

THE HISTOPATHOLOGICAL CHANGES OF PLACENTA IN HYPERTENSIVE DISORDERS OF PREGNANCY AND THEIR CORRELATION WITH FETAL OUTCOME: A CROSS-SECTIONAL STUDY

AAKRITI PANDAY^{1*}, SUMAN BUDANIA¹, TANU BANO²¹Department of Obstetrics and Gynecology, Sardar Patel Medical College, Bikaner, Rajasthan, India. ²Department of Pathology, Sardar Patel Medical College, Bikaner, Rajasthan, India. Email: aakritipandey0413@gmail.com

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ABSTRACT

Objectives: The objective of this study was to evaluate the histopathology and establish the correlation between placental changes in hypertensive disorders of pregnancy and fetal outcome.

Methods: A cross-sectional study included 100 pregnant women with singletons admitted to the labor room with gestational ages >30 weeks and 35 weeks with hypertensive disorders of pregnancy between December 2021 and November 2022, admitted to the Department of Obstetrics and Gynecology, Sardar Patel Medical College, Bikaner. All cases were examined for Shape of placenta, weight in grams, size, diameter in centimeters, and deposition. Fetomaternal outcome was also noted.

Results: Eighty percent (80) were in the age group of 21–30 years, with a mean age of 25.01±4.56 (range: 18–44 years). Only 35% of females were booked, and 63% of cases belonged to G1. Maximum cases were of pregnancy-induced hypertension (42%), followed by eclampsia (36%) and pre-eclampsia (16%), and the minimum case belonged to HELLP (1%). Although cases of placental infarction were higher in neonatal intensive care unit (NICU) admitted cases as compared to non-admitted cases (61.19% vs. 45.45%, respectively), calcification was higher in NICU-admitting cases as compared to non-admitting cases (95.52% vs. 84 vs. 5%, respectively). Syncytial knots were higher in neonatal intensive care unit (NICU) admitted cases as compared to non-admitted cases 94.03% vs 81.82%, also grade fibrosis was 44.78% vs. 27.27%, Fibrinoid necrosis (71.64% vs. 54.55%) and leukocytic infiltration (68.66% vs. 63.64%) respectively. Statistically, no significant difference was observed in all parameters.

Conclusion: Placental morphology and histopathology are affected in hypertensive pregnancies, which might be the reason for placental insufficiency in these cases.

Keywords: Fetomaternal outcome, Histopathological changes of placenta, Hypertensive disorder of pregnancy.

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INTRODUCTION

The placenta is the most vital organ interposed between mother and fetus which serves to maintain a maternofetal barrier for the exchange of blood gases, nutrients, and waste products [1]. The placenta and umbilical cord abnormalities can lead to fetal morbidity and mortality. Abnormal flow, constriction, or thrombosis in the umbilical cord have been postulated as possible etiologies of adverse prenatal outcomes. These outcomes include respiratory distress, intrauterine growth restriction, and low Apgar score seen with abnormalities of the umbilical cord and placenta [1].

Hypertensive disorders of pregnancy, especially pre-eclampsia and eclampsia, are the leading causes of maternal and fetal mortality and morbidity worldwide, accounting for 16% of direct maternal deaths. According to the Global Burden of Disease 2000 report, the pooled incidence of pre-eclampsia in developing countries was estimated to be 3.4% and it has certainly been on the rise as the years have progressed [2].

Histologically, the placenta of hypertensive disorder of pregnancy has a high incidence of infarction, retroplacental hematoma, and subchorionic fibrin areas. Fetal outcome is adversely influenced by these pathological changes occurring in placenta due to hypertensive disorder of pregnancy [3].

As pathophysiology lies in placenta, most attention is drawn to examine the placenta in recent years as it gives a valuable indication for maternal and fetal diseases, many disorders of pregnancy which are associated with high perinatal morbidity and mortality are accompanied by this pathological change in placenta [4].

