A Study of β-Human Chorionic Gonadotropin Level in Pre-Eclamptic and Normotensive Pregnant Women

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Abstract: Objectives: To study the role of β – hCG in pathogenesis of preeclampsia and its association with severity of preeclampsia. Materials and Methods: The prospective randomized study was conducted on 500 pregnant women of gestational pregnancy between 12 - 24 weeks with singleton pregnancy. According to American college of obstetrics and gynecology [ACOG, 2013], patients were classified into three groups, normal (N=250), mild pre-eclampsia (N=200) and severe pre-clampsia (N=50). Quantitative determination of hCG by sandwich enzyme immunoassay. Results were expressed as mean ±standard error. The significance of the difference between the values from different groups was determined by ANOVA. A level of P < 0.05 was defined as statistically significant. Results: Systolic and diastolic blood pressures were significantly increased in mild and severe (P < 0.001) pre-eclampsia women. The levels of urea, creatinine and uric acid were significantly increased in severe pre-eclampsia women. The serum level of maternal β-hCG was markedly raised in pre-eclampsia in comparison to controlled and parallel with the severity of pre-eclampsia. The maternal serum level of β-hCG plays one of the important role in pathogenesis of pre-eclampsia and its severity.

Keywords: β-hCG, mild Pre-eclampsia, severe Pre-eclampsia, Eclampsia.

1. Introduction

Pre-eclampsia is a multisystemic disorder involving the placenta, liver, kidneys, blood and the neurological and cardiovascular system. The symptoms of this multisystemic disorder, which appear during the second and third trimester of pregnancy are caused by the increased vasoconstriction, which result in maternal hypertension, decreased utero-placental blood flow, edema, proteinuria, abnormal clotting, liver and renal dysfunctions. A generalized dysfunction of maternal cells may underlie most of the clinical symptoms such as hypertension, fluid retention, and clotting abnormalities. Hormonal changes contribute to the physiological maternal adaptations during human gestation. Fluid balance, blood pressure, digestion, respiration, fuel and mineral metabolism, immune response, and sexual behavioral functions are reprogrammed during pregnancy and occur under modulation of hormonal changes from very early gestation to fetal delivery and beyond. Preeclampsia is responsible 25% of all fetal growth retardation and 15% preterm birth in developed countries. The incidence of preeclampsia in India is about 8-10% and maternal mortality due to be reported 8% 4.

The human chorionic gonadotropin (hCG) is a glycoprotein composed of two non covalently link subunits, α and β, and is produced by syncytiotrophoblast cells of the placenta. Maternal serum hCG peaks at 8 – 10 week of gestation and then decline to reach a plateau at 18-20 week of gestation. The free β - subunit can derive from three sources, namely, direct trophoblast cell production, dissociation of hCG into free α and free β – subunits, and by macrophage or neutrophil enzymes nicking the hCG molecule 5.

The free β – hCG circulating in maternal serum corresponds to only about 0.3 – 4 % of the total hCG. In pre-eclampsia histological examination reveals focal cellular necrosis in the syncytiotrophoblast and increased mitotic activity with cellular proliferation in the cytotrophoblast 6.

In addition the proliferating trophoblast in severe pre-eclampsia is rapidly transformed into syncytiotrophoblast within 72 hours. The normal placenta differentiates during pregnancy with the cytotrophoblast dominant in early gestation and the syncytiotrophoblast dominant in late pregnancy. Placenta vascular damage leading to decreased oxygen supply might result in increased hCG production by hyperplasic cytotrophoblastic cells. The aim of this present study was to find out the role of β– hCG in pathogenesis of preeclampsia and its association with severity of preeclampsia.

2. Materials and Methods

This study was carried out at the Department of obstetrics and gynecology, R.N.T. medical college, Udaipur, after taking approval from ethical committee from 2011 to March 2014. The prospective randomized study was conducted on 500 pregnant women of gestational pregnancy between 12 - 24 weeks with singleton pregnancy.

Patients with chronic hypertension, twin pregnancy, molar pregnancy, chromosomally abnormal fetus, diabetes, chronic renal disease, autoimmune disorders, thrombophelias, family history of diabetes mellitus and cardiovascular diseases were excluded from the study.

