

## Comparative Study of Serum Levels of Malondialdehyde, Glutathione Peroxidase and Uric Acid in Preeclampsia and Normotensive Pregnancy

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### Abstract

Preeclampsia is a challenging disease of human pregnancy that affects the mother and her foetus. It is a common obstetric syndrome of undefined aetiology affecting 7–10% of pregnant women. This study aimed to investigate the serum levels of Malondialdehyde (MDA) and glutathione peroxidase (GPx), Uric acid in preeclamptic and normotensive pregnant women. The present study showed increased levels of serum malondialdehyde, and uric acid and decreased glutathione peroxidase in preeclamptic women compared to normotensive women. Malondialdehyde is an oxidant, uric acid is a marker of renal compromise in preeclampsia and glutathione peroxidase is an antioxidant. As the sample size in the present study is less, larger studies are needed to establish the role of oxidants and antioxidants in preeclampsia.

**Key Words:** Serum levels, Malondialdehyde, Glutathione peroxidase, uric acid, Preeclampsia and normotensive pregnancy

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### I. Introduction

Preeclampsia is a multisystem disorder in pregnancy characterized by blood pressure of  $\geq 140/90$  mm of Hg on two or more occasions at least 6 or more hours apart, after 20 weeks of gestation with proteinuria of  $\geq 300$  mg/24 hours or  $\geq +1$  in a random urine sample<sup>[1]</sup>. Although the cause of Preeclampsia remains unknown, oxidative stress is one proposed feature of the maternal syndrome. The main source of ROS appears to be the placenta<sup>[2]</sup>. ROS are increased, and the levels of several detoxifying enzymes are reduced in Preeclampsia. Normal pregnancy is a state of physiological stress<sup>[3]</sup> in which there is increased production of free radicals and in parallel fashion total antioxidant capacity gradually increases leading to an oxidative balance. But, in preeclampsia there is a biochemical imbalance with increase in oxidative stress and lipid peroxidation<sup>[4]</sup>

**Pathophysiology of pre-eclampsia:** A two-stage model of Preeclampsia has been proposed. The first stage which is completed before the 20th week and prior to the appearance of clinical signs, leads to reduced uterine perfusion, placenta becomes hypoxic and releases factors into the maternal circulation that eventually cause the clinical features of Preeclampsia. One of the candidates that link the two stages is the oxidative stress, free radical production occurs in all cells as part of their normal function. There are antioxidant systems that protect against ROS, both enzymatic and non-enzymatic. In Preeclampsia decreased concentrations of several antioxidants have been observed both in the placenta and in the blood. Malondialdehyde (MDA), Glutathione peroxidase, Uric acid are some of the biochemical markers of oxidative stress.

**MALONDIALDEHYDE (MDA):** Malondialdehyde (MDA) is a product of lipid peroxidation. Methods of measuring MDA are 1. Reaction with thiobarbituric acid 2. HPLC 3. Mass spectrometry

**GLUTATHIONE PEROXIDASE:** Function of GPX was hypothesized to be protection of red blood cells against haemolysis by oxidation. Three classes of GPX, GPX1, GPX2 and GPX3 have been detected.

**Uric Acid -** Uric acid is a product of purine degradation. Conversely it can become a prooxidant in a setting of compromised antioxidant availability. In pregnancy uric acid concentrations initially fall due to the effects of estrogen, expanded blood volume and increased glomerular filtration rate. Increased uric acid often precedes clinical manifestations of the disease.

Understanding the role of oxidants and antioxidants in preeclampsia may lead to newer therapeutic interventions in future. In this context, the present study aims to estimate the levels of three oxidants namely malondialdehyde, glutathione peroxidase and uric acid in preeclamptic pregnancies.

## II. Objectives

- To evaluate the serum levels of malondialdehyde, glutathione peroxidase and uric acid in preeclamptic and normotensive women and cord blood of newborn.
- To compare the serum levels of malondialdehyde, glutathione peroxidase, and uric acid in preeclamptic and normotensive pregnant women and in the cord blood of the newborn.

## III. Methodology:

**Study design:** Prospective case-control study

**Sample size:** Convenient sample size of 50 cases and 50 controls.

**Study population:** 50 cases of preeclampsia were selected and 50 normal pregnant women who are matched for age, parity and gestational age were taken as controls.

