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PE IMPACT ON PLACENTAL MORPHOLOGY: VSM AND SK ANALYSIS

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ABSTRACT
The vasculosyncytial membrane (VSM) plays a pivotal role in fetomaternal exchange, with syncytiotrophoblasts forming syncytial knots (SKs) at the terminal villi, facilitating this exchange process. In pregnancies complicated by preeclampsia (PE), characterized by hypoxic injury, alterations in syncytial architecture can lead to further complications. To investigate these morphological changes, an observational study was conducted on 42 placentas (21 from PE cases and 21 controls) collected from the Department of Obstetrics and Gynecology. While the feto-placental index did not significantly differ between PE and control groups, neonatal and placental weights were reduced in PE cases. Notably, PE patients exhibited a statistically significant increase in SK density and VSM thickness. Specifically, VSM thickness in SKs was twice as high in PE cases compared to controls. Additionally, SKs were classified into four types (type-1, type-2a, type-2b, and type-3), with differences observed between PE and control groups. These findings highlight the adverse effects of PE on placental morphology and microscopic features, potentially contributing to fetal hypoxia.

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

INTRODUCTION

An abnormal level of blood pressure during pregnancy is known as preeclampsia or PE. Preeclampsia occurs when there is sudden onset of hypertension and proteinuria coupled with maternal dysfunction after 20 weeks of gestation [1]. A major contributor to maternal mortality and morbidity is PE, which occurs in 5-8 percent of pregnancies worldwide. In uncomplicated pregnancies, perinatal mortality may be as high as 3%; in PE, it is even three times higher [2, 3]. The maternal disease and premature birth caused by PE can cause severe maternal disease and premature birth, with a perinatal mortality rate of 1 to 3%. While some believe PE is multifactorial in nature, the precise etiology remains under extensive research. PE, however, is exacerbated and onset is slowed by the presence of the placenta [4, 5]. The maternal spiral artery is hypoxic due to inadequate trophoblast invasion into the placenta. PE is associated with shallow placentation. A normal pregnancy cannot occur with uteroplacental circulations that have low resistance or high capacitance [6]. Due to an abnormal morphology of villous morphology in PE, spiral artery remodelling is not carried out and foetal vascular development is not developed properly. During normal gestation, the diameter of the terminal villi (TV) decreases with age. In the TV, the cytotrophoblasts become subtler and their mass is contributed to the growth of the syncytium [7]. It can affect maternal hemostasis and endothelial function as it is in direct contact with maternal blood. The syncytiotrophoblast covers the outer layer of placenta, which is in direct contact with maternal blood. Syncytiums protect the body from pathogens and maternal cells while acting as secretory and transporting epitheliums [8]. As a result of an uneven distribution within the syncytiotrophoblast, a syncytial knot (SK) forms on the

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outer surface of a tertiary placental villi. At term, the number of SKs in the TV increases, reaching between 10 and 30%, whereas SKs are seldom observed in an immature placenta [9,10]. Many theories have been proposed about SKs; they have been listed as degenerative changes, aging changes, syncytial hyperplasias, and responses to trophoblast ischemia or hypoxia [11]. It is the vasculosyncytial membrane (VSM) which is the only physical barrier between maternal and fetal blood, which separates the placental villous membrane (syncytioplasm) from the fetal capillaries [12]. Maintaining the exchange surface area and the effective diffusion distance of fetomaternal surfaces are the most significant properties of the VSM. A thin VSM increases the risk of fetal hypoxia and poses a considerable threat to the fetus. Hypertensive placental villi with insufficient VSM can be attributed to failure of differentiation of trophoblasts [13]. The relationship between VSM and that of fetal hypoxia has been confirmed in almost all previous placental studies. When VSMs are altered morphologically or functionally along with other complications, preeclampsia results. The present study aims to compare normal and PE placentas with respect to their morphological and histomorphometrical changes [14].

MATERIALS AND METHODS

A total of 42 placentas were collected from the hospital for the present study. Among the placentas, 21 belonged to women with normal blood pressure during pregnancy (controls), while the remaining 42 belonged to women whose pregnancy was complicated by preeclampsia. The institutional ethical committee approved all informed written consents given by the enrolled mothers. According to Obstetrics and Gynecology, PE were selected based on the following criteria: 1) Blood pressure (BP) greater than 140/90 mm Hg manifested at least six hours apart on two occasions, 2) a proteinurea concentration of at least 300 mg per 24-hour urine collection or a protein concentration of at least 1g/l on two separate occasions at least 6 hours apart. A normal blood pressure and no proteinuria or other systemic or endocrine disorder were the criteria for inclusion of controls. Control and PE were excluded if the mothers had diabetes mellitus, obesity, severe anemia (Hb >6%), eclampsia or other endocrine disorders. As soon as the placenta is delivered, the embryonic membranes and umbilical cord are removed. The diameters of the placentas were measured and weighed. A vertical cut was made around the umbilical cord insertion and one towards the periphery of the placenta in order to take placental tissue samples. Paraffin was applied to tissue samples that had been soaked in 10% formalin saline solution for 24-48 hours. Hematoxylin and eosin were used to stain four micron-thick sections. On both groups, 1,500 TVs were examined under a microscope randomly [15]. As the smallest capillary loops surrounded by blood, they were recognized as the smallest villi. We counted capillaries randomly in selected fields per slide with an Olympus trinocular microscope (CX31) equipped with a 40× objective. We observed the desired TV using 100x objective for both VSM thickness with and without SKs. Olympus optical micrometers (stage, ocular, and reticule) were used to measure the thickness of SKs and VSMs. Using a trinocular head attached to a Sony DCR W530 digital camera (Tokyo, Japan), photographs were taken. SPSS 10 for Windows was used to analyze the data (SPSS Inc., Chicago, IL, USA). The Student paired t-test was used to determine whether there were statistically significant differences between the two groups. Data were presented as mean±standard deviation. In order to be statistically significant, a P-value less than 0.05 must be present.

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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