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Original Article

Histopathological Changes in Placenta in Pre-Eclampsia/Eclampsia: A Case-Control Study in A Tertiary Care Center

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Abstract

Background

Hypertensive disorders of pregnancy, particularly pre-eclampsia and eclampsia, remain major causes of maternal and perinatal morbidity and mortality. The placenta plays a pivotal role in their pathogenesis, with histopathological lesions correlating with adverse outcomes. This study was therefore conducted to compare various placental gross and histopathological changes in hypertensive disorders of pregnancy as compared to normotensive pregnancy.

Materials and Methods

A case-control study was conducted on 28 placentas from pre-eclamptic/eclamptic pregnancies and 28 from normotensive controls at Nobel Medical College (Sep 2024–Feb 2025). Birth weight in both groups was compared. Various gross and histological features like placental weight, umbilical cord length, insertion of placenta, infarction, calcification, chorioamnionitis, villitis, placental dysmaturity, chorionic vessel thrombosis, and subchorioinic fibrin deposition were assessed and compared. Data were analyzed using appropriate statistical tests.

Results

Placental weight and neonatal birth weight were significantly lower in hypertensive pregnancies (p=0.0001 and p=0.018, respectively). Histopathological lesions such as calcification, infarction, subchorionic fibrin deposition, chorionic vessel thrombosis, and chorioamnionitis were significantly more frequent in hypertensive cases (p<0.05 for each).

Conclusion

Significant gross and microscopic placental changes are associated with hypertensive disorders of pregnancy. Routine placental histopathology can aid in understanding disease mechanisms.

Keywords: *Eclampsia, Placenta, Pre-eclampsia*

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Introduction

Pre-eclampsia is a multisystem disorder of pregnancy, typically arising after 20 weeks of gestation, marked by new-onset hypertension and proteinuria or end-organ dysfunction [1]. Eclampsia, its most severe form, is characterized by seizures in pre-eclamptic women [2]. Globally, pre-eclampsia affects 5–8% of pregnancies and accounts for 10–15% of maternal deaths, with a notable impact in low-resource settings [3-4]. In Nepal, pre-eclampsia and eclampsia complicate approximately 2.6% and 0.5% of pregnancies, respectively [5].

The placenta plays a central role in pre-eclampsia pathogenesis, primarily due to abnormal trophoblastic invasion and inadequate spiral artery remodeling, leading to placental ischemia and systemic endothelial dysfunction [6-7]. Histopathological examination of placentas from hypertensive pregnancies frequently reveals lesions such as infarcts, increased fibrin deposition, atherosis, and syncytial knotting, which are associated with poor fetal outcomes like IUGR and stillbirth [8].

In contrast, placentas from normotensive pregnancies typically show intact villous architecture and normal vascularization. Comparative histological analysis helps identify key diagnostic and prognostic features, offering insights into disease mechanisms [9].

This study aims to evaluate and compare histopathological changes in placentas from pre-eclamptic/eclamptic and normotensive pregnancies to enhance understanding of disease progression and support the development of placental-based diagnostic tools.

Materials and Methods

It was a hospital-based, prospective case-control study done at Nobel Medical College and Teaching Hospital over six months period (September 2024 to February 2025). Ethical approval was obtained from the Institutional Review Committee (Reference No: 63/2024), and informed consent was taken from all participants. All pre-eclamptic/eclamptic placenta and equal number of normal placenta during the study period were included in this study. Inadequate biopsy sample and that not received in formalin was excluded from study. Sample size was calculated by the formula for unmatched case control study. Samadhar et al found subchorionic fibrin in placentas in 10% of control (normal pregnancy) and in 50% of cases (pre-eclampsia and eclampsia) [10]. Sample size was calculated as following:

$$n = \frac{(r+1)}{r} \cdot \frac{p(1-p)(Z_{1-\beta}+Z_{1-\alpha/2})^2}{(p_1-p_2)^2}$$

r= control to case ratio

p= proportion of the population exposed to risk = $(p_1+p_2)/2$

p_1= proportion of exposed in cases

p_2= proportion of exposed in control

$Z_{1-\alpha/2}$ = Standard normal variate for the level of significance 1.96

$Z_{1-\beta}$= Standard normal variate of power 0.84 (for power 80%)