**Cases:** Antenatal women aged 18 to 35 years of gestational age more than 28 weeks with blood pressure of more than 140/90 mm of Hg on more than 2 occasions at least 6 hours apart with proteinuria of  $\geq 1+$  ( $\geq 30$  mg/Dl) by dipstick method.

**Control:** Fifty healthy pregnant women of more than 28 weeks of gestation without hypertension matched for age, parity and gestational age with cases.

**Exclusion Criteria:** Pregnant Women

- with chronic hypertension that was present before pregnancy
- who are diabetic and on insulin therapy
- who are taking any hypolipidemic drugs
- with diagnosed liver, cardiac, renal diseases
- with multiple pregnancy
- with abruptio placenta/molar pregnancy.
- women who are not willing to participate in the study.

**Study setting:** Government Maternity Hospital, Tirupati.

**Study Period:** The study was conducted over a period of 12 months from November 2015 to October 2016

**Materials and Methodology:**

After taking informed consent, 10 ml of venous blood is taken from the anti-cubital vein of both controls and cases in a sterile bottle and taken to the biochemistry department SV Medical College within two hours. The patients were not charged for the investigation.

**Estimation of serum Malondialdehyde (MDA): Principle:** Serum is treated with 10% trichloroacetic acid, followed by addition of 0.67% thiobarbituric acid and to this 1 ml of distilled water is added. The mixture is centrifuged, and supernatant is collected. Intensity of pale pink colour is measured at 530 nm in a semi-autoanalyzer.

**Estimation of glutathione peroxidase: Principle:** Reduced glutathione reacts with 5,5'-dithiobis 2-nitro benzoic acid to form yellow coloured product 2-nitro 5-thiobenzoic acid, the intensity of which is measured at 412 nm by semi-autoanalyzer.

**Uric acid estimation: Principle:** Simple calorimetric method was employed. To 4 ml N/23 sulphuric acid, 0.5 ml serum was added and mixed. 0.5 ml 5.6% sodium tungstate was then added, mixed and centrifuged. 3 ml of the decanted supernatant was placed in a test tube, to which 0.2 ml of PTR (phosphotungstic acid reaction reagent) added, mixed well, followed by the addition of 1.0 ml 0.6 N sodium hydroxide. Reading was taken after 15 min, at 720 nm on spectrophotometer.

**Statistical analysis:** Was done using ANOVA technique for categorical variables and student-t test for continuous variables. p value of  $< 0.5$  was considered as significant. MS excel 2007 and Epiinfo version 7 was used for statistical analysis.

## IV. Results And Discussion:

The present study aimed to estimate the serum levels of malondialdehyde, which is an oxidant and glutathione peroxidase which is antioxidant & uric acid which has both oxidant and antioxidant in pre-eclamptic vs normotensive pregnancies.

This study showed increased serum malondialdehyde & uric acid and decreased concentrations of glutathione peroxidase in preeclampsia when compared to normo-tensive pregnant women. These findings are in agreement with most of the studies.

**Table 1. Demographics**

Parameters	Type	N	Mean	Std.Dev	t-value	P-Value
Age(years)	Controls	50	23.36	3.538	.453	.652
	Cases	50	23.68	3.531		
Gestational age(weeks)	Controls	50	35.34	5.177	0.059	0.953
	Cases	50	35.40	4.940		
Parity						
Primi	Controls	28	27			
Multi	Cases	22	23			

**Table 2. Birth weight**

PE/N		N	Mean	Std.Dev	t-value	P-Value
Birth weight (kgs)	Normotensive	47	2.157	0.8033	0.156	0.877
	Pre-eclampsia	50	2.130	0.9116		

**Table 3. Serum malondialdehyde**

PE/N		N	Mean	Std.Dev	t-value	P-Value
SMA	Controls	50	3.536	2.0403	10.01**	.000
	Cases	50	8.248	2.6289		