The patients were classified into three groups, Normal (N=250) mild pre-eclampsia (N=200) and severe pre-eclampsia (N=50). The diagnosis of preeclampsia was established in according with the American college of obstetrics and gynecology definition. The healthy pregnancy...
was diagnosed on the basis of clinical, biochemical, and ultrasound findings. Mild pre–eclampsia was considered having blood pressure ≥140 mm Hg systolic and ≥ 90 mm Hg diastolic, on two occasions each 4 hours apart accompanied by proteinuria at least 1 + on dipstick testing and severe preeclampsia was considered having blood pressure ≥ 160/110 mm Hg and proteinuria at least 3+ on dipstick.

Quantitative determination of hCG by sandwich enzyme immunoassay. Results are expressed as mean ± standard error. The significance of the difference between the values from different groups is determined using one way analysis of variance (ANOVA). A level of P < 0.05 is defined as statistically significant.

### Table 1: Distribution of various groups of subjects according to Severity:

<table>
<thead>
<tr>
<th>S.N</th>
<th>Group studies</th>
<th>Number of subjects (N)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Healthy pregnant women (controls)</td>
<td>250</td>
</tr>
<tr>
<td>2.</td>
<td>Pre–eclamptic primigravidas (Mild)</td>
<td>200</td>
</tr>
<tr>
<td>3.</td>
<td>Pre–eclamptic primigravidas (Severe)</td>
<td>50</td>
</tr>
<tr>
<td></td>
<td>Total</td>
<td>500</td>
</tr>
</tbody>
</table>

### Table 2: Demographic characteristics of normal pregnancy and pre–eclampsia cases:

<table>
<thead>
<tr>
<th>S. No.</th>
<th>Parameters</th>
<th>Normal Pregnancy (N = 250)</th>
<th>Mild Pre eclampsia (N = 200)</th>
<th>Severe Preeclampsia (N = 50)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Means gestational age (weeks)</td>
<td>20.2 ± 2.25</td>
<td>22.42 ± 3.25</td>
<td>21.3 ± 2.9</td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td>2.</td>
<td>Mean maternal age (years)</td>
<td>20.58 ± 2.3</td>
<td>23.2 ± 3.1</td>
<td>21.8 ± 2.9</td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td>3.</td>
<td>Mean systolic blood pressure (mm Hg)</td>
<td>114.25 ± 7.42</td>
<td>156.24 ± 7.90</td>
<td>183.86 ± 8.24</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>4.</td>
<td>Mean diastolic blood pressure (mm Hg)</td>
<td>76.61 ± 8.67</td>
<td>99.51 ± 4.87</td>
<td>113.06 ± 5.11</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

### Table 3: Laboratory data of normal pregnancy, Mild and severe pre–eclampsia:

<table>
<thead>
<tr>
<th>S. No.</th>
<th>Parameters</th>
<th>Normal Pregnancy (N = 250)</th>
<th>Mild Pre eclampsia (N = 200)</th>
<th>Severe Preeclampsia (N = 50)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Urea (mg /dl)</td>
<td>15.50e ± 2.59</td>
<td>24.52 ± 3.99</td>
<td>35.46 ± 4.94</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>2.</td>
<td>Creatinine (mg /dl)</td>
<td>0.74 ± 0.14</td>
<td>0.83 ± 0.07</td>
<td>1.46 ± 0.27</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>3.</td>
<td>Uric acid (mg /dl)</td>
<td>4.85 ± 1.31</td>
<td>5.53 ± 1.00</td>
<td>7.60 ± 0.77</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>4.</td>
<td>β–hCG (mIU / ml)</td>
<td>8091.44 ± 1493.68</td>
<td>15850.26 ± 1789.53</td>
<td>19791.70 ± 987.02</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

