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Original Research Article

Placental Pathology in Preeclampsia and Eclampsia and its Impact on Pregnancy Outcome-A Cross Sectional Study in a Tertiary Care Centre in Assam, India

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Abstract

Background: Preeclampsia and eclampsia are significant hypertensive disorders during pregnancy, contributing notably to maternal and neonatal morbidity and mortality worldwide. In India, the incidence of preeclampsia is estimated to be 7 times higher as compared to global range. Knowledge of the placental pathology in these cases is of utmost significance in understanding its pathogenesis. However, no relevant studies were done in this north eastern region of India.

Aims and Objectives: To study the spectrum of histopathological changes in the placenta in patients of Pre-eclampsia and Eclampsia**.** To see the outcome of pregnancies associated with Pre-eclampsia and Eclampsia**.**

Materials and Methods: This cross-sectional analytical study was conducted in the Department of Obstetrics & Gynaecology and the Department of Pathology, Tezpur Medical College over a period of two years from January 2019 to December 2020. Detailed clinical and laboratory evaluation was done in each of the patient. After delivery their placentas were sent for histopathological examination and results were recorded.

Results: A total of 120 pregnancies, comprising of 40 cases each of Pre-eclampsia, eclampsia and normal pregnancies were evaluated. Mean gestational age at delivery was found to be 36 weeks and 32 weeks in Pre-eclampsia and Eclampsia group respectively. 55% of newborns were found to be low birth weight in eclampsia as compared to 7.5% in normotensive control groups. The mean placental weight was statistically reduced ($p<0.001$) in pre-eclampsia and eclampsia groups as compared to control group**.** Placental necrosis was found to be the most common histopathological features in both preeclampsia (75%) and eclampsia (100%)**.** Other changes include increased syncytitial knots, perivillous fibrin deposit, calcification, hypertrophy of spiral arterioles.

Conclusion: Hypertensive disorders of pregnancies are associated with significant pathological changes in the placenta and has significant effect in the pregnancy outcome.

Keywords: Pre-eclampsia, Eclampsia, Placenta.

Introduction

Hypertensive disorders in pregnancy form one of the deadly triads, along with haemorrhage and sepsis that result in mortality and morbidity associated with pregnancy. According to the American College of Obstetrics & Gynaecology (2013b modification)[1]. Hypertensive disorder in pregnancy is classified into four categories:

1) Gestational hypertension,
2) Preeclampsia–eclampsia syndrome,
3) Chronic hypertension of any aetiology,
4) Chronic hypertension with superimposed preeclampsia

Gestational hypertension is diagnosed when hypertension develops for the first time after 20 weeks of gestation without proteinuria and returns to normal within 12 weeks of delivery. [2-6] Preeclampsia is defined as hypertension after 20 weeks of gestation along with proteinuria (> 0.3

g/24 hours).When pre-eclampsia is complicated with generalized tonic-clonic convulsion not attributable to other neurological conditions it is called eclampsia. Chronic hypertension is diagnosed when hypertension develops before pregnancy or before 20 weeks of gestation or remains high even after 12 weeks of delivery. Chronic hypertension with superimposed preeclampsia is diagnosed when chronic hypertension is complicated with new onset proteinuria. [7-13]Preeclampsia is a condition which specifically affects women with pregnancy. It is a well-known fact that the root cause of preeclampsia is the placenta; once the placenta is expelled the sign and symptoms of preeclampsia improves.

It is also established that the underlying pathophysiology of preeclampsia involves endothelial dysfunction and vasospasm due to defective placentation leading to placental hypoperfusion and hypoxia. However, the exact mechanism by which defective placentation happens in preeclampsia remains elusive. Most of the studies in the world involving placental pathology are done in Caucasians and African blacks living in Western countries [14-17]. Few studies are also done in India as well but in Assam, a state situated in the remote North-eastern corner of India, such studies involving placental pathology in preeclampsia are still very scarce. At the same time, Assam is struggling with the highest maternal mortality ratio in the country and the percentage contributed to maternal mortality by preeclampsia is as high as 22-24% which is the highest in the country. In contrast, in developed countries, death due to preeclampsia is 16% of total deaths [18-19]. That is why, we aimed to re-explore the in-depth placental histology in preeclampsia and eclampsia, focusing on their associated clinical implications. Additionally, the document will examine the impact of these pathology on pregnancy outcomes.

