

# Effects of Placental Infarctions on the Fetal Outcome in Pregnancies Complicated by Hypertension

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## ABSTRACT

**Objective:** To determine the frequency of placental infarcts and its effects on the fetal outcome in pregnancies complicated by hypertension.

**Study Design:** Case control.

**Place and Duration of Study:** Obstetrics Unit of North Colombo Teaching Hospital, Ragama, Sri Lanka, from January 2003 to January 2004.

**Patients and Methods:** Placentae of 150 normotensive women and 200 hypertensive women were studied to detect the number of placentae with infarctions. Apgar score, birth weight and the head circumference of the newborns were measured and analyzed.

**Results:** The frequency of placental infarcts was significantly higher in hypertensive group (30%) compared to normotensive group (18.7%). An association between placental infarction and low Apgar score of the newborn was seen in the hypertensive group ( $p < 0.001$ ). The difference in the birth weight of the newborns in hypertensive and normotensive groups in relation to placental infarction was statistically significant (2.2 vs. 3.1 kg,  $p < 0.001$ ). A highly significant difference was observed in the head circumference of the newborns of hypertensive group compared to normotensive group in relation to placental infarctions (30.7 cm vs. 32.3 cm,  $p < 0.001$ ).

**Conclusion:** The frequency of placental infarcts was higher in hypertensive women when compared to normotensives. Placental infarctions had an adverse effect on growth and development of the newborns. This information can be useful in planning and management of future pregnancies.

**Key words:** Placental infarcts. Hypertension. Apgar score. Birth weight. Head circumference.

## INTRODUCTION

Minor areas of infarctions are seen in about 25% of placentae from normal pregnancies.<sup>1</sup> Extensive placental infarction is usually seen in placentae from pre-eclamptic mothers when there is a vascular abnormality in the form of an acute atherosclerosis which predisposes to thrombosis.<sup>2</sup> Extravillous trophoblast infiltrating into the placental bed transforms the small caliber spiral arteries into large uteroplacental arteries. The absence of these physiological changes, coupled with other lesions such as acute atherosclerosis reduce the uteroplacental blood flow.<sup>3</sup> A secondary change found in the spiral arteries in pre-eclamptic pregnancies is an acute atherosclerosis characterized by necrosis, the presence of foam cells and inflammatory cells. Damage to these vessels often causes areas of the placenta to become infarcted.<sup>4</sup>

In a true infarction, a group of villi are infarcted due to a lesion of the maternal vessels supplying blood to the intervillous space with impairment of the integrity of the maternal circulation.<sup>5</sup> Since birth weight is directly related to the maternal blood flow to the placenta,<sup>6</sup> it follows that birth weight may also be related to whether or not the trophoblast has invaded the spiral arteries in the myometrium and increased their capacity.<sup>7</sup>

Intervillous thrombi, central infarctions and thrombi in fetal circulation were found to have significantly higher rates in pre-eclampsia.<sup>8</sup> Highly significant increase in the incidence of infarction, intervillous fibrin deposition, stromal fibrosis, and syncytial knotting were found in placentae of newborns with intrauterine growth restriction and in placentae of hypertensive mothers compared to full-term normal placentae.<sup>9,10</sup> Multiple infarctions are the main placental lesion related to intrauterine growth restriction.<sup>11</sup>

Apgar score is a scoring system to evaluate the physical condition of the newborn at birth and provide information to improve perinatal and neonatal care. An infant suffering from birth asphyxia or fetal distress at birth, therefore, has a low Apgar score.<sup>12</sup> Severe placental infarction is related to fetal distress.<sup>13</sup>

Small areas of infarction involving less than 5% villous parenchyma occur in 25% of uncomplicated

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pregnancies and are of no clinical significance.<sup>14</sup> Extensive placental infarctions of more than 10% of villous parenchyma leading to placental insufficiency can result in fetal hypoxia, intrauterine growth restriction and intrauterine death.<sup>15,16</sup>

The aim of this study was to determine the frequency of placental infarcts in hypertension and its effect on the Apgar score, birth weight and head circumference of the newborn.

## PATIENTS AND METHODS

This case control study was performed among 150 normotensive pregnant women and 200 pregnant women with hypertension complicating pregnancy. A pregnant woman with a blood pressure of less than 140/90 mmHg, throughout the pregnancy, was considered as a normotensive. Those women were recruited using a systematic sampling method. They had an uncomplicated period of gestation of 37-42 completed weeks.

