Morphological Variations of Human Placenta in Preterm Labor, Pregnancy-induced Hypertension, and Gestational Diabetes Mellitus

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Abstract

Background: Preterm birth is one of the primary causes of perinatal mortality and morbidity. Pregnancy-related conditions causing preterm labor are associated with gross morphological changes in placenta, the fetomaternal organ which is vital for maintaining pregnancy and for promoting intrauterine growth of the fetus.

Objectives: To study the morphological variations of human placenta in preterm labor, to compare the findings of the study with the morphology of human placentae of normal pregnancies, and to correlate the morphologic changes of the placenta in preterm labor with fetal outcome.

Materials and Methods: A cross-sectional study was conducted among 695 placentae delivered from the Department of Obstetrics and Gynaecology, Dr. Somervell Memorial CSI Medical College, Karakonam, during a period of 6-month from June 2016. The gross morphological and histological examinations of placentae were performed.

Results: There were 50 preterm placentae including 30 from pregnancy-induced hypertension (PIH), 10 from gestational diabetes mellitus (GDM), and 2 from anemic pregnant mothers. The preterm placentae from PIH showed a significant reduction in placental weight, diameter and thickness and significantly more incidence of infarction, retroplacental hematoma, and calcification. Histologically, placentae in PIH showed significantly large number of syncytial knots, cytotrophoblastic proliferation, fibrinoid necrosis, and villus hyalinization. Newborn babies of mothers with PIH showed significant reduction of birth weight and low Apgar score. 50% of the preterm placentae from GDM were heavier, paler, and thick.

Conclusion: Prominent risk factors of preterm labor were PIH and GDM. PIH showed significant differences in various parameters of placental morphology and histology and fetal outcome.

Key words: Fetal outcome, Gestational diabetes mellitus, Placenta, Pregnancy induced hypertension, Preterm labor

INTRODUCTION

The human placenta is the vital organ for maintaining pregnancy and promoting development of the fetus in utero. Placenta is an intrauterine fusion of fetal and maternal tissues for the purpose of physiological transfer of nutrients and oxygen from mother to fetus and transfer of waste products of metabolism from fetus to mother for continuation of fetal life. The intrauterine existence of fetus is dependent on this vital organ. Placenta has been considered as a valuable indicator for fetal and maternal diseases and conditions. Many maternal diseases or disorders are associated with high perinatal morbidity and mortality and gross pathological changes in placenta. Abnormal placenta adversely affects the fetal outcome.
As placenta is the mirror of maternal and fetal status, complications in pregnancy reflect in the placenta in a significant way both macroscopically and microscopically. Preterm birth is the primary cause of perinatal mortality and morbidity. The American College of Obstetricians and Gynaecologists (2016) defined preterm labor or premature labor as regular contractions of the uterus resulting in changes in the cervix that start before 37 weeks of pregnancy. Changes in the cervix include effacement and dilation so that the fetus can enter the birth canal.

Globally, perinatal mortality rate is 49.6 per 1000 live births. One of the major causes of perinatal mortality is preterm birth and it accounts for 6-10% of all births. Preterm labor has become a significant public health issue leading to perinatal mortality in developing countries. Among the various factors, pregnancy-induced hypertension (PIH) and gestational diabetes mellitus (GDM) are two important high-risk factors for preterm birth. Other factors that increase the risk of preterm birth include the following:

- Having a previous preterm birth
- Having a short cervix
- Short interval between pregnancies
- History of certain types of surgery on the uterus or cervix
- Multiple pregnancy and Antepartum hemorrhage
- Lifestyle factors such as low prepregnancy weight of the mother, smoking or substance abuse during pregnancy
- Anemia complicating pregnancy.

Hypertension in pregnancy is responsible for 5-8% of all maternal deaths. Hypertensive disorders of pregnancy are strongly associated with fetal growth retardation and prematurity leading to perinatal morbidity and mortality. GDM is defined as any degree of glucose intolerance with onset or first recognition during pregnancy. In women with average or high-risk (marked obesity, personal history of GDM, glycosuria, or a strong family history of diabetes), the plasma glucose concentration 1 h after a 50 g oral glucose load (glucose challenge test), followed by a diagnostic oral glucose tolerance test on the women exceeding the glucose threshold value (>140 mg/dl) at glucose challenge test confirms the diagnosis. GDM is a pregnancy-related condition causing high maternal morbidity and increased risk of perinatal morbidity and mortality.

