# Malondialdehyde (MDA) and Reduced Glutathione (GSH) Levels in Maternal and Umbilical Serum in Women with Mild and Moderate Pre-Eclampsia

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## Summary:

***Background:*** *Increased oxidative stress and lipid peroxidation associated with impairment of the anti-oxidant systems has been found to be involved in the pathogenesis of many diseases. Evaluation of such a role in pregnancy-related pathophysiological conditions seems to be important in this respect.*

***Objective:*** *The present study was designed to evaluate the possibility of the involvement of lipid peroxidation and the consequent impairment of anti-oxidant activities in pair-matched maternal and umbilical cord serum in pre-eclamptic pregnant women.*

***Subjects and Methods:*** *Fifteen healthy normotensive women, six women with mild pre-eclampsia, and six with moderate pre-eclampsia, were involved in the study in Abu-Ghraib Hospital. Serum levels of malondialdehyde (MDA) and reduced glutathione (GSH) levels in peripheral blood before and immediately after delivery and in the umbilical cord.*

***Results:*** *Before delivery, maternal serum levels of MDA and GSH were higher and lower, respectively in both cases of pre-eclampsia when compared with normal pregnant.*
*In umbilical cord serum, the appearance of MDA were lower than the corresponding maternal values, while serum levels of GSH is higher. No differences were observed between umbilical cord serum and maternal serum concerning MDA and GSH levels after delivery.*

***Conclusion:*** *This study suggests that, lipid peroxidation is involved in the pathogenesis of maternal pre-eclampsia. The presence of protective mechanism against lipid peroxides in placental system is indicated by increased level of GSH in umbilical cord serum.*

***keywords:*** *lipid peroxidation, anti-oxidant status, pre-eclampsia, malondialdehyde, reduced glutathione*

## Introduction:

Pre-eclampsia is a pregnancy-specific condition that increases maternal and infant mortality and morbidity [1], Observed after the 20th week of pregnancy with systolic blood pressure of ≥ 140 mm Hg or diastolic blood pressure of ≥ 90 mm Hg accompanied by significant proteinuria [2]. The etiology is still unclear but impaired detoxification or enhanced levels of reactive (oxygen) metabolites may contribute to the development or maintenance of pre-eclampsia [3, 4].

Many evidences indicated that, this imbalance is present in both the maternal and placental compartments, and that the interaction between these two compartments result in the clinical manifestations of this disorder [5].

The source of lipid peroxides in pre-eclampsia is unknown, but it has been suggested that poorly perfused placental tissues may evoke the free radical process, and the initiation of generalized lipid peroxidation [6]. Orhan *et al* in 2003 reported an increased rate of production of thromboxane $A_2$ and lipid peroxides from placenta in pre-eclampsia [7].

Glutathione, as one of the major detoxifying and free radical scavenging system, may play a role in controlling the disease [8, 9].

This study was designed to evaluate the suspected role of oxidative stress during the pathophysiology of pre-eclampsia through the measurement of lipid peroxidation parameter (MDA) and the soluble anti-oxidant (GSH) in the peripheral blood of mothers and umbilical cord blood.

### Subjects and Methods:

Twenty-seven out patient primigravidas pregnant women attending the Abu-Ghraib Hospital at the day of delivery were selected to participate in this study. None of the women had cardiac, hepatic, or renal dysfunction. None of them had any obstetrical abnormalities (diabetes, rhesus immunization). None had essential hypertension.

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All women were performed verbally that they will participate in the study and their consent was obtained.

The levels of blood pressure, and protein in urine were determined at the time of sampling. The women were classified into:

1. Fifteen healthy normotensive women in the 3rd trimester of pregnancy served as control group.(10 by vaginal delivery, and 5 by caesarian section).
2. Twelve pregnant women, in the 3rd trimester of pregnancy served as pre-eclamptic un-treated control group. This group can be classified according to the severity of the disease into [10]:

a. Mild pre-eclampsia (n=6), their mean arterial blood pressure (MABP) (107 ± 1.4 mm Hg). (4 by caesarian section and 2 by vaginal delivery).

b. Moderate pre-eclampsia (n=6), their mean arterial blood pressure (MABP) (123 ± 8.7 mm Hg).( all by caesarian section).