### 3. Result

Distribution of various group of subjects according to severity are shown in table 1. (i) mild pre –eclampsia cases of those who showed ≥ 140 mm Hg systolic or ≥ 90 mm Hg diastolic one 2 occasions at least 4 hrs apart after 20 wks gestation in women with a previously normal blood pressure. (ii) Severe pre –eclampsia cases of those who showed ≥ 160 mm Hg systolic or ≥110 mm Hg diastolic, on 2 occasions 4 hours or more apart while the patient is an bed rest. (ACOG, 2013) Out of 250 pre –eclampsia patients, 200 were mild preeclampsia and 50 were severe preeclampsia. The clinical results of mild and severe pre –eclampsia patients were compared (Table 2 & Table 3). Demographic data of women with preeclampsia and healthy normotensive controls are shown in Table 2. No significant difference was observed in terms of gestational age & maternal age when compared normotensive controls and pre–eclampsia groups. Systolic and diastolic blood pressures were significantly increased in mild and severe (P < 0.001) pre-eclampsia women, when compared with normotensive controls.

The levels of urea, creatinine and uric acid were found to be significantly increased in severe pre –eclampsia women (Table – 3). β–hCG levels were significantly higher in mild & severe (P < 0.001) preeclamptic women, as compared to normotensive controls. (Table – 3).

### 4. Discussion

In preeclampsia the rise of blood pressure is due to vasoconstriction and impaired angiogenesis leading to hypoxia and hyperplasia of trophoblastic cells which causes hyper secretion of placental hormone ultimately leading to high level of circulation β– hCG. Human chorionic gonadotropin(hCG), a glycoprotein hormone is produced in excess by normal and neoplastic trophoblastic conditions like twin and molar pregnancies. High – levels of circulating β – hCG are found in preeclampsia. As pre- eclampsia is probably a trophoblastic disorder, elevated β – hCG is thought to reflect early placental damage or dysfunction, therefore, the study of pathologic changes and secretary reaction of the placenta may prove essential for understanding this disease. There in general agreement that the placenta remains the main source of hCG in patients with pre– eclampsia, whether the cause of the high circulating levels of the hormone by placenta is still debated. Some advocate that hCG secretion may be increased as a consequence of abnormal placental invasion or placental immaturity. It may also be linked to the trophoblast response to hypoxia with the development of hyper secretory state.

The syncytiotrophoblast is a differentiated trophoblast found in early gestational period transformed from the cytotrophoblast. Although the mechanism of regulation of gestational hCG remains largely unknown, it is generally accepted that hCG, are only secreted by syncytiotrophoblasts. In preeclampsia, the cytotrophoblast transformed into syncytiotrophoblast. Human placenta synthesizes steroid, protein, and glycoprotein hormones throughout gestation. The production of hCG by the placenta in early pregnancy is critical for implantation and maintenance of the blastocyst. Since it is postulated that preeclampsia is likely a trophoblastic disorder. Remzi Gokdeniz et al, found a strict relationship between severe pre – eclampsia and elevated serum β – hCG levels.
indicating that should be an abnormal placential secretory function in patients with severe pre – eclampsia. In 1934, Smith et al talked about increasing hCG levels in severe preeclampsia for the first time.

Luckas M et al, Benn PA et al & Ashour AM et al indicate that an unexplained elevation of serum hCG significantly correlated with the occurrence of preeclampsia. But pouta et al and Aguilina et al demonstrated no relation between levels of serum hCG and severity of pre – eclampsia. Stamilio et al also found no association between severe pre – eclampsia and elevated second trimester hCG level. In the present study like all other investigations the serum hCG level was found significantly increased in pre – eclampsia than control mothers (P ≤ 0.00001) with remarkably raised in severe preeclampsia than mild (P ≤ 0.00001).

5. Conclusion

Preeclampsia remains a major cause of perinatal morbidity worldwide. Exact etiology is still not defined. It usually presents clinically toward the end of pregnancy, after the disease process is well established. The new markers provide an opportunity to study the early natural history of disease and possibly to conduct treatment trials. The present study confirmed the elevated levels of β-hCG are associated with preeclampsia in second trimester. These findings suggest that severe pre-eclamptic women have higher hormonal changes than mild preeclampsia, and this reflect the abnormal placentation in these patients.

References


Author Profile

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