Materials and Methods

Study Design and Setting: This study is a cross-sectional analytical study. It is conducted in the Department of Obstetrics & Gynaecology and the Department of Pathology, Tezpur Medical College over a period of two years from January 2019 to December 2020. A certificate from the institutional ethical committee is obtained before starting this study.

Study Population: A total of 142 pregnant women were initially enrolled in the study after applying inclusion and exclusion criteria, with the final analysis conducted on data collected from 120 participants. The study population was categorized into three groups based on clinical diagnosis:

Control Group: 40 women with normal pregnancies.

Preeclampsia Group: 40 women diagnosed with preeclampsia.

Eclampsia Group: 40 women diagnosed with eclampsia.

Inclusion Criteria

- Women of reproductive age.
- Gestational age between 28 – 40 weeks
- Confirmed diagnosis of preeclampsia or eclampsia based on clinical definitions.
- Willingness to participate and give consent after explaining the aim of the study.

Exclusion Criteria

- Women with pre-existing essential hypertension, diabetes mellitus, gestational diabetes, renal disease, autoimmune disease and thrombophilic condition
- Multiple gestations.
- Congenital anomaly and fetal hydrops
- Positive viral biomarkers like HIV, HBsAg, HCV
- Use of any drugs
- Any significant medical or obstetric complications that could confound the results.

Pregnant women were enrolled into the study as per inclusion and exclusion criteria which are evaluated after proper history taking, clinical examination and laboratory investigations. The participants blood samples are collected under aseptic and antiseptic measures and sent to laboratory for evaluation. Their obstetric managements were done as per protocol. After delivery, the placentae were washed to remove any clotted blood. Placental tissues were collected from the central and marginal areas. Additional sections were also taken from grossly abnormal lesions. Placentae were preserved in 10% neutral buffered formalin. The following gross features are recorded: Weight of trimmed placentae without cord and membranes, length of umbilical cord, diameter of placental disc, thickness of placental disc, insertion point of umbilical cord, diameter of umbilical cord, color of umbilical cord, number of vessels in umbilical cord, number of twists per representative 10 cm of length of umbilical cord, presence of true knots and/or pseudo knots in umbilical cord, insertion of membranes and their completeness, thickness of membranes, appearance of chorionic plate, appearance of basal plate, complete presence of cotyledons, examination of serial cut sections, and any added abnormality like infarct, and areas of gross necrosis plaques, hematomas etc. The tissues were processed using ascending grades of ethyl alcohol, xylene, and paraffin wax in an automatic tissue processor. The tissues were embedded in paraffin wax and cut at four-micron intervals using a rotary microtome. They were stained with

hematoxylin-eosin and observed under light microscope.

Statistical Analysis: Statistical analysis was performed using appropriate software (SPSS version 25). Descriptive statistics were calculated for all variables, and comparisons between groups were made using chi-square tests for categorical variables and t-tests for continuous variables.

A p-value of less than 0.05 was considered statistically significant, in line with standard practices in clinical research.

Result

Table 1: Gestational age

Gestational age	Normal	PE	E
$28^{+0} – 33^{+6}$ early preterm	0	3	2
$34^{+0} – 36^{+0}$ late preterm	3	10	20
$37^{+0} – 40^{+0}$ term	37	27	18

Table 2: Birth weight of the new-borns

Birth weight	Normal	PE	E
<2kg	0	9	10
2-2.5	6	10	11
2.6 – 3.5	29	21	19
>3.5	5	0	0

Table 3: Placental weight among normal, PE and E cases

Weight	Normal	PE	E
>400 gms	35	24	13
<400 gms	5	16	27

The data from a total of 120 women were analysed which were categorized into three distinct groups: 40 women with normal pregnancies (control group), 40 women diagnosed with preeclampsia, and 40 women diagnosed with eclampsia.

The findings are presented in detail, focusing on pregnancy outcomes and histopathological findings.