Methyl dopa were given to patients in the pre-eclampsia groug to control hypertension.

Mid-stream urine samples were collected from patients to perform the following tests, routine general urine examination, a test for protein using Albustix (ames company) [11].

Venous blood samples were collected from women on the day of delivery and immediately after delivery. Cord blood was obtained immediately post-partum from the umbilical vein after clamping of the cord. Serum was aspirated after centrifugation of blood and kept frozen unless worked immediately.

MDA levels, as a parameter of lipid peroxidation was determined in serum according to the method of Buege and Aust [13]. Total thiol contents of serum, which can be used as indicator for reduced glutathione were measured according to the method of Ellman [14]. Total serum protein was determined according to the method of Lowry [15].

To test the differences between groups, ANOVA and student's t-test were made. Differences were considered significant with $P < 0.05$.

**Results:**

Characterization of women according to some clinical and laboratory parameters is given in table 1.

Serum MDA contents were detectable in a significantly higher level in all pre-eclamptic patients before delivery compared to normotensive pregnant controls

($P < 0.05$). The levels are being 2-times higher than that of the controls in mild pre-eclampsia and 4-times higher than that of the controls in moderate pre-eclampsia. There was also a highly significant increase in MDA contents in moderate pre-eclampsia when compared to mild cases ($P < 0.05$). (Table 2).

Serum GSH levels in mild pre-eclamptic women were significantly lower than their corresponding levels in normotensive controls group. ($P < 0.05$), and significantly lower levels were observed in moderate pre-eclampsia compared to controls.($P < 0.05$). There were significantly lower levels of serum GSH in moderate pre-eclamptic women compared to mild cases before delivery. ($P < 0.05$).(Table 2).

Concerning serum MDA contents in both mild and moderate pre-eclamptic women after delivery, there were significantly lower levels when compared to MDA contents before delivery ($P < 0.05$). Furthermore, serum levels of reduced glutathione were significantly increased in both mild and moderate pre-eclamptic patients when compared to their levels before delivery. ($P < 0.05$). (Tables 3 and 4).

Concerning serum MDA contents of the umbilical cord, there was a non-significant differences between normotensive, mild and moderate pre-eclamptic women.($P > 0.05$), while there was a significant increase in umbilical GSH levels in both mild and moderate pre-eclamptic patients when compared to normotensive controls. ($P < 0.05$).(Table 5).

With the regard to the serum contents of MDA in umbilical cord, the levels were significantly lower than before delivery in maternal serum in both mild and moderate pre-eclamptic groups.($P < 0.05$).(Tables 6 and 7).

Serum levels of reduced GSH were significantly increased in umbilical cord when compared to the maternal values in both mild and moderate pre-eclamptic women before delivery. ($P < 0.05$). (Tables 6 and &7).

No differences were detected between umbilical cord serum and maternal serum, concerning the levels of MDA and GSH after delivery. ($P > 0.05$). (Tables 8 and 9).

**Discussion:**

The data presented in this study showed that an increased level of serum MDA and a decreased level of serum GSH in women with mild or moderate cases of pre-eclampsia before delivery compared to normotensive pregnant controls. Our results are consistent with previous reports [4, 7], which allowed us to speculate that there were abnormally increased levels of lipid peroxides.

Lipid peroxides are toxic compounds that damage endothelial cells, increase peripheral vasoconstriction and increase thromboxane $A_2$ synthesis and decrease prostacycline synthesis [16, 17, 18, 19].