Nowadays, when medicolegal problems threaten the practicing obstetrician, a study of placenta with histology can prove the exact pathology behind perinatal death and is a legal shield to the doctor from the consumer forum. It is fanciful to assume that every adverse perinatal outcome is associated with an abnormal placenta, and equally fanciful to expect that every abnormal placenta will result in adverse perinatal outcome. Hence, the placenta is the most accurate record of the infants' prenatal experience. The placental study provides a record, to plan the future care of the mother and the child. Even though there are clinical studies emphasizing the diagnosis and the perinatal intercurrent diseases of hypertensive syndromes in pregnancy, few of these studies establish the clinical forms of the specific hypertensive syndromes with the associated morphological placental alterations [5,6]. The lack of studies on placental morphology and the etiopathogenesis of the different clinical standards for hypertensive syndrome, together with the need to objectively characterize these morphological placental lesions, justify this study.

Aim

The aim of this study was to evaluate the histopathology and establish the correlation between placental changes in hypertensive disorders of pregnancy and fetal outcome.

METHODS

A cross-sectional study included 100 pregnant women with singletons admitted to the labor room with gestational ages >30 weeks and 35 weeks with hypertensive disorders of pregnancy between December 2021 and November 2022, admitted to the Department of Obstetrics and Gynecology, Sardar Patel Medical College, Bikaner. All cases were

examined for Shape of placenta, weight in grams, size, diameter in centimeters, and deposition. All pregnant females admitting to the labor room with gestational age <30 weeks and >35 weeks with hypertensive disorder of pregnancy, multiple pregnancy, pregnancy with other medical disorders, and not willing to participate were excluded from the study. After obtaining approval from the institutional research ethical committee and written informed consent from a patient with hypertensive disorder having blood pressure >140/90 with singleton pregnancy >30 weeks in labor or having induction of labor were selected. Information regarding her age, address, socioeconomic status, and dietary habits were noted. Special inquiry was made regarding smoking and drug use, and previous antenatal checkups were noted. On admission, a complete history of present complaints, obstetric history, menstrual history, past medical and surgical history, and family history were taken. General physical examination was done to assess both maternal and fetal conditions. Abdominal examination and per vaginal examination were done. Blood samples for complete blood count, RBS, urine R/M, and viral markers were sent. After delivery, cord blood was drained, and placentas were collected and fixed with 10% formalin. Shape of placenta, weight in grams, size, diameter in centimeters, and deposition were examined. Fetomaternal outcome was also noted. The investigation was started after receiving ethical approval from the institute. Written informed consent was obtained from all the study subjects.

Statistical analysis

The data were collected and tabulated with the help of collected and tabulated with the help of appropriate software. Continuous data were represented as mean and standard deviation and were analyzed by one-way analysis of variance. Frequency variables were presented as number and percentage and were analyzed by Chi-square tests.

RESULTS

Among the 100 cases, 80% (80) were in the age group of 21–30 years, with a mean age of 25.01±4.56 (range: 18–44 years). Only 35% of females were booked, and 63% of cases belonged to G1 and 2 cases belonged to G4. According to ultrasonography findings, we have found that 39% of cases belonged to 34 weeks, 27% belonged to 35 weeks, 22% belonged to 32 weeks, and so on (Table 1).

Maximum cases were of pregnancy-induced hypertension (PIH) (42%), followed by eclampsia (36%) and pre-eclampsia (16%), and the minimum case belonged to HELLP (1%) (Fig. 1).

The mean systolic blood pressure and diastolic blood pressure was 165.96±14.99 mmHg and 105.32±8.60 mmHg, respectively. We have found that 98% of cases had pedal edema and only 2 cases had pallor. On ultrasonography, 52% of placenta belonged to Grade III and 48% of cases belonged to Grade II. The mean diameter in cm, biparietal diameter (mm), weight (g), number of cord vessels and Cord length (cm) was 17.66±1.88 cm, 410.87±54.32 g, 3±0.00, 44.55±4.23 cm, respectively. On histopathological examination of placenta, 92% of cases belonged to calcification, followed by syncytial knots: 90%, infarction: 56%, grade leukocytic infiltration: 67%, grade fibrinoid necrosis: 66%, infarction: 56%, and grade fibrosis: 56% (Table 2).