A pregnant woman with an absolute rise in blood pressure of at least 140/90 mmHg, if the previous blood pressure is not known or rise in systolic pressure of at least 30 mmHg or a rise in diastolic pressure of at least 15 mmHg over the previously known blood pressure,<sup>17</sup> was considered as hypertension complicating pregnancy. Furthermore, they were classified into the sub-groups using a simple modified classification.<sup>18</sup>

Essential hypertension group included women who were diagnosed as having pre-pregnancy hypertension or had a history of hypertension before 20 weeks of gestation. Pregnancy induced hypertension without proteinuria was considered hypertension after the 20<sup>th</sup> week of gestation having less than 100 mg/dl protein in urine. Pregnancy induced hypertension with proteinuria (pre-eclampsia) was hypertension after the 20<sup>th</sup> week of gestation having 100-300 mg/dl proteins in urine. Severe pre-eclampsia and eclampsia was defined in women with blood pressure of 160/110 mmHg and above and severe proteinuria of 1000 mg/dl with or without fits.

Urinary protein estimation was performed by Human test combine 9SG dipstick method. Women with any other illness other than hypertension were excluded from the study. Socio-demographic data of the women were noted. Women were informed about the study and written consent was obtained at the time of recruitment. Ethical clearance was obtained from the Research, Higher Degrees and Ethics Committee of Faculty of Medicine, University of Colombo.

Immediately after delivery, after assessing the Apgar score, the birth weight and the head circumference of the newborns were measured. The placentae were fixed in 10% formalin for few weeks. A series of 0.5 cm thick

vertical strips were cut across the fetal and maternal surfaces of the placentae and central and peripheral sections were taken from each slice. In addition, sections were taken from gross lesions, red areas and white plaques.<sup>19</sup> Sections were stained with hematoxylin and eosin and the areas of true infarction were detected by light microscopy.

Placental infarcts were grouped according to the extent of infarction. When infarctions were absent, it was marked 0, infarction involving less than 5% of villous parenchyma=1, infarcts involving 5-10% parenchyma=2 and infarcts involving more than 10% of the villous parenchyma as 3. To determine the relationship between placental infarcts and birth weight, head circumference and Apgar score of the newborn, the placentae were dichotomized into placental infarcts present or absent. Strength of association was determined by calculating risk ratio and statistical significance was assessed using the chi-square test for categorical variables and t-test for numeric variables.  $P < 0.05$  was considered as significant. Epi Info version 6 was used for data entry and initial analysis. Multivariate analysis was performed using STATA version 8.2.

## RESULTS

The mean age and the parity of hypertensive and normotensive mothers were comparable. Out of 200 hypertensive women, 60 placentae showed evidence of infarcts (30%) (Table I).

**Table I:** Age and parity of the study sample and frequency distribution of the placental infarcts in hypertensive and normotensive groups.

|                        | Hypertensive group<br>n=200 |      | Normotensive group<br>n=150 |      |
|------------------------|-----------------------------|------|-----------------------------|------|
| Mean (SD) age in years | 29.6 (5.8)                  |      | 27.8 (4.8)                  |      |
| Parity                 | Number                      | %    | Number                      | %    |
| 1                      | 92                          | 46.0 | 69                          | 46.0 |
| 2 and 3                | 86                          | 43.0 | 62                          | 41.3 |
| > 3                    | 22                          | 11.0 | 19                          | 12.7 |
| Placental infarction*  |                             |      |                             |      |
| 0                      | 140                         | 70.0 | 122                         | 81.3 |
| 1                      | 30                          | 15.0 | 28                          | 18.7 |
| 2                      | 10                          | 5.0  | -                           | -    |
| 3                      | 20                          | 10.0 | -                           | -    |

\* Placental infarcts absent-0 < 5% -1 5-10%-2 >10%-3

In the normotensive group, 18.7% of placentae showed small areas of infarction. In the hypertensive group, there were 34 women with essential hypertension, 97 women with pregnancy induced hypertension without proteinuria, 37 women had pre-eclampsia and 32 women had severe pre-eclampsia and eclampsia. Extensive areas of infarctions were seen in 53.1% of placentae of women with severe pre-eclampsia and eclampsia.

Of the 200 hypertensive women, 196 delivered a live baby at or after 37 weeks of gestation. There were

4 intrauterine deaths with cord around neck in 2 of them. Therefore, association between hypertension and infarctions on the fetus was determined by analyzing 196 live births (Table II).

**Table II:** Relationship between the blood pressure, placental infarcts and Apgar score among live births.

|               | Apgar  | Infarction |        |       | Risk ratio | X <sup>2</sup> | Significance |
|---------------|--------|------------|--------|-------|------------|----------------|--------------|
|               |        | Present    | Absent | Total |            |                |              |
| Hypertensives | Low    | 31         | 33     | 64    | 2.37       | 16.76          | p < 0.001    |
|               | Normal | 27         | 105    | 132   |            |                |              |
|               | Total  | 58         | 138    | 196   |            |                |              |
| Normotensives | Low    | 11         | 25     | 36    | 1.83       | 3.30           | p = 0.069    |
|               | Normal | 19         | 95     | 114   |            |                |              |
|               | Total  | 30         | 120    | 150   |            |                |              |
| Total         | Low    | 42         | 58     | 100   | 2.24       | 20.35          | p < 0.001    |
|               | Normal | 46         | 200    | 246   |            |                |              |
|               | Total  | 88         | 258    | 346   |            |                |              |

Overall risk ratio  $MHX^2$  -18.728; Risk ratio -2.19; P < 0.001

Presence of placental infarction was associated with low Apgar score. This association was stronger (risk ratio = 2.37) and significant (p < 0.001) among hypertensives. Though this association was present to a lesser degree (risk ratio=1.83) among normotensives, it failed to reach statistical significance (p=0.069).

