Macroscopic Changes in the Human Placenta in Hypertensive Disorders of Pregnancy in Indian Women: A Cross-sectional Study

ABSTRACT

Introduction: Hypertension (HTN) is a common complication in 6-10% of pregnancies and is one of the prime factors for foetal, as well as, maternal fatalities and morbidities. Significant pathological changes are seen in the placenta in hypertensive pregnancies before affecting the foetus. These changes may serve as an early warning system for detecting foetal issues like low birth weight and growth restriction. Early detection and intervention of morphological changes in the placenta and umbilical cord can help prevent adverse foetal outcomes.

Aim: To study the macroscopic changes in the placenta in women with HTN induced by pregnancy compared to non hypertensive pregnant women.

Materials and Methods: The present cross-sectional descriptive study was conducted in the Department of Anatomy and the Department of Obstetrics and Gynaecology, Ramaiah Medical College Hospital, Bengaluru, Karnataka, India, between December 2017 and January 2019. A sample size of 43 each was taken for non hypertensive and hypertensive subjects, including those with preeclampsia and chronic HTN with superimposed preeclampsia. The placental morphological parameters, routine biochemical tests and neonatal outcomes of both groups were analysed statistically using the Shapiro-Wilk test, Independent t-test and Chi-square test. A probability value less than 0.05 was considered for statistical significance.

Results: The mean age of participants was 28.35±3.026 years in the hypertensive group and 26.23±2.636 years in the control group. The circular, oval and irregular shapes were 29 (65.9%), 10 (22.7%) and 4 (9.3%) in non hypertensive subjects and 33 (78.6%), 7 (16.27%) and 3 (7.1%) in the hypertensive subjects, respectively. The surface area (mean-142.44±49.69; p-value<0.001), radius (mean-6.622±1.24; p-value<0.001), circumference (mean-37.419±6.091; p-value<0.001), the quantum of cotyledons (mean-13.09±3.344; p-value<0.001) were lesser in the hypertensive group than the non hypertensive subjects. There were differences in placental and foetal weight among non hypertensive and hypertensive subjects, but the differences were insignificant. The Appropriate for Gestational Age (AGA) babies were more in non hypertensive subjects.

Conclusion: The present study found hypertensive pregnancies to be associated with a greater occurrence of unfavourable foetal outcomes. Furthermore, it highlights the importance of investigating the placenta’s physical attributes and their association with foetal outcomes to develop standard operating protocols for diagnostic and therapeutic approaches in normal/complicated pregnancies.

INTRODUCTION

Hypertension (HTN) is a common complication in 6-10% of pregnancies and is one of the prime factors for foetal growth and development [2]. The health of the placenta is critical for a healthy baby. During pregnancy, the placenta facilitates haemopoiesis, foetal circulation, nutrition, removal of waste, hormone secretion, exchange of gases and immunity of the foetus [2]. The growth of the human foetus is limited by the inability of the placenta to supply nutrients and oxygen to the foetus, leading to foetal under-nutrition, poor growth and low birth weight [3]. It has been suggested that placental nutrient transfer is significantly affected by blood flow and morphological features like surface area and thickness of the placenta [4].

The placenta is currently the focus of interest because significant pathological changes are seen in it before affecting the foetus. Hence, the changes in the placenta may serve as “an early warning system” for foetal issues [5]. There are significant macroscopic placental changes resulting in foetal growth restriction and hypoxia [6]. Uteroplacental vascular thrombosis leads to placental ischaemia and accelerated placental maturation resulting in calcification. These are the most common gross morphological changes in severe Pregnancy-induced Hypertension (PIH) [7,8]. HTN is associated with increased vascular resistance leading to decreased uteroplacental perfusion and foetal stem artery constriction resulting in an adverse foetal outcome [9]. All these changes result in a much smaller placental size. The placental weight and size are inversely proportional to the degree of PIH [7,9]. Studies have shown lower neonatal birth weight in PIH, and it has been positively correlated with placental weight. In addition, the mean placental surface area is also significantly lower with an inverse association between surface area and disease severity. Interestingly, the placental surface area also directly correlates with foetal distress [7,9]. In PIH, the umbilical cord diameter has been reported to be low. The site of cord insertion is more likely to be eccentric, central or marginal. This is thought to be associated with impaired placental perfusion leading to poor foetal outcomes and low birth weight [10-12]. By identifying morphological placental and umbilical cord changes, early intervention by delivery may prevent poor foetal outcomes.

Placental changes in women with hypertensive disorders have been studied. None of these studies have included the full spectrum of anatomical parameters or compared placental changes with all measures of foetal outcome. The primary aim was to study the macroscopic changes in the placenta in women with HTN induced by pregnancy compared to non hypertensive pregnant women. The objective was to associate the macroscopic placental changes with antenatal biochemical parameters and neonatal outcomes.

