Original Research Article

A Prospective Study on Placental Changes in Pre-Eclamptic Women and Correlation of Severity of Hypertension with Placental Changes and their effect on Neonatal Outcome

Authors

Dr Priyanka Agrawal¹, Dr Subhash Kumar Agrawal², Dr Sarita Singh³

¹Assistant Professor, Department of Pathology, S.S. Medical College, Rewa, MP
²Assistant Professor, Department of Anaesthsiology, S.S. Medical College, Rewa
³PG Student, Department of Obs & Gyanecology, S.S. Medical College, Rewa, MP

Corresponding Author
Dr. Subhash Kumar Agrawal
Department of Anaesthsiology, S.S.Medical College, Rewa, MP 486001, India
Email: drsubhash24@gmail.com, mob 9589717934

Abstract

Context: Placenta forms a functional unit between mother and fetus. Preeclampsia is regarded as a risk factor in pregnancy and it leads to placental insufficiency. This, in turn causes both maternal and fetal morbidity and mortality. The present study intends to compare morphological and histological changes of placenta in pre-eclampsia and correlate severity of hypertension with histopathological changes of placenta and correlate these changes with perinatal outcome.

Study Design: A descriptive type of study.

Place and period of study: Department of Pathology, Anaesthesia and Gynecology, S.S.Medical College, Gandhi Memorial Hospital, Rewa(M.P.) from 1st July 2016 to 30th June 2017.

Materials: 200 cases were taken. 90 cases were of Mild Preeclampsia, 78 cases were of Moderate and 32 cases were of Severe Preeclampsia were taken for this study.

Method: Samples were grouped in three groups on the basis of severity of Preeclampsia. All samples were studied morphologically and histologically.

Result: To summarise the results of this study was the birth weight and placental weight significantly decreases from moderate group of preeclampsia and also placental infarction, calcification, syncytial knot, basement membrane thickening and fibrinoid necrosis significantly increases from the moderate preeclampsia and is highest in severe preeclampsia.

Conclusion: In the present study all the morphological and histopathological variants of placenta are affected very less in cases of mild preeclampsia but there is a significant increase in the changes from the moderate group and the perinatal outcome was also comparatively poor in this group. Till now, antihypertensives are started when B.P. >160/110 mmhg, means from severe preeclampsia. But on the basis of the results of this study we recommend early initiation of antihypertensive treatment, it will be helpful in improving the perinatal outcome.

Keywords: Placenta, Preeclampsia, Morphology, Histopathology, perinatal outcome.
Introduction

Placenta forms a functional unit between mother and fetus. Placenta maintains an accurate record of infant’s prenatal growth. Pregnancy induced hypertension is associated with macroscopic and microscopic changes in the placenta. The maternal utero-placental blood flow is decreased in pre-eclampsia. Maternal vasospasm leads to fetal hypoxia. Pregnancies with moderate to severe PIH have smaller, irregular placenta, marginal insertion of umbilical cord, calcification and abnormal trophoblastic proliferation were observed these changes are directly proportional to the severity of the disease and perinatal outcome become worse with advancing grades of pregnancy induced hypertension and utero-placental insufficiency.

The objective of present study is intended to compare morphological and histological changes of placenta in pre-eclampsia and correlate severity of hypertension with histopathological changes of placenta and perinatal outcome.

Materials and Methods

Sample size was of 200. The cases with systolic blood pressure greater than 140 mmhg, diastolic blood pressure greater than 90 mmhg on two measurements taken 6 hour apart, association with proteinuria more than 300 mg in 24 hour urine included in the study these cases further divided as

Group-1: Mild preeclampsia-systolic B.P. 140-160 mmhg & Diastolic blood pressure <100 mmhg.

Group-2: Moderate preeclampsia-Systolic B.P. 140-160 mmhg diastolic blood pressure >100 mmhg to <110 mmhg.