Therefore,

r = 1 (Assumed)

P1 = 0.5

P2 = 0.1

P = (p1 + p2)/2 = (0.5 + 0.1)/2 = 0.3

Thus, $n = \frac{1+1 \times 0.3(1-0.3)(0.84+1.96)^2}{1(0.5-0.1)^2}$

$= 2 \times \frac{0.3 \times 0.7 \times 7.84}{10.16}$

$= 20.58$

Calculated sample size was 21. A convenience sampling method was used. A total of 28 placentas from pregnancies complicated by pre-eclampsia/eclampsia and 28 from normotensive pregnancies were included in this research. Placentas were collected fresh post-delivery, weighed, and examined for gross features including weight, cord anomalies, umbilical cord length, insertion type and meconium staining of fetal surface. Specimens were fixed in 10% formalin, grossed by the Swiss roll technique, and were processed for histopathological study as per standard guideline. Hematoxylin and Eosin (H&E) staining was performed, and histopathological features including infarction, calcification, fibrin deposition, villous maturity, vessel thrombosis, subchorionic fibrin deposition, and chorioamnionitis were assessed by experienced pathologists.

All data were entered in Microsoft excel and data analysis was done by SPSS 17 software. Quantitative variables such as placental weight, birth weight, and cord length were analyzed using unpaired t-tests. Categorical histopathological features were compared using Chi-square or Fisher's exact test, with $p<0.05$ considered statistically significant.

Results

We examined placental tissues from normotensive and pre-eclamptic/eclamptic pregnancies. A total of 28 samples were received during the study period (Sep 2024-Feb 2025). Birth weight of the newborn and placental weight were significantly reduced in preeclamptic/eclamptic

pregnancies. Similarly, the umbilical cord was notably shorter in hypertensive pregnancies compared to normal pregnancies. Eccentric placental insertion was also found to be significantly more frequent in hypertensive pregnancies (Table 1).

Histopathological examination showed that calcification, infarction, placental floor infarction, chorionic vessel thrombosis, and chorioamnionitis were significantly more frequent in hypertensive disorders of pregnancy compared to normotensive pregnancies (Table 2).

Table 1: Comparison of birth weight and gross description of placentas in pregnancies complicated by pre-eclampsia/eclampsia and the control group

Parameters	Pre-eclampsia/ Eclampsia (n=28)	Control (n=28)	P value
Birth weight, mean (Kg)±SD	2.9±0.38	3.1±0.21	*0.018
Weight of placenta, mean (gm)±SD	253.5±5.27	341.7±7.74	*0.0001
Umbilical cord length mean (cm)±SD	47±7.4	49.7±6.59	*0.155
Umbilical cord insertion:			
Central, n (%)	12(42.8)	21(75)	**0.02
Ecentric,n (%)	16(57.2)	07(25)	
Any cord artery anomalies, n (%)	0(0)	0(0)	NA
Meconium staining of fetalsurface,n (%)	7(25)	3(10.7)	***0.29

* Calculated by unpaired t-test as mean difference in normotensive Vs hypertensive pregnancies.
** Calculated by Chi Square test as frequency difference in normotensive Vs hypertensive pregnancies.
***Calculated by Fisher Exact test as frequency difference in normotensive Vs hypertensive pregnancies.

Table: 2 Comparison histological findings of placentasin pregnancies complicated by pre-eclampsia/eclampsia and the control group.

Parameters	Pre-clampsia/ clampsia (n=28)	Control (n=28)	P value
Subchorionic fibrin deposition, n (%)	20(71.4)	3(10.7)	*0.29
Calcification, n (%)	10(35.7)	1(3.6)	*0.005
Infarction,n (%)	9(32.1)	0(0)	*0.001
Features of dysmaturity, n (%)	8(28.6)	4(14.3)	*0.329
Villitis of unknown origin. n (%)	5(17.8)	2(7.1)	*0.421
Placental floor infarction. n (%)	10(35.7)	2(7.1)	*0.021
Chorionic vessel thrombosis/ Obliterative Vasculopathy. n (%)	16(57.1)	2(7.1)	*0.0001
Chorioamnionitis. n (%)	16(57.1)	2(7.1)	*0.0001
Retroplacental hematoma. n (%)	2(7.1)	0(0)	*0.49

*Calculated as frequency differences in normotensive Vs hypertensive pregnancies by Fisher exact test.

