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HISTOMORPHOMETRIC ALTERATIONS IN PREECLAMPTIC PLACENTAS: IMPACT ON FETO-MATERNAL EXCHANGE AND PREGNANCY OUTCOMES

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ABSTRACT

Background: Preeclampsia (PE) is a hypertensive disorder of pregnancy associated with significant maternal and fetal complications. Structural and histomorphometric changes in the placenta, particularly alterations in syncytial knots (SKs) and vasculosyncytial membranes (VSMs), contribute to placental dysfunction and fetal hypoxia. This study aims to compare placental morphology and histological changes between normotensive and preeclamptic pregnancies to understand their impact on fetal outcomes. Methods: A total of 42 placentas were collected at Sri Lakshmi Narayana Institute of Medical Sciences & Hospital in 2021, with 21 from normotensive pregnancies (control group) and 21 from preeclamptic pregnancies (PE group). Placental weights, diameters, and thicknesses were measured, and histological sections were analyzed using hematoxylin and eosin (H&E) staining. 1,500 terminal villi (TVs) were examined for SK density, VSM thickness, and SK variations. Statistical analysis was performed using SPSS version 10, and a p-value < 0.05 was considered significant. Results: PE placentas exhibited significant increases in SK density and diameter compared to controls ($p < 0.0001$). The thickness of VSM in PE placentas was twice as high as in controls, further impairing fetoplacental circulation. Type 3 SKs, which indicate severe placental dysfunction and fetal hypoxia, were exclusively found in PE placentas. Placental weight was significantly lower in the PE group ($p < 0.0001$), and neonatal birth weights were also reduced ($p = 0.001$). No significant differences were observed in placental thickness or diameter between groups. Conclusion: The structural abnormalities observed in PE placentas, particularly increased VSM thickness and SK density, suggest compromised feto-maternal exchange and placental insufficiency. These alterations may contribute to fetal hypoxia and low birth weight, supporting the role of placental morphometry as an indirect measure of placental function and pathology. Understanding these histopathological changes in PE could help improve early detection and management strategies for high-risk pregnancies.

Key words: Vasculosyncytial membrane (VSM), Syncytial knots (SKs), Preeclampsia (PE), Placental morphology, Fetal hypoxia.

INTRODUCTION

Preeclampsia (PE) is a pregnancy-related hypertensive disorder characterized by a sudden onset of high blood pressure and proteinuria, often accompanied by maternal organ dysfunction after 20 weeks of gestation [1]. Affecting 5-8% of pregnancies worldwide, PE is a leading cause of maternal morbidity and mortality. In healthy pregnancies, perinatal mortality is approximately 3%, but this risk triples in cases of PE [2,3]. This condition significantly contributes to maternal complications and preterm birth, with perinatal mortality rates ranging from 1% to 3%. While PE is widely recognized as a multifactorial disorder, its precise etiology remains a subject of ongoing research. However, the presence of the placenta plays a crucial role in both the onset and progression of PE [4,5].

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One of the hallmarks of PE is inadequate trophoblast invasion, which leads to hypoxia in the maternal spiral arteries. This results in shallow placentation, preventing the uteroplacental circulation from achieving low resistance and high capacitance, which are essential for a healthy pregnancy [6]. In PE, abnormal placental development is linked to poor spiral artery remodeling and impaired fetal vascular formation. During normal gestation, the terminal villi (TV) diameter decreases as pregnancy progresses, with cytotrophoblasts reducing in prominence and the syncytium expanding [7]. The syncytiotrophoblast, which forms the outermost layer of the placenta and remains in direct contact with maternal blood, plays a critical role in maternal hemostasis and endothelial function. This layer serves as both a protective barrier against pathogens and maternal immune cells and functions as a secretory and transport epithelium [8].

Syncytial knots (SKs)—aggregations of syncytiotrophoblast nuclei—form on the outer surface of tertiary placental villi due to uneven nuclear distribution. These structures are rarely seen in early placental development but increase to 10-30% at term [9,10]. The exact role of SKs remains controversial, with hypotheses suggesting they are degenerative changes, aging effects, syncytial hyperplasia, or responses to trophoblast ischemia or hypoxia [11].