Anemia exerts profound changes on the maternal circulatory system and has serious effects on both mother and fetus. Anemia in mother leads to hypoxia which results in low birth weight of baby and premature delivery.

The prevalence of these risk factors of preterm labor shows geographical variations.

This research work has been conducted with the objectives to find the prevalence of preterm labor and to study the morphological variations of human placenta in conditions leading to preterm labor at Dr. Somervell Memorial CSI Medical College, Karakonam, a health-care facility in rural South Kerala, India.

Objectives
- To study the morphological variations of human placenta in preterm labor
- To compare the findings of the study with those of human placentae of normal pregnancies
- To correlate the morphologic changes of placenta in preterm labor with fetal outcome.

MATERIALS AND METHODS

A cross-sectional study was conducted among placentae from 659 pregnant ladies admitted in the labor room, Department of Obstetrics and Gynaecology, Dr. Somervell Memorial CSI Medical College, Karakonam, South Kerala, India, during a period of 6-month from June 2016.

Placentae from those pregnant women who delivered before 37 weeks of pregnancy were considered as the preterm group. Placentae from mothers having normal, uncomplicated pregnancy formed the normal group.

Inclusion Criteria
Those pregnancies with preterm labor.

Exclusion Criteria
All pregnant mothers with a history of hypertension or diabetes mellitus detected before pregnancy.

Before the study, approval from the Institutional Ethics Committee and permission from the Head of the Department of Anatomy and Head of Department of Obstetrics and Gynecology were obtained. Informed consent was taken from the parents of the newborns.

Definitions
- Pregnant mothers who had blood pressure at or above 140/90 mm Hg on at least two occasions 6 h apart diagnosed for the first time after 20 weeks of gestation, with or without edema and/or proteinuria formed the PIH group.
- Mothers having a fasting plasma glucose level >126 mg/dl, or an occasional plasma glucose >200 mg/dl detected for the first time after pregnancy were included as having GDM.
Pregnant mothers with hemoglobin (Hb) level <11 g/dl formed the anemic group. According to the WHO classification, anemic group was divided into 3 groups:

- Group a - Mild anemia (Hb level 11-10 g/dl)
- Group b - Moderate anemia (Hb level 10-7 g/dl)
- Group c - Severe anemia (Hb level <7 g/dl).

**Method of Data Collection using Pretested Schedule**

Clinical findings of mothers were collected from case sheets, along with recording of their obstetric and medical history. Their investigation reports were noted (blood sugar, urea, creatinine, Hb levels, urine for albumin, pus cells, and ophthalmic examinations). Mothers were considered to be hypertensive if the blood pressure was 140/90 or above mm of Hg. Mothers with blood sugar levels higher than normal as per definition were considered to have gestational diabetes.

Placentae were collected immediately after vaginal delivery and cesarean section and were washed in running tap water. The placentae along with cord were coded. Any abnormality of cord and membranes was noted and were cutoff by sharp scissors. The placentae were cleaned and excess water was removed with blotting paper. Then, placentae were immersed in 10% formalin.

Examination of placenta was done for gross and histological studies.

Size, shape, surface area and thickness of placentae, number of cotyledons, presence of infarction, calcification, and site of insertion of umbilical cord were noted. The placentae weight was taken using standard weighing machine.

Placental tissues were taken from the following sites for histological studies:

- Margins – at 12, 3, 6, 9 O’ clock positions
- Near the insertion of the umbilical cord
- Center of the placenta
- Umbilical cord at placental junction and cut end
- Infarcted area if any
- Fibrotic area if any.

Placental tissues were stained and examined under microscope for number of syncytial knots, fibrinoid necrosis, cytotrophoblastic cell proliferation, calcification, and hyalinization of villi in the preterm group in comparison to normal group.

Neonatal outcome in the form of birth weight, Apgar score, presence of any congenital anomalies, need for neonatal resuscitation, and admission to newborn intensive care unit were noted. Fetal-placental weight ratio was calculated in each case.