Discussion

In this study, significant differences were observed between placentas from pre-eclamptic/eclamptic and normotensive pregnancies, with key findings aligning with existing literatures. Average birth weight was significantly lower in hypertensive pregnancies (p=0.018), likely due to placental insufficiency resulting from poor perfusion and reduced nutrient exchange [11-12] Similar findings were observed by others [11-12]. Placental weight was also significantly reduced in these cases (p=0.018), consistent with abnormal trophoblastic invasion, impaired spiral artery remodeling, and chronic uteroplacental ischemia hallmarks of hypertensive disorders [13]. Another study reported similar results [14]. While umbilical cord length did not differ significantly, the site of cord insertion showed a notable difference, with a significantly higher prevalence of eccentric insertion in hypertensive pregnancies (p=0.02). Comparable findings were observed in another study [14]. Eccentric insertion may further compromise perfusion, potentially contributing to adverse outcomes like, intrauterine growth restriction (IUGR), and preterm birth [15-16]. Meconium staining was observed in a slightly higher number of hypertensive cases, though without statistical significance (p=0.29). This may be due to limited sample size, although prior studies suggest increased meconium staining may indicate fetal stress in hypertensive pregnancies [17]. Histopathologically, subchorionic fibrin deposition was significantly more frequent in pre-eclamptic/eclamptic cases (p=0.01). It is likely a consequence of endothelial dysfunction and heightened inflammatory response, contributing to placental hypoperfusion and increased fibrin accumulation at the maternal-fetal interface [18]. Placental calcification was significantly associated with hypertensive pregnancies (p=0.005). While typically a feature of placental aging, premature and excessive calcification in eclampsia may result from hypoxia-induced damage due to impaired blood flow [19]. Similarly, placental infarction a pathological outcome of localized ischemia was significantly more common in hypertensive cases (p=0.001), reinforcing the role of vascular compromise in disease pathogenesis [20]. No statistically significant difference was found in placental dysmaturity or villitis between the groups (p=0.32 and p=0.42, respectively), though other studies have reported higher incidences in hypertensive conditions [6]. These findings may reflect sample size limitations or inter observer variability in histopathological evaluation. A significantly higher incidence of placental floor infarction was observed in hypertensive pregnancies (p=0.021). A similar pattern was reported in a different study [21]. Placental

floor infarction, characterized by extensive fibrin deposition and trophoblastic necrosis, indicates profound ischemic insult and is increasingly recognized as a marker of poor maternal perfusion [21].

Chorionic vessel thrombosis was also significantly more common in the pre-eclamptic/eclamptic group (p=0.001), underscoring the central role of vascular pathology in the etiology of eclampsia. Disruption of vascular homeostasis likely renders chorionic vessels prone to thrombotic occlusion, impairing fetal circulation [22]. Lastly, the incidence of chorioamnionitis was markedly higher in hypertensive pregnancies (p=0.001). "Similar outcomes have been documented in other research [23]. This could be due to increased vulnerability to infection related to placental insufficiency, inflammation, and iatrogenic factors [23]. Overall, these findings highlight the multifaceted placental changes associated with hypertensive disorders of pregnancy and underscore the importance of vascular pathology in their pathogenesis.

This study was limited by a small sample size, potentially affecting the statistical significance of certain findings. As a single-center study, generalizability is limited. Diagnostic assessment was restricted to gross and histopathological examination without advanced techniques. Additionally, lack of postnatal follow-up prevented correlation with neonatal outcomes.

Conclusion

This study reveals significant placental changes in pre-eclamptic/eclamptic pregnancies, including lower placental and birth weights, more frequent pathological lesions, and abnormal cord insertion underscoring placental insufficiency and vascular pathology in hypertensive pregnancy disorders.

Recommendation

Future studies should involve larger, multi-center cohorts to improve generalizability and statistical power. Incorporating advanced diagnostic tools such as Doppler imaging, immunohistochemistry, and molecular analyses may deepen understanding of disease mechanisms. Longitudinal follow-up is essential to link placental changes with neonatal outcomes. Emphasis should be placed on early detection strategies and standardized placental evaluation protocols to enhance diagnosis and management of hypertensive disorders in pregnancy.

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