There was a significant association between hypertension and birth weight in both hypertensive and normotensive pregnancies but the association between placental infarction and birth weight was significant only among hypertensives. These results were obtained by doing an ANOVA, where birth weight was the outcome variable and hypertension, placental infarction and their interaction was considered as predictors.

There was a significant association between hypertension and head circumference in both hypertensive and normotensive pregnancies but the association between placental infarction and head circumference was significant only among hypertensives. These results were obtained by doing an ANOVA where head circumference was the outcome variable and hypertension, placental infarction and their interaction was considered as predictors (Table III).

**Table III:** Fetal characteristics (birth weight and head circumference) by maternal blood pressure and placental infarction.

| Placental infarction | Count   | Hypertension group weight in grams |     |       | Normotensive group weight in grams |     |       | F-value | p-value  |
|----------------------|---------|------------------------------------|-----|-------|------------------------------------|-----|-------|---------|----------|
|                      |         | Mean                               | SD  | [N]   | Mean                               | SD  | [N]   |         |          |
| Placental infarction | Absent  | 2619                               | 671 | [138] | 3092                               | 343 | [122] | 37.25   | p<.0.001 |
|                      | Present | 2223                               | 747 | [58]  | 3139                               | 441 | [28]  |         |          |
| Placental infarction | Count   | Head circumference in centimeters  |     |       | Head circumference in centimeters  |     |       | 20.1    | p<0.001  |
|                      |         | Mean                               | SD  | [N]   | Mean                               | SD  | [N]   |         |          |
| Placental infarction | Absent  | 32.3                               | 2.1 | [138] | 33.0                               | 1.1 | [122] | 20.1    | p<0.001  |
|                      | Present | 30.7                               | 2.6 | [58]  | 32.3                               | 1.0 | [28]  |         |          |

## DISCUSSION

Pre-eclampsia is a serious complication of pregnancy

associated with altered uteroplacental circulation. A variety of changes in placental villi are known to occur in hypertension complicating pregnancy. These changes are directly proportional to the severity of the disease and perinatal outcome becomes worse with advancing grades of pregnancy induced hypertension.<sup>20</sup> In pregnancies, complicated by pre-eclampsia, placental infarction is one histological feature representing severe focal uteroplacental ischaemia and the extent and incidence increase with the increasing severity of the illness.<sup>21</sup> High prevalence of inflammation, infarction, ischemia, intervillous hemorrhage was seen in placentae of pregnancy induced hypertension with intrauterine growth restriction.<sup>22</sup> Severity of hypertension adversely affect both fetus and the placenta.<sup>23</sup> In keeping with the similarities of the previous studies, this study also showed that the frequency of placental infarction is higher in hypertension when compared to normotensive pregnancies and the frequency was increased with the severity of the illness.

Fetal hypoxia is not infrequent near term and may lead to fetal distress or death. Risk is increased if placental function has been impaired by pre-eclampsia.<sup>24</sup> Newborn babies of mothers with poorly controlled hypertension were small for dates and had birth asphyxia.<sup>25</sup> This study results show that the newborn babies with a low Apgar score at birth, showed evidence of infarction in their placentae. Significant association between the placental infarcts and Apgar score of the newborns was seen among hypertensives.

Pregnancy complicated by hypertension is commonly associated with placental insufficiency resulting in fetal growth restriction.<sup>26</sup> Placental infarctions are the second common type of placental pathology seen in low birth weight infants.<sup>27</sup> In this study, a statistically significant difference in the birth weight of newborns of the hypertensive group in relation to placental infarcts was seen when compared to normotensive group (p=0.001). Birth weight as well as head circumference both considered as parameters for intrauterine growth restriction<sup>28</sup> have been found to have a statistically significant difference in the newborns of hypertensive group in relation to placental infarctions. Having found a significant relationship of infarction to birth weight and head circumference of the newborns in the present study, it is obvious that diminution of placental functional reserve affects the fetus in utero, which may have resulted in reduction in birth weight and head circumference.

## CONCLUSION

Placental infarcts are seen in about 30% placentae of women with hypertension. An association was seen between placental infarcts and low birth weight and

reduced head circumference, placental infarcts have an adverse effect on the fetal outcome.

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