Keywords: Calcification, Eclampsia, Foetus, Pregnancy-induced hypertension, Preeclampsia
MATERIALS AND METHODS

A cross-sectional descriptive study was conducted in the Department of Anatomy and the Department of Obstetrics and Gynaecology, Ramaiah Medical College, Bengaluru, Karnataka, India, from December 2017 to January 2019. Prior ethical clearance was obtained from the Institutional Ethics Committee (IEC). Written informed consent was obtained from all participants.

Sample size calculation: Based on a previous study conducted by Udainia A and Jain ML, the mean placental weight was found to be 495 with a standard deviation of 114.11 in the control group as compared to 405.67 with a standard deviation of 101.64 in the PIH group [13]. In the present study, based on this finding, considering a similar mean difference and power of 90%, and an alpha error of 1%, the sample size was calculated to be 43 in each group.

Inclusion criteria: Inclusion criteria: Antenatal women presenting to the Labour Room of the study Institution both nulliparous and multiparous women, and with normal vaginal and caesarean section deliveries were included in the study.

Exclusion criteria: Women with maternal anaemia, gestational diabetes mellitus, multiple pregnancies, cardiac and renal diseases and cases with manual removal of retained placentae were excluded from the study.

Study Procedure

Placentae from the non hypertensive and hypertensive subjects were collected from the hospital, and the findings were compared with the patients’ history and biochemical investigations during their routine antenatal visits. The haematological and biochemical reports were taken from the patients’ files. Placentae were washed in tap water and blood clots were removed. The formaldehyde-preserved samples were examined for various parameters. The parameters observed were:

A. Maternal

1. Blood pressure: Based on the National High Blood Pressure Education Program’s (NHBPEP) classification [14], the hypertensive subjects were grouped as given below:

   - Group-1: Gestational HTN-BP ≥140/90 mmHg for the first time during pregnancy; No proteinuria
   - Group-2: Preeclampsia-BP ≥140/90 mmHg after 20 weeks’ gestation; proteinuria ≥300 mg/24 hours or ≥1+ dipstick
   - Group-3: Eclampsia-BP ≥160/110 mmHg after 20 weeks’ gestation; proteinuria ≥2000 mg/24 hours or ≥2+ dipstick
   - Group-4: Chronic HTN with superimposed preeclampsia: New onset proteinuria ≥300 mg/24 hours in hypertensive women but no proteinuria before 20 weeks’ gestation
   - Group-5: Chronic HTN-BP ≥140/90 mmHg before pregnancy or diagnosed before 20 weeks’ gestation or HTN first diagnosed after 20 weeks’ gestation and persistent after 12 weeks postpartum

2. Placental parameters:

   - Shape: circular, oval or irregular
   - Attachment of umbilical cord: eccentric, marginal or central
   - Weigh (in grams): measured using a digital weighing scale (before preserving the placentæ in formalin solution).
   - Diameter (in centimeters): Two diameters measured at right angles to each other. The mean of the two maximum diameters was considered. All measurements were performed by a single observer.
   - The surface area (in cm²) was calculated using π(radius)²
   - Thickness (in centimeters): the maternal surface of the placenta was arbitrarily divided into three equal zones by drawing two circles. With a long needle, the thickness was measured at points 1-the center of the central zone; points 2a and 2b from the middle zone; points 3a and 3b from the peripheral/outer zone. The mean of five measurements was considered for thickness [Table/Fig-1].

   [Table/Fig-1]: Measurement of placental thickness.

   - Mean quantum of cotyledons: on the maternal side of the placenta
   - Presence or absence of calcification and retro placental clots.

3. Biochemical parameters:

   - Serum Creatinine
   - Platelet count
   - Liver Function Test (Only Aspartate Aminotransferase (AST) and Alanine Transaminase (ALT)). Parameters of the third trimester were taken for measurement.

STATISTICAL ANALYSIS

The data were analysed using the Statistical Package for Social Sciences (SPSS) software version 18.0. The normality of the data was analysed using the Shapiro-Wilk test. Descriptive statistics on macroscopic variables were described in terms of mean with standard deviation. The foetal outcome was summarised in terms of percentage. Independent t-test was used to analyse the differences in macroscopic changes in HTN and non hypertensive subjects. The Chi-square test was utilised to compare foetal outcomes in hypertensive and non hypertensive subjects. A probability value less than 0.05 was considered for statistical significance.

RESULTS

In the study, in Group-1, there were 24 samples; in Group-2, there were 13 samples; in Group-3, there were four samples; Group-4 had nil samples; and Group-5 had two samples. The mean age of participants was 28.35±3.026 years in the hypertensive group and 26.23±2.636 years in the control group.