Statistical analysis was made using Chi-square test and Student’s t-test.

**RESULTS AND DISCUSSION**

Among 695 placentae delivered from the Department of Obstetrics and Gynaecology, Dr. Somervell Memorial CSI Medical College, Karakonam, during a period of 6-month from June 2016, 50 placentae were from preterm labor. The gross morphological and histological findings of preterm placentae were compared with a normal group of significantly comparable maternal age and parity.

The prevalence of preterm labor was 7.19% in this study (Table 1).

Prominent risk factors of preterm labor in this study were PIH (60%) and GDM (20%) (Table 2) (Figure 2).

In this study, 26.7% hypertensive placentae were irregular in shape (Figure 2). A study conducted by Agarwal et al. did not show a significant variation of shape in hypertension.

The incidence of infarction among placentae of the PIH was 36.7% and the same of the nonhypertensives was 6.7% in the present study.

Udaina et al. and Majumdar and Dasgupta, and Corrêa et al. made similar observation in their study.

In this study, the presence of infarction was related to low birth weight and intrauterine death (IUD) of fetus (Table 3).

**Table 1: Distribution of placentae-based on term of delivery**

<table>
<thead>
<tr>
<th>Category</th>
<th>Number of placentae (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Term</td>
<td>645 (92.806)</td>
</tr>
<tr>
<td>Preterm</td>
<td>50 (7.194)</td>
</tr>
<tr>
<td>Total</td>
<td>695 (100)</td>
</tr>
</tbody>
</table>

**Table 2: Distribution of preterm placentae (N=50) and risk factors**

<table>
<thead>
<tr>
<th>Risk factor of preterm labor</th>
<th>Number of cases (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pregnancy induced hypertension</td>
<td>30 (60)</td>
</tr>
<tr>
<td>Gestational diabetes mellitus</td>
<td>10 (20)</td>
</tr>
<tr>
<td>Low prepregnancy weight of mother</td>
<td>4 (8)</td>
</tr>
<tr>
<td>Anemia</td>
<td>2 (4)</td>
</tr>
<tr>
<td>Multiple (twin) gestation</td>
<td>1 (2)</td>
</tr>
<tr>
<td>Antepartum hemorrhage</td>
<td>1 (2)</td>
</tr>
<tr>
<td>Cervical incompetence</td>
<td>1 (2)</td>
</tr>
<tr>
<td>Hypothyroidism</td>
<td>1 (2)</td>
</tr>
<tr>
<td>Total</td>
<td>50 (100)</td>
</tr>
</tbody>
</table>


Placental features such as placental weight, diameter, thickness, and number of cotyledons were significantly less in PIH (Figure 3) compared to normal group (Table 4).

Similar findings were reported from other studies also. In the studies by Udaina et al., Majumdar and Dasgupta, and Vijayalakshmi and Kittali observed that marginal insertion of cord was significantly associated with hypertensive placentae.

In the PIH group of this study, five placentae showed abnormal insertion of cord. Among them, four placentae showed marginal insertion (Figure 4) and one showed velamentous insertion while the placentae of normotensive group showed central insertion of umbilical cord. There was insignificant association between insertion of umbilical cord and PIH ($P > 0.05$).

Histology of Placenta in PIH

Placentae in PIH showed significantly large number of syncytial knots, cytotrophoblastic proliferation, fibrinoid necrosis, and villus hyalinization compared to normal group in this study.

In the present study, fetal-placental weight ratio was not showing statistically significant relation between the two groups. Another study by Vijayalakshmi and Kittali has reported increased F/P weight ratio in the hypertension complicating pregnancy.