**Table 4. Level of blood pressure and serum markers**

		SBP	DBP	SMA	SGP	SU
SBP	Pearson correlation	1	0.873**	0.751**	-0.745**	0.752**
	P value		0.000	0.000	0.000	0.000
DBP	Pearson correlation	0.873**	1	0.750**	-0.667**	0.686**
	P value	0.000		0.000	0.000	0.000
SMA	Pearson correlation	0.751**	0.750**	1	-0.835**	0.805**
	P value	0.000	0.000		0.000	0.000
SGP	Pearson correlation	-0.745**	-0.667**	-0.835**	1	-0.814**
	P value	0.000	0.000	0.000		0.000
SU	Pearson correlation	0.752**	.686**	0.805**	-0.814**	1
	P value	0.000	0.000	0.000	0.000	

\*\* . Correlation is significant at the 0.01 level (2-tailed).

**Table 5. Serum glutathione peroxidase**

PE/N		N	Mean	Std.Deviation	t-value	P-Value
SGP	Normotensive	50	35.102	4.4066	11.906**	0.000
	Pre-eclampsia	50	25.118	3.9670		

**Table 6. Serum uric acid**

PE/N		N	Mean	Std.Dev	t-value	P-Value
Serum Uricacid	Normotensive	50	4.356	1.2231	0.12.66**	0.000
	Pre-eclampsia	50	8.041	1.6552		

## Demographics

**Age:** In the present study, women of 18-30 years have been included. The mean age of pregnant women in the present study is 23.36 years in controls and 23.68 years in cases. So the two groups are similar with respect to age. Other studies have included women in age group ranging from 18 to 40 years with mean age of 26.7 years [5]

**Gestational age:** In the present study, women above 28 weeks of gestation are enrolled. The mean gestational age among cases is 35.40 weeks & among controls is 35.34 weeks. Cases & controls are matched for gestational age in the present study. Other authors [6] enrolled women with gestational age of more than 20 weeks. Some studies showed a mean gestational age of 36.4 and 37.7 weeks in normotensive and pre-eclamptic women [7]. This can be explained by the fact that women with pre-eclampsia are induced prematurely to avoid maternal & fetal complications.

**Parity:** There is an almost equal distribution of primigravida & multipara in both groups. Some studies included only primigravida [5]. Whereas others included primigravida & multigravida [7]. Some studies didn't mention the parity of the patients [6]. Some studies enrolled non-pregnant, pregnant & postpartum women [8].

In the present study cases & controls are matched for age & gestational age, so the base line characters of two groups are similar.

**Birth Weight:** In the present study, the mean birth weight in normotensive group is 2.16 kg and in preeclampsia group it is 2.13 kg. There is no statistically significant difference between the two groups in terms of birth weight. All the other studies showed significantly lower birth weight among preeclamptic women when compared to normotensive women [7].

**Malondialdehyde:** In the present study we have observed that serum MDA levels have been significantly increased [ $p < 0.0001$ ] in preeclamptic women as compared to normal pregnant women. These findings agree with those of other studies. Other studies showed lower levels of MDA in last trimester than in the first and second trimesters [9].

**Serum Glutathione Peroxidase:** Present study showed a significant reduction in maternal glutathione peroxidase concentrations in preeclamptic samples compared to normal pregnant controls. This is in concurrence with other studies [8].

**Uric acid:** The present study showed increased levels of serum uric acid in preeclamptic women as compared to normotensive women. This is similar to a study by Tatjana *et al.* Punthumapol & Kittichonpanish [10] found that uric acid was higher in severe preeclampsia but not in mild preeclampsia.

The present study found a linear correlation between both systolic & diastolic blood pressures and serum uric acid level. This is corroborated by other studies. Many of the authors believed that uric acid is the earliest and consistent parameter in pre-eclampsia and a better predictor of fetal risk than blood pressure. In contrast a study done by Hickman *et al.* [11] concluded that serum uric acid was an unreliable indicator for developing hypertension.

## V. CONCLUSION

The present study showed increased levels of serum malondialdehyde, and uric acid and decreased glutathione peroxidase in preeclamptic women compared to normotensive women. Malondialdehyde is an oxidant, uric acid is a marker of renal compromise in preeclampsia and glutathione peroxidase is an antioxidant. As the sample size in the present study is less, larger studies are needed to establish the role of oxidants and antioxidants in preeclampsia.

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