Study of oxidative stress and uric acid in pregnancy induced hypertension

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Abstract

Background: Pregnancy induced hypertension is a leading cause of morbidity and mortality in pregnant woman. Preeclampsia and Eclampsia Sepsis and Haemorrhage are the prime killers in pregnancy.
Aim: This study is aimed to assess the role of oxidative stress by estimating Malondialdehyde MDA), Glutathione –s-transferase (GST) and its severity by estimating serum uric acid levels in PIH.
Materials and Methods: The study comprised of 60 third trimester pregnant woman. Among those 24 were clinically diagnosed Preeclamptic cases, 16 were eclamptic cases and 20 were Normotensive antenatal controls. Plasma MDA, GST levels and serum uric acid levels were estimated and compared in them.
Results: Mean values of plasma MDA, GST and serum uric acid levels in cases were 5.14 ±1.88nmol/ml, 44.49 ±14.48IU/L, 7.21±1.63mg/dL and in controls mean values were 1.7±0.87nmol/ml, 70.98±12.68IU/L, 4.38±1.24mg/dL respectively.
Conclusion: Mean values of plasma MDA, serum Uric acid levels were significantly higher and plasma GST levels were significantly lower in pregnancy induced hypertension cases when compared with normotensive antenatal controls.

Keywords: Glutathione –s-transferase (GST), Malondialdehyde (MDA), Pregnancy induced hypertension, uric acid

1.Introduction

Pregnancy induced hypertension (PIH) is a leading cause of fetal growth retardation, infant morbidity, mortality and maternal death. In India maternal mortality due to Pregnancy induced hypertension is 15.6%[1]. It is categorized into Preeclamptic and Eclamptic toxemia. Preeclampsia is characterized by a clinical trial of Hypertension (>140/90 mm of Hg), proteinuria and edema developed after 20 weeks of gestation. Eclampsia is its severe form with superadded convulsions.

Preeclampsia contributes to more than 40% of iatrogenic premature deliveries[2]. In PIH spasm of small systemic arteries leads to ischemia, hypoxia necrosis and dysfunction in organs and tissues. Vasospasm results in endothelial dysfunction and damage decreased production of vasodilator factors like nitric oxide, prostaglandinE2, ProstaglandinI2, and increased vasoconstrictive factors like Endothelin, Thromboxane A2, Platelet derived growth factor. Nitric oxide syntheses (NOS) is inhibited by large amounts of free radicals, ROS and lipoperoxidative products like MDA resulting in decreased synthesis of nitric oxide and thus resulting in vasospasm[3].

Oxidative stress is an important factor in the pathogenesis of PIH. Malondialdehyde is an aldehyde is an end product of lipid peroxidation, Glutathione –s- transferase is an antioxidant enzyme. In this study we are trying to evaluate the oxidative stress and antioxidant status in pregnancy induced hypertension. Uric acid is used to assess the severity of the disease.
1.1 Aim
This study is aimed to assess the oxidative stress and antioxidant status severity in PIH by estimating lipid peroxidation marker plasma Malondialdehyde (MDA), Glutathione -S- Transferase (GST), and serum uric acid in both cases and controls and comparing them.

2. Materials and methods
Present study was carried out in Department of Biochemistry and Department of Obstetrics and Gynecology of S.V Medical College Tirupati on a total of 60 pregnant women in third trimester. Among those 24 were clinically diagnosed Preeclamptic cases, 16 were eclamptic cases and 20 were Normotensive age matched antenatal controls.

2.1 Inclusion criteria
Cases: Pregnant woman in third trimester clinically diagnosed to have PIH with blood pressure >140/90 mm of Hg on 2 separate occasions more than 6 hrs apart with bilateral pedal edema, proteinuria are taken as preeclampsia cases and those with overwhelming convulsions as eclampsia cases.
Controls: Age matched normotensive third trimester pregnant woman with no pedal edema, proteinuria and convulsions

2.2 Exclusion criteria
Include pregnant woman in first and second trimesters; Woman with previous H/O Hypertension, Diabetes, chronic renal failure, congestive cardiac failure, convulsions and Gout; Pregnant woman with anemia, chronic infections, sepsis, asthma etc. and pregnant woman taking antioxidant drugs.

2.3 Sample collection
After taking informed consent, 6ml of venous blood sample was collected from antecubital vein in aseptic conditions immediately after admission, before commencement of treatment. 4ml of sample is collected into EDTA containing test tubes to obtain plasma for estimating MDA, GST and 2ml of sample is used to obtain serum to estimate uric acid in it. Plasma MDA is estimated by Thiobarbituric acid method (TBA), plasma GST is measured using 1-Chloro-2,4-dinitrobenzene as substrate. Plasma and serum samples are analysed for uric acid by Brown method in Aimil colorimeter after proper standardization.