Insertion of Umbilical Cord

Majumdar and Dasgupta and Duley observed that preterm labor and preterm birth associated with increased fetal mortality.

| Table 3: Gross appearance of placentae (normal vs. pregnancy induced hypertension) |
|---------------------------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| Placental features              | Component       | Placental features | Placental features |
|---------------------------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| Shape                           | Discoid         | 22 (73.3)       | 30 (100)        | 5.894           | $P < 0.001$     |
|                                 | Irregular       | 8 (26.7)        | 0 (0.0)         | 1.433           | $P > 0.05$      |
| Presence of hematoma            | Yes             | 2 (6.7)         | 0 (0.0)         | 2.821           | $P < 0.01$      |
|                                 | No              | 28 (93.3)       | 30 (100)        | 2.635           | $P < 0.01$      |
| Presence of infarction          | Yes             | 11 (36.7)       | 2 (6.7)         |                 |                 |
|                                 | No              | 19 (63.3)       | 28 (93.3)       |                 |                 |
| Presence of calcification       | Yes             | 17 (56.7)       | 7 (23.3)        |                 |                 |
|                                 | No              | 13 (43.3)       | 23 (76.7)       |                 |                 |

In this study, Apgar score of new born babies was found to be significantly low in the hypertensive group ($P < 0.001$) (Table 5).

The means of Apgar score of babies at birth of PIH and nonhypertensive groups were $6.9 \pm 1.8$ and $9 \pm 0$ and the same at 5 min were $8.5 \pm 0.8$ and $10 \pm 0$, respectively (Table 6).

There were two cases of IUDs in the PIH group.

Similar finding was observed by Pandure and Ghosh who found that preterm labor and preterm birth associated with increased fetal mortality.
Comparison of Placentae in Normal versus Gestational Diabetes

This study was found that in gestational diabetes; there was increased birth weight of babies. The placentae of gestational diabetic mothers showed significant increase in size, weight, and volume in the present study (Figures 5 and 6).

Radaelli et al. (2003), Segregur et al. (2009), and Fahima Akhter et al. found that placentae of diabetic mothers show significant increase in size, weight, volume, area, thickness, diameter, and circumference than those of normal mothers.

Furthermore, placentae from diabetic mothers showed significant increase in villous edema, fibrin deposition, calcification, and congestion of blood vessels.

Comparison of Placentae in Normal versus Anemia

In this study, the placental weight and volume were reduced in anemia (Hb 9 g/dl) complicating pregnancy. Chavez and Corral M (2003) stated that there is increase in placental weight and placental weight/newborn baby weight ratio in placenta from anemic pregnancies. Huang et al. (2001) stated that placental volume was significantly increased in anemic group and the uniform enlargement of placenta was a physiological compensatory growth.

CONCLUSION

The prevalence of preterm labor was 7.19% in the present study. Prominent risk factors of preterm labor were PIH and GDM. 60% of preterm placentae from PIH were delivered by early induction for the sake of mother and new born. PIH showed significant differences in various parameters of placental morphology and histology and fetal outcome. There were two cases of preterm IUD in the PIH group. In GDM, there was increased birth weight of babies. Placenta from pregnancy with combined PIH and GDM were normal in size and volume. The preterm placentae of gestational diabetic mothers showed significant increase in size, weight, and volume in the present study. Examination of the placentae
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Table 6: Comparison of fetal outcome (normal vs. PIH)

<table>
<thead>
<tr>
<th>Variable</th>
<th>PIH=30</th>
<th>Normal=30</th>
<th>Difference of means</th>
<th>“t”</th>
<th>df</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth weight</td>
<td>30</td>
<td>30</td>
<td>2.5±0.7</td>
<td>0.4</td>
<td>2.973</td>
<td>58</td>
</tr>
<tr>
<td>Apgar score at birth</td>
<td>28</td>
<td>30</td>
<td>6.9±1.8</td>
<td>2.1</td>
<td>6.294</td>
<td>56</td>
</tr>
<tr>
<td>Apgar score at 5 min</td>
<td>28</td>
<td>30</td>
<td>8.5±0.8</td>
<td>1.5</td>
<td>10.13</td>
<td>56</td>
</tr>
</tbody>
</table>

PHI: Pregnancy-induced hypertension, SD: Standard deviation

Figure 5: Placenta from gestational diabetes mellitus (weight 750 g)

Figure 6: (a and b) Placenta from gestational diabetes mellitus

gives valuable information about the perinatal health of the new born baby and the mother.

ACKNOWLEDGMENT

We are indebted to all the participant parents of newborns for the kind consent. We are thankful to Dr. Jasmine and Dr. Vishnu for helping in data collection and photography.

REFERENCES


Source of Support: Nil, Conflict of Interest: None declared.