Among speculation regarding the etiology of enhanced lipid peroxidation in pre-eclampsia, has one line of thought indicated a possible deficiency of anti-oxidant GSH, a naturally-occurring tripeptide ( γ glutamyl cysteinyl glycine) whose nucleophilic and reducing properties play a central role in the metabolic pathways of most aerobic

**Table 4 MDA contents and GSH levels in maternal serum of moderate pre-eclampsia before and after delivery.**

| | Moderate pre-eclamptic un-treated control before delivery N= 6 | Moderate pre-eclamptic un-treated control after delivery N= 6 |
|---|---|---|
| MDA (nmol/mg protein) | 3.69 ± 0.6 | 0.852 ± 0.2 *** |
| GSH (µg/mg protein) | 0.089 ± 0.03 | 0.513 ± 0.05 *** |

****: P < 0.0005*

**Table 5: MDA contents and GSH levels in umbilical cord serum of normotensive, mild and moderate pre-eclampsia.**

| | Umbilical cord serum of normotensive pregnant controls N=15 | Umbilical cord serum of mild pre-eclamptic women N=6 | Umbilical cord serum of moderate pre-eclamptic women N=6 |
|---|---|---|---|
| MDA (nmol/mg protein) | $(0.873 \pm 0.13)_a$ | $(0.81 \pm 0.27)_a$ | $(0.88 \pm 0.18)_a$ |
| GSH (µg/mg protein) | $(0.59 \pm 0.29)_a$ | $(0.66 \pm 0.01)_b$** | $(0.63 \pm 0.02)_b$*** |

***: P < 0.005 ***: P < 0.0005*

*Each value is the mean ± SD. Values with non-identical subscripts (a,b,) within each parameter are significantly different.(P < 0.05)*

**Table 6: MDA contents and GSH levels in umbilical cord serum of mild pre-eclamptic.pregnant women.**

| | Mild pre-eclamptic women before delivery N=6 | Umbilical cord serum of mild pre-eclamptic women N=6 |
|---|---|---|
| MDA (nmol/mg protein) | $(1.91 \pm 0.37)_a$ | $(0.81 \pm 0.27)_b$*** |
| GSH (µg/mg protein) | $(0.11 \pm 0.02)_a$ | $(0.66 \pm 0.01)_b$*** |

****: P < 0.0005*

**Table 7: MDA contents and GSH levels in umbilical cord serum of moderate pre- eclamptic pregnant women.**

| | Moderate pre-eclamptic women before delivery N=6 | Umbilical cord serum of moderate pre-eclamptic women N=6 |
|---|---|---|
| MDA (nmol/mg protein) | $(3.69 \pm 0.6)_a$ | $(0.88 \pm 0.18)_b$*** |
| GSH (µg/mg protein) | $(0.089 \pm 0.03)_a$ | $(0.63 \pm 0.02)_b$*** |

****: P < 0.000*

**Table 8: MDA contents and GSH levels in umbilical cord serum of mild pre-eclamptic pregnant women.**

| | Mild pre-eclamptic women after delivery N=6 | Umbilical cord serum of mild pre-eclamptic women N=6 |
|---|---|---|
| MDA (nmol/mg protein) | (0.793 ± 0.23) | (0.81 ± 0.27) |
| GSH (µg/mg protein) | (0.623 ± 0.09) | (0.66 ± 0.01) |

**Table 9: MDA contents and GSH levels in umbilical cord serum of moderate pre- eclamptic pregnant women.**

| | Moderate pre-eclamptic women after delivery N=6 | Umbilical cord serum of moderate pre-eclamptic women N=6 |
|---|---|---|
| MDA (nmol/mg protein) | (0.852 ± 0.2) | (0.88 ± 0.18) |
| GSH (µg/mg protein) | (0.513 ± 0.05) | (0.63 ± 0.02) |

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cells[20]. The role of GSH in biological systems includes protection against reactive oxygen compounds, other toxic compounds of endogenous and exogenous origin and free radicals. Furthermore, GSH is the substrate for gluthathione peroxidase, an enzyme involved in the detoxification of lipid peroxides [21]. In addition, the conjugation of GSH with the foreign compounds is mediated in biological system by glutathione S trasferase enzyme [22], thus GSH depletion in pre-eclamptic women may also be attributed to the presence of such foreign metabolites leading to increased conjugation with GSH through glutathione S transferase.

