology of many hypertensive pregnancy-related conditions including preeclampsia and gestational hypertension[23].

Most common target of free radical attack and incidence of biomolecular deterioration is lipid peroxidation of membrane lipids. It generates a variety of hydroperoxide and aldehyde products that are highly reactive with cellular components and extracellular matrix. Malondialdehyde (MDA) is a well-known toxic aldehyde end product of lipid peroxidation[24]. Excess endogenous aldehyde production (lipid peroxides) plays a significant role in blood pressure elevation by binding sulphydryl groups of membrane proteins, altering Ca2+ channels and increasing cytosolic free Ca2+ that cause further extensive membrane damage leading to peripheral vascular resistance and hypertension[24].

Increased lipid peroxides in preeclampsia might be related to increased placental thromboxane formation which causes increased cyclo-oxygenase activity that would increase the free radical formation. Low density lipoproteins(LDL) are more susceptible for free radical oxidation. They can be protected from free radical-induced oxidation by an enzyme PON1[25].

PON1 activity is inhibited by reactive oxygen species and, the serum PON1 expression is down-regulated by oxidative stress. Under conditions of oxidative stress, PON1 can be oxidized which leads to structural and functional modification of Apo A-1[25].

The decrease in PON1 activity may play an important role in pathogenesis of early PE detection through increased susceptibility to lipid peroxidation[25]. The susceptibility of lipoproteins to oxidation processes may be interpreted as a decrease in antioxidant mechanisms[26].

The present study was undertaken to study the serum malondialdehyde (MDA) levels and serum paraoxonase (PON1) activity in women with pregnancy induced hypertension(PIH) and their variation in mild and severe PIH.

In this study, subjects were divided into 2 groups. Group 1 comprising of normal pregnant females (controls) and Group 2 comprising of patients diagnosed with pregnancy induced hypertension (cases).

Group 2 was further divided into 2 subgroups based on blood pressure and proteinuria as mild PIH and severe PIH.

Serum malondialdehyde (MDA) and serum paraoxonase (PON1) were assessed in these groups.

In the present study, age group was 18 – 35 years.The Mean ± SD of serum MDA in Group 1 was 2.812 ± 0.7395 nmol/ml and in Group 2 was 5.087± 1.245 nmol/ml. The increase was statistically significant (P<0.0001). Because, MDA is formed from lipid peroxidation in an event of oxidative stress, it could be involved in endothelial dysfunction and thus increased in PIH.

The results were in accordance with the following studies:

In a study of Oxidative Stress in Patients of Pregnancy Induced Hypertension conducted by Dhananjay V et.al., there was highly significant increase in serum level of MDA in hypertensive pregnant women(4.6±0.9 nmol/ml) when compared to normal pregnant women (2.7±0.4nmol/ml). MDA is considered to be the most sensitive & final stage of peroxidation and as a marker of pro-oxidant level and indicator of oxidative stress.They concluded that Oxidative stress has the potential for being used as a marker for PIH[27].

In the present study, the Mean ± SD of serum MDA in mild PIH was 4.357 ± 0.9257(IU/L) and in severe PIH was 6.016 ± 0.9484 (IU/L). Serum MDA levels were increased in severe PIH when compared to mild PIH.

Unpaired t-test was performed to determine if there was statistically significant difference between 2 subgroups. MDA differed significantly in the subgroups with a P-value of < 0.0001.

The results were in accordance with the study conducted by Shikha Saxena et.al., to determine the association of serum malondialdehyde (MDA) level with severity of PIH. The study subjects were divided into four groups as women with gestational hypertension (Group I), with PE (group II), with eclampsia(Group III) and normotensive pregnant women(Group IV). MDA level in PIH group III (eclamptic) was found significantly higher (P<0.001) when compared with the other two PIH groups. Also, a strong positive and statistically significant correlation was observed between systolic BP and MDA (r = 0.567 and P-value of < 0.0001). This indicated that the severity of PIH is associated with increase in blood pressure, both systolic and diastolic. The strong significant relationship between MDA and systolic-diastolic blood pressure in PIH suggests an increased susceptibility to vascular disease and development of PIH which is associated with oxidative stress in these patients[28].