Gestational Age: The mean gestational age at delivery was significantly lower in the eclampsia group (32 weeks) compared to the preeclampsia group (36 weeks) and the control group (39 weeks). This difference was statistically significant ($p < 0.001$), indicating that eclampsia is often associated with premature delivery, likely due to the severity of maternal conditions.

Birth Weight: Low birth weight, defined as less than 2.5 kg, was observed in 32.5% of neonates from the preeclampsia group and a striking 55% from the eclampsia group. In contrast, only 7.5% of neonates in the control group were classified as low birth weight ($p < 0.001$). This indicates a substantial risk of low birth weight associated with both preeclampsia and eclampsia.

Histopathological Findings: Histopathological examination of placental tissues revealed critical differences among the groups, providing insights into the underlying pathological changes associated with preeclampsia and eclampsia.

Placental Weight: The mean placental weight was significantly lower in the preeclampsia (450 grams) and eclampsia (400 grams) groups compared to the control group (600 grams) ($p < 0.001$). This reduction in placental weight may reflect impaired placental development and function.

Necrosis: Areas of necrosis were identified in 75% of preeclamptic and 100% of eclamptic placentae, while only 5% of normal placentae exhibited this feature ($p < 0.001$). The presence of necrosis suggests compromised placental perfusion and function.

Perivillous Fibrin Deposit: This pathological finding was present in 42.5% of preeclamptic and 40% of eclamptic placentae, compared to only 10% in normal placentae ($p < 0.001$). The accumulation of fibrin can indicate placental insufficiency and is associated with adverse pregnancy outcomes.

Calcification: Calcifications were noted in 35% of preeclamptic and 50% of eclamptic placentae, while only 5% of normal placentae showed this feature ($p < 0.001$). These calcifications may reflect chronic placental damage and are often associated with poor fetal outcomes.

Thrombi: The presence of thrombi was found in 27.5% of preeclamptic and 47.5% of eclamptic placentae, while only 2.5% of normal placentae exhibited this feature ($p < 0.001$). Thrombus formation can disrupt normal placental blood flow, further compromising fetal health.

Syncytial Knots: Increased syncytial knots were observed in 27.5% of preeclamptic and 57.5% of eclamptic placentae, compared to 27.5% in normal placentae ($p < 0.001$). This finding is indicative of abnormal placental maturation and function.

Hypertrophy of Spiral Arteriole: Hypertrophied spiral arterioles were observed in 27.5% of preeclamptic placentae and 32.5% of eclamptic placentae, compared to only 2.5% in normal placentae ($p < 0.001$). This finding indicates abnormal remodelling of uterine arteries, which is crucial for adequate placental perfusion.

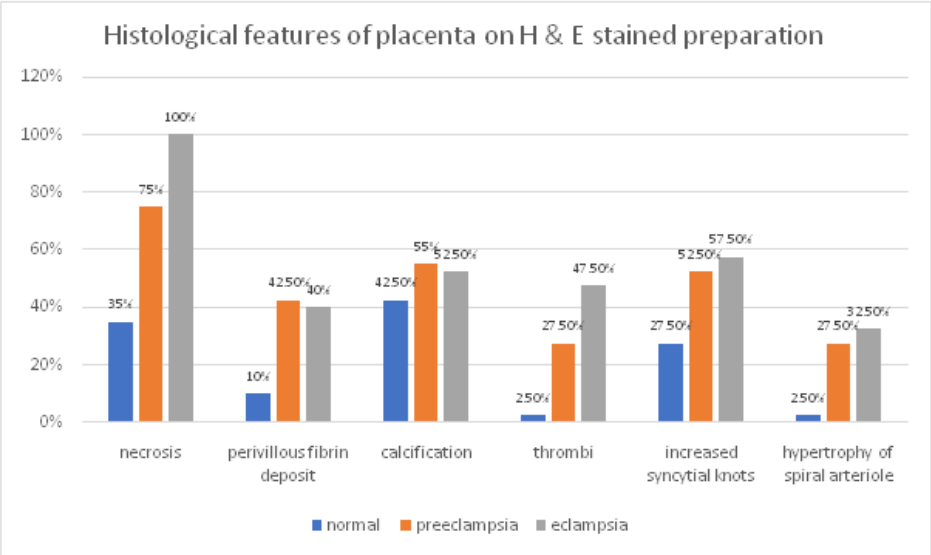

Figure 1: Bar diagram-Histological features of placenta on H & E stained preparation