Group-3: Severe preeclampsia –systolic blood pressure >160 mmhg, diastolic blood pressure >110 mmhg.

Pregnant women with gestational age 28 to 40 week with B.P. more than 140/90 mmhg with proteinuria were included in study.

Cases with hypertension prior to this pregnancy and hypertension secondary to other causes, associated Cardiac diseases, Renal disorder, Diabetes mellitus, Multiple gestations, Anemia, Pregnancy ≤ 28 weeks of gestation, Postdated pregnancies and Placenta praevia / abnormalities of placental insertion were excluded from the study.

After delivery weight of newborn baby were recorded. The shape, weight, diameter, thickness, no of cotyledons of the placenta and insertion of umbilical cord in placenta was assessed. Later the placental was cut into vertical strips (bread loaf manner) of 0.5 cms thickness and the gross lesions were re-examined. Evaluation of histological features as Syncytial knots, Vasculosyncytial membrane, Villous Stromal Fibrosis, Fibrinoid necrosis and Basement membrane thickening were assessed

Table 1: Histological features of normal placenta

<table>
<thead>
<tr>
<th>Sl. No</th>
<th>Parameters</th>
<th>Characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Syncytial knots</td>
<td>Present on 11-30% of terminal villi</td>
</tr>
<tr>
<td>2</td>
<td>Vasculosyncytial membrane</td>
<td>Present on 6-30% of terminal villi</td>
</tr>
<tr>
<td>3</td>
<td>Villous stromal fibrosis (Fibrotic villi)</td>
<td>Present in 3% of terminal villi</td>
</tr>
<tr>
<td>4</td>
<td>Fibrinoid necrosis (Intravillous fibrinoid)</td>
<td>Present in 0-3% of terminal villi</td>
</tr>
<tr>
<td>5</td>
<td>Basement membrane thickening</td>
<td>Present in 0-3% of terminal villi</td>
</tr>
</tbody>
</table>

All the gross and histological features were compared between the placenta of the PIH group.

Results

- Out of 200, 90 cases were of Mild Preeclampsia, 78 cases were of Moderate and 32 cases were of Severe Preeclampsia.
- Out of 200, 66 babies (43%) were between 2000-2500 gms followed by 58 (29%) babies were birth weight between 2500-3000 gms. In severe preeclampsia, maximum number of babies (71%) were weight less than 2 kg.
Out of 200, 117 (58.5%) placenta having weight 400-500 gms followed by 22% between 300-400 gm. In mild and moderate preeclampsia, maximum number of cases having placental wt between 400-500gm while in severe preeclampsia it was between 300-400gm. Result were statistically significant.

- Increase in severity of preeclampsia mean placental weight decreases and with decrease in mean placental weight mean baby birth weight decreases.
- Placental Diameter decreases with increase in Severity of Preeclampsia.
- Average Thickness decreases with increase in Severity of Preeclampsia.
- Number of Cotyledons decreases with increase in Severity of Preeclampsia.
- Out of 200 in 127 (63.5%) cases placenta were having calcification. Calcification increases with increase in severity of preeclampsia.

Out of 200, 168 cases (84%) having syncytial membrane <6%. Paucity of vasculo syncytial membrane seen in all cases of severe preeclampsia.

- Stromal villous fibrosis increases with increase in severity of preeclampsia
- Out of 200, 111 (55%) placenta having basement membrane thickening >3%. majority of placenta of severe preeclampsia were having basement membrane thickening >3%.

Increase in grading of infarction increases with severity of preeclampsia. In mild preeclampsia 41% cases were having infarction in placenta while in severe preeclampsia cases 100% of cases were having infarction.

Out of 200 cases, 111 (55.5 %) placenta were having syncytial knot in more than 30% of villi. In women of severe preeclampsia 29 placenta (90.6%) were having syncytial knot in >30% of villi.
Out of 200, 119 (59.5%) placenta were having fibrinoid necrosis between 3–10%.