Fifty-four percent of cases belonged to vaginal delivery and the rest 46% belonged to C-section. Ninety-four percent of cases belonged to live birth and 6% belonged to IUFD. The mean weight (kg) was 1.98±0.44 kg, respectively, with a range of min and max 1–2.6 kg. According to Apgar score, 42% of cases belonged to score 4–5 moderately depressed (below normal) at 1 min, while at 5 min, one case was in critically low condition and 15% of cases belonged to moderately depressed (below normal) condition. Sixty-six percent of babies were admitted to neonatal intensive care unit (NICU) and 65% of cases had signs of fetal distress. We have found that 76% of cases belonged to discharged, 17% belonged to expired, and 5% belonged to stillbirth (Table 3).

Table 1: Baseline characteristics of study subjects

Age group	Number	Percentage
≤20	11	11
21–30	80	80
31–40	7	7
>40	2	2
Booking status		
Booked	35	35
Unbooked	65	65
Gravida		
G1	63	63
G2	23	23
G3	12	12
G4	2	2

Table 2: Placental characteristics of study subjects

Grading	Number	Percentage		
II	48	48		
III	52	52		
Histopathology				
Infarction	56	56		
Calcification	92	92		
Syncytial knots	90	90		
Grade fibrosis	39	39		
Grade fibrinoid necrosis	66	66		
Grade leukocytic infiltration	67	67		
Macroscopic study	Mean	SD	Minimum	Maximum
diameter in cm	17.66	1.88	13	22
Weight (g)	410.87	54.32	296	554
Number of cord vessels	3	0	3	3
Cord length (cm)	44.55	4.23	34	54

Table 3: Fetal outcome among study subjects

Live birth or stillbirth	Number (n = 100)	Percentage
Live birth	94	94
IUFD	6	6
Weight (in kg) mean (SD)	1.98	0.44
Apgar score	At 1 min.	At 5 min.
Critically low (0–3)	0	1
Below normal (4–6)	42	15
Excellent (7–10)	52	78
NICU admission		
Signs of fetal distress	65	65
NICU admission present	66	66
Outcome		
Discharged	77	77
Expired	17	17
Intrauterine fetal death	6	6

NICU: Neonatal intensive care unit

Patients admitted to NICU, out of them, 42% of cases belonged to respiratory distress/low birth weight (LBW) and 20% respiratory distress, 2% of cases were only LBW and only one case was observed with hydronephrosis/LBW (Fig. 2).

Although cases of placental infarction were higher in NICU-admitted cases as compared to non-admitted cases (61.19% vs. 45.45%, respectively), calcification was higher in NICU-admitted cases as compared to non-admitted cases (95.52% vs. 84 vs. 5%, respectively). Syncytial knots were higher in neonatal intensive care unit (NICU) admitted cases as compared to non-admitted cases 94.03% vs 81.82%, also grade fibrosis was 44.78% vs. 27.27%, Fibrinoid necrosis (71.64% vs. 54.55%) and leukocytic infiltration (68.66% vs. 63.64%)