Concerning umbilical cord serum, the result of this study showed that, there were a significant lower levels of serum MDA and significant higher levels of serum GSH when compared to maternal serum before delivery (tables 6 and 7), while a non significant differences in these two parameters in cord serum when compared to their corresponding levels to that of maternal values after delivery. (Tables 8 and 9). A possible explanation for that, lipid peroxides were increased abundantly in pre-eclamptic women, but not in their placentas, and their presence consumes GSH in maternal serum before delivery and not in placenta which harbors anti-oxidant but not lipid peroxides.

Moreover, no differences in the serum level of MDA were detected between umbilical cord serum of normotensive, mild and moderate pre-eclamptic women, while there was a significant increase in umbilical GSH levels in both cases of pre-eclampsia compared to nomotensive controls. (Table 5).These findings are in conflict with some published reports indicating that glutathione levels in serum from pre-eclamptic women are lower than in serum from normal pregnant women [23, 24]. In contrast, other authors have reported that, glutathione and glutathione peroxidase enzyme were elevated in the decidua and placenta in pre-eclamptis, [8].

This study gives support to those few studies considering lipid peroxidation as an important factor in the pathogenesis of pre-eclampsia. The rise in anti-oxidant GSH is probably of compensatory nature responding to increased lipid peroxides load in pre-eclampsia. Further studies are needed to clarify the relations between lipid peroxidation and anti-oxidative function and their pathophysiological significance in pre-eclampsia.

**Table 1: A description of women according to some clinical parameters:**

| Variables | Control normotensive pregnant N=15 | Mild Pre-eclamptic un-treated control N=6 | Moderate pre-eclamptic untreated control n=6 |
|---|---|---|---|
| Age (year) | 26 ± 5.6 | 27.5 ±3.7 NS | 24.5 ± 3.7 NS |
| SBP (mm Hg) | 117.33 ± 4.5 | 140.83 ± 2.04*** | 156.7± 10.1*** |
| DBP (mm Hg) | 77.33 ± 4.2 | 90.83 ± 2.04*** | 106.6 ± 8.2*** |
| MABP (mm Hg) | 90.67 ± 3.4 | 107.5 ± 1.4*** | 123.3 ± 8.7*** |
| Urinary protein (g/L) | 0 | 0.15 ± 0.05** | 1.66 ± 0.82** |
| Weight (Kg) | 65 ± 2.8 | 75 ± 3** | 84 ± 2.5** |
| Gestational age at the day of delivery (wks) | 35 ± 4.6 | 36 ± 2.7 NS | 36 ± 2.9 NS |

*Data are shown as mean ± SD values. The P-values refer to the differences from the control group.*
***: P < 0.005 ***: P < 0.0005*
*NS = non significance from control group*

**Table 2: MDA contents and GSH levels in maternal serum of normotensive pregnant control, mild and moderate pre-eclampsia before delivery.**

| | Normotensive pregnant control N=15 | Mild pre-eclamptic un-treated control N=6 | Moderate pre-eclamptic un-treated control N=6 |
|---|---|---|---|
| MDA (nmol/mg protein) | $(0.906 \pm 0.19)_a$ | $(1.91 \pm 0.37)_b$*** | $(3.69 \pm 0.6)_c$*** |
| GSH (µg/mg protein) | $(1.046 \pm 0.29)_a$ | $(0.11 \pm 0.02)_b$*** | $(0.09 \pm 0.03)_c$*** |

****: P < 0.0005*
*Each value is the mean ± SD. Values with non-identical subscripts (a,b,c) within each parameter are significantly different.(P < 0.05)*

**Table 3: MDA contents and GSH levels in maternal serum of mild pre-eclampsia before and after delivery.**

| | Mild pre-eclamptic un-treated control before delivery. N=6 | Moderate pre-eclamptic un-treated control after delivery. N=6 |
|---|---|---|
| MDA (nmol/mg protein) | 1.91 ± 0.37 | 0.793 ± 0.23 *** |
| GSH (µg/mg protein) | 0.11 ± 0.02 | 0.623 ± 0.09 *** |

****: P < 0.0005*

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