2.4 Statistical analysis
Data analysed by epi info 3.5.4 software by student’s t test.

3. Results
Table 1: Mean & S.D values in pregnancy induced hypertension cases and normotensive controls

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Mean &amp; S.D IN Controls</th>
<th>Mean &amp; S.D IN Cases</th>
<th>t- Value</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>MDA(nmol/L)</td>
<td>1.7 ± 0.87</td>
<td>5.14 ± 1.88</td>
<td>7.8</td>
<td>&lt;0.0001*</td>
</tr>
<tr>
<td>GST(IU/L)</td>
<td>70.98 ± 12.68</td>
<td>44.49 ± 14.48</td>
<td>6.8</td>
<td>&lt;0.0001*</td>
</tr>
<tr>
<td>Uric Acid (mg/dl)</td>
<td>4.38 ± 1.24</td>
<td>7.21 ± 1.63</td>
<td>6.9</td>
<td>&lt;0.001*</td>
</tr>
</tbody>
</table>

* Significant p-value <0.05

Fig 1: Bar diagram showing comparison between mean values of MDA, GST, Uric acid in PIH cases and normotensive controls

Table 2: Mean & S.D Values in preeclampsia and eclampsia cases

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Mean &amp; S.D in Preeclampsia cases (n=24)</th>
<th>Mean &amp; S.D in Eclampsia cases (n=16)</th>
<th>t-value</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>MDA(nmol/L)</td>
<td>4.621 ± 1.76</td>
<td>5.93 ± 1.89</td>
<td>2.9</td>
<td>0.05</td>
</tr>
<tr>
<td>GST(IU/L)</td>
<td>48.31 ± 13.48</td>
<td>38.77 ± 14.77</td>
<td>2.7</td>
<td>0.05</td>
</tr>
<tr>
<td>Uric Acid (mg/dl)</td>
<td>7.1 ± 1.48</td>
<td>7.41 ± 1.89</td>
<td>0.7</td>
<td>Not significant</td>
</tr>
</tbody>
</table>
4. Discussion

Our study was carried out on sixty third trimester women, 40 were pregnancy induced hypertension cases and 20 were normotensive antenatal controls. Among the 40 PIH cases 24 (60%) were preeclamptic cases and 16 (40%) were eclamptic cases. Mean and standard deviation of Plasma MDA, GST, Uric acid among cases and controls obtained was shown in Table 1 and their comparisons is shown as a bar diagram in Fig 1. Our study shows significant increase in levels of MDA and uric acid and a significant decrease in levels of GST in pregnancy induced hypertension. Several Studies are there showing similar findings[1]-[7].

Our study shows a significant variation in MDA, GST levels and a non significant variation in uric acid levels between preeclamptic and eclamptic cases as shown in Table 2 and Fig 2.

ROS functions as signal transducers but their overproduction can cause severe health problems they oxidize many biomolecules including membrane lipids. Lipid peroxides and oxygen species are involved in pathogenesis of PIH. In a healthy individual oxidation by free radicals and neutralization by antioxidants remains in balance, when the Reactive oxygen species (ROS) overwhelm the antioxidant defenses of the host it results in oxidative stress. Malondialdehyde is the terminal compound of lipid peroxidation and is used as a marker of oxidative damage induced by ROS[4].

Glutathione –s-transferase is an antioxidant enzyme its levels were significantly lower in PIH cases GST conjugated glutathione to toxic reactive compounds 4- hydroxynonenal & cholesterol α oxide which are generated during oxidation of membranes, thus GST protects cell s from oxidative stress by detoxifying secondary ROS produced when ROS reacts with cellular constituents.[5][6].

Increased lipid peroxidation product (MDA) levels and decreased antioxidant (GST) levels clearly indicates role of oxidative stress in PIH.

Uric acid differentiates PIH from chronic hypertension. In chronic hypertension uric acid levels are within the normal range. Hyperuricemia results due to decreased renal excretion that occurs as a consequence of preeclampsia and it also occurs due to tissue ischemia and oxidative stress .Uric acid impairs nitric oxide generation in endothelial cells and induces hypertension and vascular disease in PIH[7].

Few studies are there showing no evidence of oxidative stress in PIH[8][9].

5. Conclusion

Our study shows a clear significant role of oxidative stress in pregnancy induced hypertension and its severity. Supplementation of antioxidants in pregnant women as a prophylaxis may bring down the incidence of PIH.

References