Majority of babies were born alive in mild (95.55%) and in moderate (89.74%) preeclampsia group while in severe preeclampsia group only 78.1% of babies were born alive. Incidence of stillbirth and early neonatal death was 21.8% & 28.1% respectively in severe preeclampsia group.

Table 2 - Correlation of perinatal outcome with placental weight and histopathological changes

<table>
<thead>
<tr>
<th>Variable</th>
<th>Number</th>
<th>Alive babies</th>
<th>Still Birth</th>
<th>NICU ADMISSION</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Neonatal Death</td>
</tr>
<tr>
<td>Placental Weight</td>
<td>&lt;300</td>
<td>10</td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>300-400</td>
<td>44</td>
<td>24</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>400-500</td>
<td>117</td>
<td>99</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>&gt;500</td>
<td>29</td>
<td>24</td>
<td>1</td>
</tr>
<tr>
<td>Infarction</td>
<td>Absent</td>
<td>81</td>
<td>71</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Mild</td>
<td>79</td>
<td>6</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Moderate</td>
<td>31</td>
<td>17</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Severe</td>
<td>9</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td>Syncytial Knot</td>
<td>&lt;30</td>
<td>89</td>
<td>84</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>&gt;30</td>
<td>111</td>
<td>65</td>
<td>8</td>
</tr>
<tr>
<td>Stromal Fibrosis</td>
<td>3%</td>
<td>31</td>
<td>27</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>4-6%</td>
<td>77</td>
<td>58</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>&gt;6%</td>
<td>92</td>
<td>39</td>
<td>9</td>
</tr>
<tr>
<td>Basement Membrane Thickness</td>
<td>&lt;3%</td>
<td>89</td>
<td>69</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>&gt;3%</td>
<td>111</td>
<td>71</td>
<td>6</td>
</tr>
<tr>
<td>VSM</td>
<td>&lt;5%</td>
<td>168</td>
<td>117</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td>&gt;5%</td>
<td>32</td>
<td>22</td>
<td>3</td>
</tr>
</tbody>
</table>

Above table shows correlation of placental weight, infarct, syncytial knot, stromal fibrosis with fetal outcome was significant, while correlation with basement membrane thickening and vasculosyncytial membrane was not significant.
**Discussion**

Pregnancies complicated by PE are reflected in the placenta both macroscopically and microscopically. Although the placenta adapts well to the hypoxic condition in PE, the compensatory changes that occur are insufficient. These compensatory changes cause mal-development and inadequate placental mass, causing placental dysfunction that leads to oxidative stress and chronic fetal hypoxemia. In preeclampsia, placenta tend to be smaller as compared to uncomplicated pregnancy. Blood flow to placenta is reduced in hypertensive disorder of pregnancy and result in unduly small fetus. Moreover due to hypoxia placenta weight is also reduced. In the present study comparing preeclamptic placentas to control placentas, the mean placental weight, thickness, diameter, and surface area were decreased and were found to be more significant. Mean weight of placenta in mild, moderate and severe preeclampsia group were 484.88gm, 420.16 gm & 357.37gm respectively. This study shows that weight of placenta reduces significantly (p<0.0001) as severity of preeclampsia increases. The macroscopic changes found in our study are analogous to the findings of other PE cases in the literature. With severity of preeclampsia percentage of calcification increased supported by others. The calcification indicates an ‘aging’ of the placenta that occur near the end of pregnancy. But it may be a sign of premature ageing in the cases of PIH. Thus study showed that area of infarction increases with increase in severity of preeclampsia. Infarction in any organ develop due to rapid loss of arterial blood supply. Placental infarction ,it represent villous tissue that has died due to rapid loss of intervillous (maternal) circulation. Excess of placental infarction can attributed to abnormality of spiral arteries which predispose to thrombosis and vessel rupture. In mild preeclampsia group 41% cases were having infarction, in moderate group 64.1% cases and in severe 100% cases were having infarction.