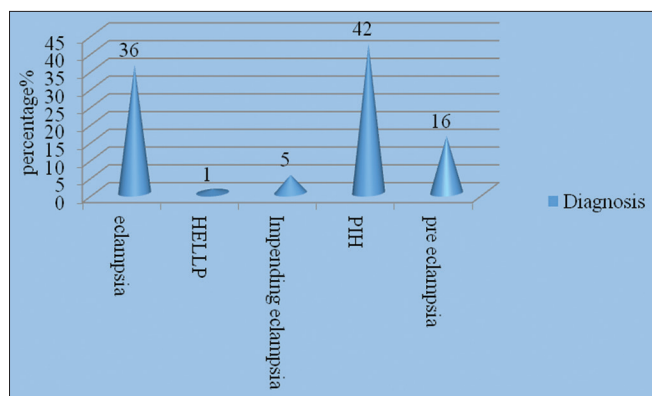


Fig. 1: Distribution of the cases according to diagnosis

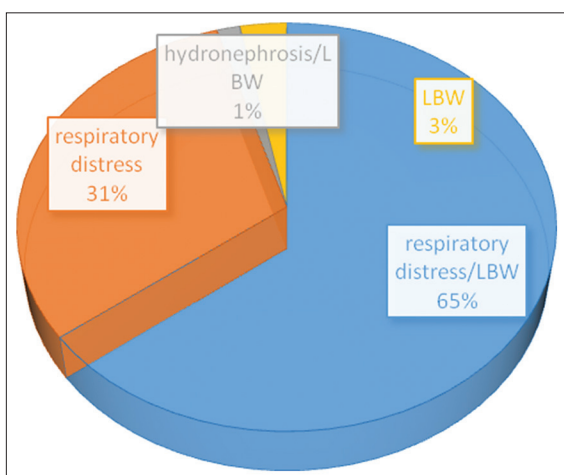


Fig. 2: Reasons of neonatal intensive care unit admission

Table 4: Association of histopathological findings of placenta with NICU admission

NICU admission	Present (n = 67)		Absent (n = 33)		p-value
	No	%	No	%	
Placental infarction	41	61.19	15	45.45	0.20NS
Calcification	64	95.52	28	84.85	0.145NS
Syncytial knots	63	94.03	27	81.82	0.119NS
Grade fibrosis	30	44.78	9	27.27	0.14NS
Fibrinoid necrosis	48	71.64	18	54.55	0.141NS
Leukocytic infiltration	46	68.66	21	63.64	0.78NS

NICU: Neonatal intensive care unit

Table 5: Association of type of PIH with histopathological findings of placenta

Histopathological findings	Eclampsia (n = 36)		PIH (n = 42)		Pre-eclampsia (n = 22)		p-value
	No	%	No	%	No	%	
Placental infarction	21	58.33	21	50.00	14	63.64	0.545NS
Calcification	34	94.44	36	85.71	22	100.00	0.108NS
Syncytial knots	34	94.44	34	80.95	22	100.00	0.029S
Grade fibrosis	15	41.67	11	26.19	13	59.09	0.034S
Fibrinoid necrosis	23	63.89	26	61.90	17	77.27	0.442NS
Leukocytic infiltration	29	80.56	22	52.38	16	72.73	0.025S

PIH: Pregnancy-induced hypertension

respectively. Statistically, no significant difference was observed in all parameters (Tables 4 and 5).

DISCUSSION

In the present study, out of 100 cases, the maximum number of cases was found to be 80% (80) in the age group of 21–30 years, followed by 11% (11), 7% (7), and 2% (2) in the groups of 20 years, 31–40 years, and >40 years, respectively. The mean SD of age was 25.01±4.56 (range: 18–44 years). Chhatwal et al. [7] studied a similar age group of 27.60±4.37 (20–39), and Kambale et al. [8] studied a similar age group of 20–25 years.

According to the diagnosis, 42% of the cases in the current study belonged to PIH and 36% to eclampsia. This is in accordance with the previous observation of Chhatwal, 2018 [7], and Parmar et al., 2019 [9].

In the present study, the distribution of the cases according to physical examination, where we have found that 98% of cases belonged to pedal edema followed by nil in rest all. Also observed that Chhatwal 2018 [7] 45.2% had moderate-to-severe edema.

In the present study, a quantitative analysis of macroscopic study of placenta, we observed that the mean diameter of placenta in cm, BPD (mm), weight (g), number of cord vessels. Cord length (cm) was 17.66±1.88 cm, 410.87±54.32 g, 3±0.00, 44.55±4.23 cm, respectively, with a range of min and max 13–22, 29–554, 3–3, and 34–54, respectively. Low parameters were observed low in terms of mean diameter, mean weight, and cord length as compared with normal weight is 500 g, cord length of normal length 55 cm, normal placental diameter 22–25 cm.