In both hypertensive and non hypertensive subjects, the placenta was circular, oval and irregularly shaped. The circular, oval and irregular shapes were 29 (65.9%), 10 (22.7%) and 4 (9.3%) in non hypertensive subjects and 33 (78.6%), 7 (16.27%), and 3 (7.1%) in the hypertensive subjects, respectively [Table/Fig-2].
The current study showed a higher incidence of eccentric insertion, n=27 (61.4%) followed by central, n=12 (27.3%) and marginal, n=4 (9.3%) in the non hypertensive subjects. In comparison, insertion was central in 20 (46.5%), followed by marginal in 13 (30.1%) and eccentric in 10 (23.3%) hypertensive subjects. The p-value was <0.001 and hence, statistically significant. Statistical significance was observed for placental radius, circumference, surface area and quantum of cotyledons. The difference in foetal weight was not significant between the two groups [Table/Fig-3].

A higher incidence of calcified areas, 20 (46.5%) was noted in the hypertensive subjects; however, 2 (4.5%) were also seen in the non hypertensive subjects. Statistical significance was seen for calcified areas (p-value<0.001). Retroplacental clots were observed in 18 (41.86%) hypertensive and 10 (23.25%) non hypertensive subjects [Table/Fig-4].

Among the biochemical parameters observed in the hypertensive group, platelet count, serum creatinine values, AST, and ALT levels were within the normal range in most of the hypertensive group [Table/Fig-5].

On comparing the foetal outcome, it was found that almost 38 (94.95%) neonates with IUGR, 14 (20.28%) with AGA, and 3 (75%) with IUD/SB had a placental weight of less than 450 grams, indicating poor foetal outcomes and supporting the well known theory of a small placenta being associated with a small baby. The p-value was not statistically significant (0.029) [Table/Fig-7].

DISCUSSION

The placenta was circular, oval and irregular in both groups in the present study, similar to observations in studies reported by Goswami PR and Shah SN (2016), Kirwara S et al., (2009), Kumar VS et al., (2015), Shresha I et al., (2022), and Wubale Y and Tolera G (2018), except in the studies by Ranga MKSS et al., (2017) where the order of attachment was eccentric, central and marginal, respectively [9,12,16,20-22]. In the hypertensive subjects, the incidence of the site of cord insertion showed different patterns in various studies [9,12,16,20-22]. The placental thickness was less in the hypertensive group in various studies except the current study. The calcification was higher in the hypertensive subjects with respect to non hypertensive subjects in various studies [Table/Fig-8] [9,16,19,22-24].

The quantum of cotyledons in the present study was in line with those reported by Salmani D et al., (2014) in non hypertensive subjects, while in the hypertensive subjects, the cotyledons observed were more than the present study in other studies [Table/Fig-9] [11,15,16,18,19,25,26].

The placental surface area in the present study in the non hypertensive and hypertensive subjects.
to that observed by Sirpurkar M and Anjankar VP (2017) [223.6±108.5 and 188.4±89.6 in two groups, respectively] [27]. PIH significantly reduces placental weight and its dimensions and gives rise to characteristic histological changes. All these factors are responsible for ischaemia and the compromised uteroplacental blood flow leading to low foetal weight [28].

The placental circumference in the current study in the non hypertensive and hypertensive subjects was 47.045±6.65 cm and 37.419±6.091 cm, respectively, which was slightly less than that observed in the study by Kumar VS et al., (2015) in non hypertensive and hypertensive subjects with 45.1 cm and 41.1 cm, respectively [16].

The weight of the placenta and the foetal weight in the hypertensive and hypertensive subjects was 47.045±6.65 cm and 37.419±6.091 cm, respectively, which was slightly less than that observed in the study by Kumar VS et al., (2015) in non hypertensive and hypertensive subjects with 45.1 cm and 41.1 cm, respectively [16].

The difference between the non hypertensive and hypertensive subjects was higher in hypertensive subjects with 4.26% and 1.39% in two groups, respectively [27].

The differences between the non hypertensive and hypertensive subjects in parameters like placental radius, circumference, surface area and quantum of cotyledons were found to be statistically significant. The abnormal values of biochemical parameters and adverse foetal outcomes are higher in hypertensive subjects but need testing on a larger sample size to establish whether the differences are statistically significant.

**Limitation(s)**

A larger sample size in each group of hypertensive subjects needs to be tested for all parameters to establish statistically significant observations, which can lead to the categorisation of placental morphological changes in groups of hypertension (NHBPEP) classification.

### CONCLUSION(S)

The hypertensive disorders of pregnancy adversely affect the morphological and morphometric features of the placenta, biochemical values such as serum creatinine, platelet count, AST and ALT levels, foetal weight, and foetal outcomes. The study calls attention to further research to establish the statistical significance of the above findings. It stresses the importance of placental examination and research by a trained professional for the proper identification of causes of poor pregnancy outcomes in hypertensive disorders of pregnancy to improve the modus operandi.

<table>
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**Table/Fig-10**: Comparison of foetal weight and placental weight in different studies [13,16,19,22,25-27,29-32].
Acknowledgement

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REFERENCES