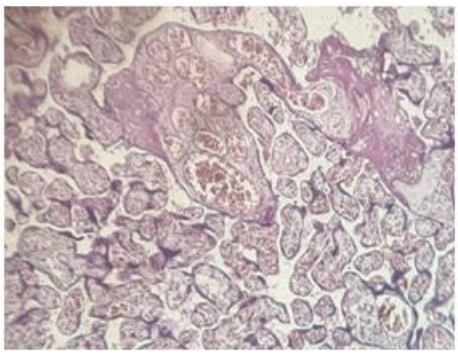

Figure 2: Photomicrograph showing Increased syncytial knots. (H&E, 40x)

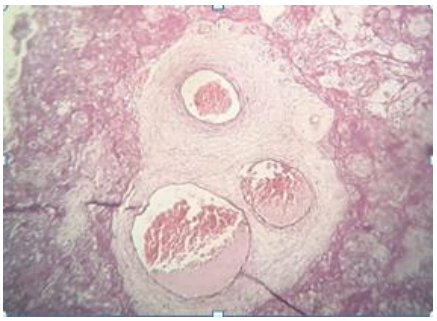

Figure 3: Photomicrograph showing Hypertrophied Spiral arteriole (H&E, 40x)

Syncytial knots (Figure 2) are aggregates of syncytial nuclei at the surface of terminal villi and are indicator of villous maturity. However, they are also associated with some pathological condition of placenta like preeclampsia. In our study we found that 52.5% and 57.5% of preeclamptic and eclamptic placentae showed increased syncytial knots respectively as compared to 27.5% of normal placenta.

Vasculopathies are common in preeclampsia and eclampsia which are characterised histologically with hypertrophied spiral arterioles. In our study

we found that preeclampsia and eclampsia are associated with hypertrophied spiral arteriole in 27.5% and 32.5% of placentae, respectively. Only 2.5% of normal placentae showed hypertrophied spiral arterioles. The figure 3 shows spiral arteriole hypertrophy as well as thrombi inside lumen indicating vascular thrombosis. Spiral arterial thrombosis is found in 27.5% and 47.5% of preeclampsia and eclampsia respectively as compared to 2.5% of normal placentae.

Discussion

Recent studies have underscored the critical role of placental abnormalities in the development of preeclampsia, revealing various histopathological changes that indicate impaired placental perfusion. In the present study, the mean placental weight was found significantly lower among the preeclamptic and eclamptic women as compared to normal pregnancy[20-21].

However, even though the weight of preeclamptic women were lower than normal ones, the difference was not significant. Other features like presence of necrotic area and haematoma were also found more in the diseased group as compared to the normal placentae [22-23]. In the present study, calcifications are significantly more in the diseased group which is consistent with that of Narsimha et al. Histopathological examination of placental tissues revealed notable differences between the groups, particularly the presence of hypertrophied spiral arterioles and spiral arterial thrombosis in the placentae of women diagnosed with preeclampsia and eclampsia. These observations are consistent with previous research, which documented similar histological changes in preeclamptic patients [24-25]. Such findings suggest abnormal trophoblastic invasion and impaired remodelling of uterine arteries, which are essential for ensuring adequate placental perfusion. This supports the hypothesis that preeclampsia is characterized by inadequate placental blood flow, leading to a cascade of pathological changes that adversely affect both maternal and fetal health [26]. Light microscopy has been instrumental in identifying these morphological changes, allowing for a detailed assessment of placental architecture and function. The findings from light microscopy studies align with those from electron microscopy as well, which have demonstrated structural abnormalities in the placental vasculature of preeclamptic women [27].

Conclusion

Pathological changes in placenta like necrosis, increased syncytial knots, perivillous fibrin deposits, hypertrophy of arterioles, provide useful insights in the pathogenesis of Pre-eclampsia and Eclampsia which has significant impact on the pregnancy outcomes. This study undermines the importance of further studies on various factors affecting feto- maternal circulation leading to these disorders which could provide useful information for better patient management.

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