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Research Article

Investigation of Placentas of Preeclamptic Patients with Very Premature Membrane Rupture

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Abstract



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Purpose: In this study, placental histological differences between the control group and the PROM+preeclampsia group were evaluated.**Materials and Methods:** In our study, placentas were obtained from a total of 90 pregnant patients (regardless of age), including 45 control and 45 PROM+Preeclampsia pregnant patients, by obtaining informed consent form.**Results:** In the control group, placental structures appeared normal with regular chorionic villi, properly organized trophoblast layers, minimal syncytial nodes, and limited fibrin accumulation. Villous capillary endothelial cells were thin and elongated, while stromal cells were well-placed without signs of bleeding or inflammation. In the PROM+preeclampsia group, villous degeneration, trophoblastic apoptosis, vascular congestion, endothelial hyperplasia, and increased fibrin deposition were observed. The intervillous area showed extensive hemorrhage and immune cell infiltration, with numerous Hoffbauer cells in the villous stroma and marked decidual cell degeneration near the maternal plate.**Conclusion:** In our study, placental histopathological changes observed in the PROM+preeclampsia group show that this condition may seriously affect the placental structure.**Keywords:** placenta, PROM, histopathology, preeclampsia

INTRODUCTION

Preeclampsia (PE) is one of the most common pregnancy complications leading to maternal and fetal mortality and morbidity worldwide. It is considered the second most common major cause of abnormal pregnancy outcomes ¹. PE is most commonly seen after the 20th week of pregnancy with high blood pressure (140/90 mmHg) and proteinuria (albumin >300 mg per 24 hours) ². The prevalence of PE has been reported to be 2-8% of all pregnancies in various countries of the world, even among different ethnic groups living in the same country ³. Important risk factors for PE include previous history of hypertension, autoimmune system, kidney disease, high blood sugar level, maternal weight, age of the pregnant women, ethnicity and family history ⁴.

Premature membrane rupture (PROM) is the rupture of the membranes one hour before the onset of uterine contractions, regardless of gestational age. According to gestational age, PROM can be divided into two categories: term PROM after 37 weeks of gestation and preterm PROM (pPROM) before 37 weeks of gestation. PROM is one of the common obstetric complications, but its accurate incidence is difficult to estimate due to the

wide variation reported in the current literature. Recent data suggest that it complicates approximately 3-10% of all pregnancies ⁵. PROM is a potential risk factor for both maternal and infant mortality and morbidity. Neonatal complications associated with PROM include prematurity, trauma, fetal distress, intraventricular hemorrhage, respiratory distress syndrome, and intrauterine infection. These complications ultimately lead to poor fetal development during pregnancy ⁶.

Our aim in this study was to examine histopathological changes in the placentas of preeclamptic patients diagnosed with PROM.

MATERIALS AND METHODS

Obtaining Placentas

Our study was initiated with the approval of the Ethics Committee of Dicle University Faculty of Medicine dated 17.05.2023 and numbered 186. In our study, placentas were obtained by obtaining informed consent forms from a total of 90 pregnant patients (regardless of age), 45 controls and 45 PROM+Preeclampsia pregnant patients. A postpartum consent form was obtained from the mothers who applied to the Gynecology and Obstetrics Clinic of Dicle University Faculty of Medicine

Hospital. After the placentas were washed with physiological serum, they were placed in 10% buffered neutral formalin under appropriate conditions in the operating room for tissue follow-up and taken to the Dicle University Faculty of Medicine Histology and Embryology Department Laboratory.

Tissue Tracking for Light Microscopic Examination

Placentas taken to the Dicle University Medical Faculty Histology and Embryology Department laboratory were taken from both the central maternal and central fetal sides of the placenta for tissue tracking, and then placed in buffered 10% neutral formalin in numbered transparent glass sample bottles. Tissue pieces taken from the central maternal and fetal sides were kept in transparent glass sample bottles for 16 hours for fixation. After the fixation stage, the tissue pieces were kept under running tap water for 12 hours to remove formalin solution. Then, the tissue pieces were kept in 50%, 70%, 80%, 90% and 96% alcohols for a total of 8 hours and finally, they were kept in absolute alcohol (99.9%) for 2x20 minutes to complete the dehydration process. The tissues were kept in xylene for 2x15 minutes to remove alcohol and the transparency process was performed. After waiting in paraffin for 2x1

hours in an oven set at 58oC for infiltration, tissue pieces were embedded in paraffin blocks for blocking¹². After the embedding process, 5µm thick sections were taken from each paraffin block with the help of a fully automatic rotary microtome (Leice RM2265, Germany). Hematoxylin-Eosin (H-E) staining were applied to the obtained sections. Preparations were examined under a light microscope using the Zeiss Imager A2 light and Zen 3.00 software program.