The vasculosyncytial membrane (VSM) serves as the only physical interface between maternal and fetal circulation, forming the fetomaternal exchange barrier [12]. This structure is critical for maintaining the surface area and diffusion efficiency of nutrient and gas exchange. A thin VSM increases the risk of fetal hypoxia, posing a serious threat to fetal health. In hypertensive pregnancies, abnormal trophoblast differentiation leads to insufficient VSM formation, impairing placental function [13]. Previous placental studies have consistently confirmed the association between fetal hypoxia and VSM alterations. Morphological and functional changes in the VSM, along with other placental abnormalities, contribute to the development of PE.

The present study aims to compare placental morphology and histomorphometric changes between normal pregnancies and those complicated by PE, providing further insights into the structural alterations associated with this condition [14].

MATERIALS AND METHODS

This study was conducted at Sri Lakshmi Narayana Institute of Medical Sciences & Hospital in 2021. A total of 42 placentas were collected for analysis, of which 21 were from women with normal blood pressure during pregnancy (control group), and 21 were from women diagnosed with preeclampsia (PE group). Ethical approval was obtained from the Institutional Ethics Committee, and informed written consent was secured from all participating mothers.

PE cases were identified based on Obstetrics and Gynecology criteria, which included:

1. Blood pressure (BP) exceeding 140/90 mmHg, recorded on two separate occasions at least six hours apart.
2. Proteinuria levels of at least 300 mg per 24-hour urine collection or protein concentration of at least 1g/L, measured twice at an interval of at least six hours.

The control group consisted of women with normal blood pressure and no signs of proteinuria or systemic or endocrine disorders. Both PE and control groups excluded participants with diabetes mellitus, obesity, severe anemia (Hb >6%), eclampsia, or other endocrine disorders.

Immediately after delivery, the embryonic membranes and umbilical cord were removed, and the diameters and weights of the placentas were recorded. Placental tissue samples were collected by making one vertical incision near the umbilical cord insertion and another towards the periphery. The tissue samples were then fixed in 10% formalin saline solution for 24-48 hours, followed by paraffin embedding. Sections of four microns in thickness were stained with hematoxylin and eosin (H&E) for histological examination.

A total of 1,500 terminal villi (TVs) were randomly analyzed under a microscope in both groups [15]. TVs were identified as the smallest capillary loops surrounded by blood. Capillary counts were performed in randomly selected fields per slide using an Olympus trinocular microscope (CX31) with a 40× objective lens. The thickness of vasculosyncytial membranes (VSM) with and without syncytial knots (SKs) was examined using a 100× objective lens.

Measurements of SK and VSM thickness were conducted using Olympus optical micrometers (stage, ocular, and reticule). Images were captured using a Sony DCR W530 digital camera (Tokyo, Japan) mounted on a trinocular microscope.

Data analysis was performed using SPSS version 10 for Windows (SPSS Inc., Chicago, IL, USA). A paired Student's t-test was used to evaluate statistical differences between the PE and control groups, with results presented as mean ± standard deviation. A p-value of less than 0.05 was considered statistically significant.

RESULTS

In this study, 42 placentas were examined morphologically and histologically (21 from control and 21 from PE). There was a difference of 3.8 weeks in the mean gestational age among PE and control groups (P=0.002). The mean systolic BP of PE and controls were 144.64±10.55 and 115.2±6.80, respectively while the mean diastolic BP of PE and controls were 97.71±5.5 and 75.47±5.23, respectively. Statistical significance was found in both systolic and diastolic blood pressure (P0.001). Th e mean weight of the placenta was found 465.36±81.45 g

(range, 250 to 550 g) in controls and 422.38±130.49 g (range, 200 to 700 g) in PE and the difference in weight between two groups were statistically significant (P<0.0001). Feto-placental index did not differ between PE and controls (P>0.9186), but neonatal weight was significantly lower in PE than in controls. There were no significant differences between PE and controls in placental thickness or diameter. (Table 1). In relation to density of SKs, the VSM thickness was twofold increased in PE than the normal but the ratio of VSM thickness without SKs was 1:1.13. There was also a noticeable increase in SK density and diameter in PE compared to the control (Table 2). There was an increase in SK density in PE compared to the control, as well as an increase in VSM in PE compared to the control. A statistically significant relationship was found between the placenta weight and the neonate's gross weight (P<0.0001) in the PE cases.