With respect to placental diameter too, various studies have found it to be lower in hypertensive cases as compared to normotensive cases. Samaddar et al. [10] found a statistically significant reduction in diameter and thickness among cases compared to controls Samaddar et al. [10] observed that morphometric parameters in the hypertensive group revealed that there is a decrease in mean placenta diameter and mean placenta thickness in comparison with normal women.

The weight of placenta is an important and functionally significant parameter as it is related to villous area and fetal metabolism. The mean±SD of weight of the placenta was 410.87±54.32 g. This observation was correlated well with the previous studies done by various workers. Chhatwal 2018 [7], and BAR p. K 2019 [11].

This study depicts the distribution of the cases according to ultrasonographic study of placenta, where we have found that 52% of cases belonged to III and 48% of cases belonged to II. Dutta et al. [12] found that 97.62% of cases (41 out of 42) in the control group showed Grade II changes as opposed to 57.14% of cases (24 out of 42) in the study group before 34 weeks.

Histological changes of placenta from the hypertensive mothers also showed a 92% significant increase in calcification, perivillous fibrin deposition also in Samaddar et al. [10] study, 44% of the placentas in the hypertensive group showed evidence of calcification.

Grade fibrinoid necrosis was observed 66%, also Al-Bakri *et al.* observed that the histological study of placenta with gestational hypertension showed a significant increase in syncytial knots and calcification and hyalinization area also fibrinoid necrosis are observed hypertensive disorders of pregnancy adversely influence the morphology of placenta.

In the present study, according to mode of delivery, where we have found that 54% of cases belonged to vaginal and the rest 46% of cases belonged to C-section. Similar to the present study, preterm deliveries were high in hypertensive groups in the published literature.

In our study, the mean fetal birth weight (kg) was 1.98±0.44 kg, respectively, with a range of min and max 1–2.6 kg. Similarly, Samaddar *et al.* [10] found a statistically significant reduction in birth weights of newborns to hypertensive mothers which were significantly lower than those of normotensive mothers.

In this study, distribution of the cases according to Apgar at 1 min and 5 min, where we have found that 42% of cases belonged to score 4–5 moderately depressed (below normal) at 1 min while at 5 min, one case was in critically low condition and 15% of cases belonged to moderately depressed (below normal) condition. Similarly, Kambale *et al.*, 2021, [8] observed that in PIH placentae with fetal low Apgar score, and fetal loss was found.

In our study, although cases of placental infarction were higher in NICU-admitted cases as compared to non-admitted cases (61.19% vs. 45.45%, respectively), calcification was higher in NICU-admitting cases as compared to non-admitting cases (95.52% vs. 84 vs. 5%, respectively). Syncytial knots were 94.03% vs. 81.82%, respectively, and grade fibrosis was 44.78 vs. 27.27%. Fibrinoid necrosis (71.64% vs. 54.55%) and Leukocytic infiltration (68.66% vs. 63.64%). Statistically, no significant difference was observed in all parameters.

In 2020, Yadgiri *et al.* [13], in their study, observed that morphological and histological feature changes were correlated with fetal mortality and morbidity. Moreover, they observed that there was an increase in fetal mortality and morbidity in hypertensive patients with the above histological changes in their placentas.

The placental infarction was observed in eclampsia cases 34%, in PIH cases 36%, and in pre-eclampsia cases 100% with $p=0.545$ NS. A significant difference was observed in syncytial knots were observed more in pre-eclampsia, grade fibrosis were observed more in pre-eclampsia and leukocytic infiltration were observed more in eclampsia ($p=0.029S$, $p=0.034S$, and $p=0.025S$). Our findings of increased calcification found in preeclampsia and eclampsia patients are consistent with the findings of some other studies as well [14].

CONCLUSION

The findings of the present study thus suggest that placental morphology and histopathology are affected in hypertensive pregnancies, which might be the reason for placental insufficiency in these cases. Separate research is needed to determine how these morphological and histopathological changes affect maternal and perinatal outcome needs to be studied separately.

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AUTHORS' CONTRIBUTION

All the authors have contributed equally.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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