These results were in between those present in literature. Villi with syncytial knot were increased with increase in severity of preeclampsia. In mild preeclampsia group, 27.77 % cases were having syncytial knot >30%, in moderate group 73% cases, and in severe preeclampsia group 90.6% cases were having syncytial knot >30%. These results were higher than those present in literature.

In present study, vasculosyncytial membrane decreased with increase in severity of preeclampsia, in mild preeclampsia <5% vasculosyncytial in 77.77% and >5% in 22.22%, in moderate preeclampsia <5% in 84.6% and >5% in 15.38% and in severe preeclampsia <5% in 100%. In a similar study vasculo-syncytial membrane were less in hypertensive group as compared to normotensive group and this difference was highly significant. Similar results were found in earlier studies as significantly less vasculo-syntial membranes in hypertensive group. And less than 6% vasculo-syncytial membrane count is an indication of either immaturity or regression. A study showed PIH worsens the uteroplacental ischemia. The villous abnormalities such as cytotrophoblastic hyperplasia and basement membrane thickening are due to diminution of uteroplacental blood flow. The proliferation of villous cytotrophoblastic cells is thought to be in response to chronic placental ischemia and these cells perhaps secrete basement membrane substrate leading to high basement membrane thickness. In present study, villi with < 3% basement membrane thickening found in 72.22%, 26.92% and 9.37% in mild, moderate and severe preeclampsia and villi with >3% basement membrane thickness in 27.77%, 73.03% and 90.6% in mild, moderate and severe preeclampsia. Thus, the present study showed that, there is significantly increased (p<0.0001) basement membrane thickening in severe PIH group. Basement membrane thickening in other studies also is higher in hypertensive group as compared to normotensive population.
In mild preeclampsia group, in 17.77% of cases stromal fibrosis was present in >6% of villi, in moderate group 62.82 % cases and in severe group 84.3 % cases were have stromal fibrosis in >6% of villi. The results were statistically significant (p<0.0001) as severity of preeclampsia increases.

Fibrinoid necrosis is the hallmark of immunological reaction in the villous tissue. It has been claimed that anti-trophoblastic antibodies may be found in the serum of the pregnant women and the level of this antibody are unduly high in the serum of preeclampsia. It has been possible that in both normal and preeclampsia pregnancies an antibody –antigen reaction occurs in the trophoblast. With increase in severity of hypertension percentage of villi with fibrinoid necrosis were increased. Fibrinoid necrosis was seen in more than >10% of villi in 13.33% , 57.69% , and 75% cases of mild , moderate ,and severe preeclampsia respectively. These findings were stastically significant p(p<0.0001%) and similar to those in literature.

Incidence of still birth (21.8%) and neonatal death (28.1%) was high in severe preeclampsia group. In other studies 10% neonate were with Apgar score less than 5 and 10% were stillbirth.

To summarise the results of present study, the birth weight and placental weight significantly decreases from moderate group of preeclampsia and also placental infarction, calcification, syncytial knot, basement membrane thickening and fibrinoid necrosis significantly increases from the moderate preeclampsia group.

**Conclusion**

The intrauterine existence of fetus depends on one vital organ, the “placenta”. Placenta is the organ by means of which the nutritive, respiratory and excretory function of fetus is carried on. Placenta maintains an accurate record of infant’s prenatal growth. The histomorphological feature of placenta is important determinant of both baby birth weight and fetal growth.

In the present study all the morphological and histopathological variants of placenta are affected very less in cases of mild preeclampsia but there is a significant increase in the changes from the moderate group and the perinatal outcome was also comparatively poor in this group. Till now, antihypertensives are started when B.P. >160/110 mmhg, means from severe preeclampsia .But on the basis of the results of this study we recommend early initiation of antihypertensive treatment, it will be helpful in improving the perinatal outcome.

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