Table 1: A comparison of neonatal and gross placental parameters between controls and preeclampsia (PE) patients

Variables	Control (n=21)	PE (n=21)	*t*-value	*P*-value
Gestational age (y)	36±2.4	35.4±3.56	3.07	0.002
Neonatal wt (g)	2,4900.89±509.87	2,294.41±856.72	1.469	0.001
Placental wt (g)	458.34±80.47	419.83±129.51	1.809	0.0001
Placental diameter (cm)	15.69±2.27	16.38±2.69	0.479	0.137
Placental thick (g)	1.71±0.55	1.54±0.65	0.993	0.184
Feto-placental index	5.44±0.83	5.41±1.12	0.1031	0.9187

Table 2: An evaluation of micromorphometric differences between controls and pre-eclamptic patients with syncytial knots (SKs) and vasculosyncytial membranes (VSMs).

Variables	Control (n=21)	PE (n=21)	*t*-value	*P*-value
SKs density (μm^3)	1.59±0.78	2.54±1.63	20.77	0.0001
SKs diameter (μm)	17.46±6.45	22.14±9.56	2.89	0.004
VSM thickness (μm)	2.45±1.19	3.14±1.06	14.09	0.0001
VSM thickness in relation to SKs (μm)	2.88±1.44	5.21±2.87	27.36	0.0001

Table 3: Placentas of control and preeclampsia (PE) patients with different types of syncytial knots.

Variables	Type 1	Type 2	Type 3
Control	31	19	NIL
PE	24	19	4

DISCUSSION

According to our study, the thickness of VSMs in PE was twofold greater than that in SKs. Additionally, there was an increase in the density and diameter of the SKs. A statistically significant difference was found between the VSM and SKs studies in PE in the present study. SKs of type 3 were only found in PE placentas with increased VSM thickness, as determined by the present study. PE is characterized by hypoxic conditions due to the aforementioned structural changes causing functional disturbances of the placenta. Type 3 TV SKs along with VSM thickness would indicate fetal hypoxia even if type 1 and 2 SKs were present in PE. A fetal vascular network transports oxygen from the intervillous space into the terminal villus, where it diffuses into capillaries and eventually reaches the fetus. This study found that increasing VSM thickness in PE reduced fetoplacental circulation and SK accumulation, even worsening the condition in some cases. Associated with increased uteroplacental vascular pathology in PE is fetal intrauterine distress due to increased thickness of the VSM. Compared to normotensive pregnancies, pregnancies with PE often result in low birth weights and smaller newborns. According to this study, there is a significant difference between the PE and control groups in the density and thickness of SKs and VSMs, indicating that structural changes in the villous syncytiotrophoblast impair placental function.

CONCLUSION

The structural changes in the placenta lead to the functional changes in the placenta. This means that morphometry can be used as an indirect method of studying placental pathophysiology and physiology in this context. Oxygen delivery from the mother to the fetus can be affected by placental morphology and cellular architecture. The development of neonatal birth weight is directly related to the placental weight of the PE. The gestational age also plays a major role in maternal and perinatal outcomes, along with placental weight and fetal weight. Under hypoxia injury, SKs and VSMs are supposed to become more dense, thereby promoting the release of soluble syncytial factors. Hypoxia injury disrupts the syncytial architecture. When VSM is thickened, it impairs the maintenance of feto-maternal exchange and triggers aponecrosis of syncytiotrophoblasts as SKs,

resulting in mother's systemic inflammation. Proteinuria and hypertension, the clinical hallmarks of PE, are believed to result from those factors pathologically activating the maternal endothelium.

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