Hypertension develops through increased chemokine and cytokine expression, induction of the renin-angiotensin system and increased vascular C-reactive protein (CRP) expression in mother. As the severity of the PIH increases, there is increase in the severity of the patho-physiological phenomena leading to the accentuation of blood pressure. The increased MDA level in PIH is known to be due to increased generation of reactive oxygen species and reduction in anti-oxidants activity. Reactive oxygen species thus produced can cause enhanced lipid peroxidation in PIH which play a significant role in patho-physiology of PIH[28].

Riza Madazli et.al., conducted a study in which a strong correlation was detected between malondialdehyde and blood pressure (r = 0.75) in both control and pre-eclamptic patients. This indicates a correlation between the severity of the disease process and the level of lipid peroxidation. Reactive oxygen species can cause cellular damage by oxidising nucleic acids, proteins and membrane lipids.

They concluded that uncontrolled lipid peroxidation may play an important role in the pathophysiology of preeclampsia[29].

Similar findings were observed in the study done by ArashRafeeinia et.al.,Mean and SD of serum MDA were 2.96±1.40; 4.50±1.20;4.92±0.86nmol/ml; (P<0.0001) in healthy pregnant females, mild PE and severe PE respectively. The elevation of serum MDA shows the significance of additional oxidative stress process which occur in preeclampsia patients. Increased level of MDA in preeclampsia women suggest that excessive MDA production may play an important role in the pathophysiology of these patients[30].

Sheena P.S., who conducted a study to compare oxidative stress in different subgroups of PIH, found that the mean value of MDA was found to be significantly increased in (P<0.001) in PIH group than that of the normal control group and also within subgroups[31].

Increased activation of neutrophils, macrophages and T cells along with exaggerated placental response result in elevated formation of reactive oxygen species like superoxide radical, hydroxy radical. This will cause an increase in lipid peroxidation damage to vascular endothelium, membranes of cells and organelles which is evidenced by elevation of MDA level[31].

In the present study, the Mean ± SD of serum PON in Group 1 was 335 ± 71.69(IU/L) and in Group 2 was 225.3 ± 39.65(IU/L). There was a statistically significant decrease in group 2 when compared to group 1(P<0.0001). The decrease in the activity of serum PON could be due increased oxidative stress in PIH.

Serum PON-1 was further estimated in subgroups i.e., mild and severe PIH. The Mean ± SD of serum PON1 in mild PIH was 248.4 ± 35.28(IU/L) and in severe PIH was 195.8 ± 21.10(IU/L). Activity of serum PON1 decreased in severe PIH when compared to mild PIH. Analysis by unpaired t test showed this difference to be statistically significant(P<0.0001).

The results were in accordance with the following studies:

HafizeUzun et.al.,studied circulating Oxidized Low-Density Lipoprotein and paraoxonase activity in

preeclampsia. The study groups included 41 pregnant women with preeclampsia and 33 normotensive pregnant women. Serum concentrations of MDA and oxLDL were significantly higher, while PON1 activity was significantly lower in preeclampsia compared with normotensive controls ($P < 0.001$, $P<0.001$, and $p < 0.001$, respectively). Also, a positive correlation was detected between oxLDL and MDA ($r = 0.876$), and a negative correlation was detected between MDA and PON1;oxLDL and PON1($r = –0.837$ and $r = –0.759$, respectively). These results suggested that elevated oxidative stress and oxidized LDL, dyslipidemia and decreased PON1 activities may cause damage to vascular endothelium and contribute to the etiology of preeclampsia[32].

Antioxidants avidly react with and eliminate active oxygen species before they can inflict oxidative damage to vital components, such as DNA or cell membranes. Unlike chain-breaking antioxidants, HDL prevents accumulation of lipid peroxides on LDL and in the vessel wall for several hours and continues to do so long after fat-soluble antioxidants are exhausted, and this activity appears to be due to PON1[32].

According to Yahya Y. Z. Fareed et.al., serum PON activity was lower significantly in preeclamptic group compared to normal pregnant group($P<0.001$). The decrease serum PON1 activity in PE patients may contribute to atherosclerotic heart disease and/or the inactivation of the enzyme itself due to oxidative stress[25].

Anil B. Bargale et.al., determined serum superoxide dismutase and paraoxonase-1 activity in preeclampsia patients. Study included 30 preeclamptic women as cases and 30 normal pregnant women as controls. Cases were again subcategorized into mild and severe preeclampsia. PON-1 activity was significantly decreased ($P<0.001$) in PE patients as compared to normal pregnant women. But, among the preeclampsia group serum PON-1 activity did not change according to severity of disease[33].

In a study conducted by KS Meera et.al., PON1 activity in preeclampsia cases (113.31±13.01U/L) were significantly lower than in normal pregnant controls (130.72±14.44 U/L;$t=4.906$;$P<0.001$) while MDA levels were significantly higher [art 8]The increased MDA levels in preeclampsia is known to be due to increased generation of reactive oxygen species and increased oxygen demand along with reduction in activities of enzymes like superoxide dismutase, glutathione peroxidase and decrease in concentration of antioxidants like Vitamin C and Vitamin E. Decreased PON1 activity can cause damage to the vascular endothelium[34].

In preeclampsia there is altered lipid metabolism with increased lipid peroxidation and decreased antioxidants. LDL is more susceptible to oxidation. It readily gets oxidized by MDA, to form oxidized LDL which is taken up by macrophages via scavenger receptors and form foam cells which in turn results in atherogenesis. Ox-LDL particles might be involved in vascular endothelial damage[35].

PON-1 which is bound to HDL acts as an antioxidant that protects the LDL from the oxidative modifications. The reduction in the activity of PON-1 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. Hence prevention of LDL oxidation by PON may play an important role in preventing the development of PE[36].

In a study conducted by Hayder M. Al-Kuraishy et.al., PON-1 was significantly decreased ($P < 0.01$) while MDA serum levels were significantly increased in PE compared to the women with normal pregnancy and concluded that PE is associated with the augmentation of oxidative stress and reduction of endogenous antioxidant capacity related to PON-1[37].

Preeclampsia has been associated with atherogenic wall changes in the uteroplacental bed. These changes consequently result in necrosis of vessel wall and accumulation of lipid laden foam cells with oxidized LDL. In preeclampsia, the placental damage is progressive and can be compensated for some time depending on the severity of initial placental defect and intrinsic placental antioxidant capacity. Low antioxidant levels may aggravate prooxidant injury on endothelial cells, altering prostacyclin / thromboxane balance and culminating in preeclampsia. Prevention of LDL oxidation by PON prevents endothelial damage[38].

It can be considered that abnormal trophoblastinvasion and inadequate uterine artery remodelling occurs in preeclampsia, which causes uteroplacental imperfusion and injury to placenta which may lead to generation of oxidative stress. The generated free radicals enhance the lipid peroxidation products(LPO) and lead to formation of lipid hydro peroxide which could damage the endothelial cell membrane and cause endothelial cell dysfunction[33].

Normally, “healthy-HDL” includes active PON1, which suppresses the formation of oxidized lipids and lipoproteins. “Dysfunctional-HDL” has reduced PON1 activity that potentially leads to greater formation of MDA, which activates lectin-like oxidized LDL receptor-1 (LOX 1). The LOX-1 is an oxLDL receptor expressed in vascular endothelium and a multiligand receptor implicated in endothelial dysfunction[39].

Limitation of the study

- The study should have been carried out on a larger group of population.
- More patients with eclampsia could have been included in the study.
- Lipid profile could have been estimated and correlated with PON1 activity.

Conclusion

In this study, significant increase levels of serum MDA were found in women with PIH when compared to controls. Serum MDA levels also increased significantly in the subgroups i.e., MDA levels are more in severe PIH when compared to mild PIH. Serum paraoxonase(PON1) activity was decreased significantly in cases when compared to controls. PON 1 activity varied in subgroups. There was significant decrease in severe PIH when compared to mild PIH.Thus, it can be concluded that serum MDA and PON1 may be considered as important factors in the pathogenesis of PIH. Furthermore, variation of serum MDA levels and PON1 activity in subgroups indicate their role as severity marker. Hence it can be suggested that serum MDA and PON1 can be estimated for predicting the severity of the disease and in its management to avoid complications and serious maternal and fetal outcomes.

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