RESULTS

Hematoxylin-Eosin Findings of Control group

In the control group, placental structures were observed as normal. Chorionic villi exhibited an oval and regular structure, while syncytiotrophoblasts were found in the outer part and cytotrophoblasts in the inner part. Syncytial nodes were few in number and fibrin accumulation was limited. Endothelial cells in villous capillaries were long and thin, fibers were regular in the root villous connective tissue, and stromal cells were properly placed. No bleeding or lymphocyte infiltration was observed in the intervillous area (Figure 1 and Figure 2).

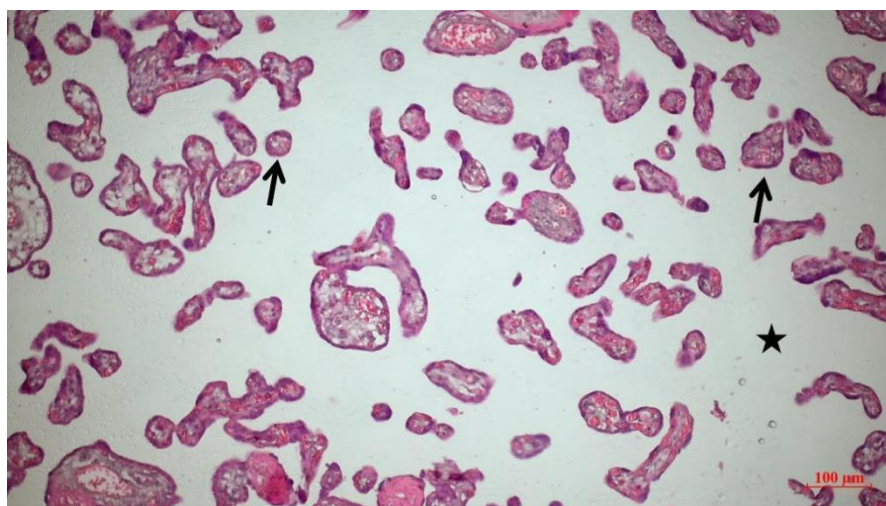


Figure 1: Placental section of the Control Group. Arrow: villus, star: intervillous area, Hematoxylin Eosin Staining, Bar: 10 µm, Magnification: 10X

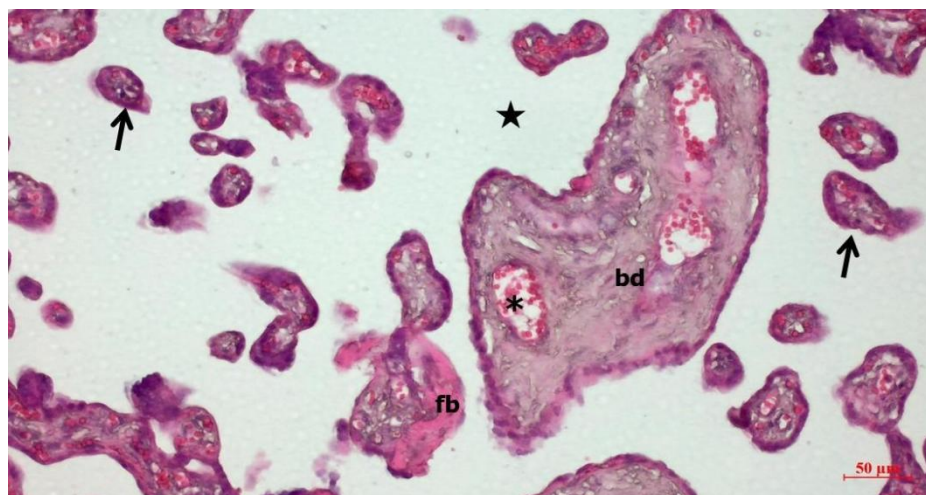


Figure 2: Close-up placental section of the Control Group. Arrow: villus, arrowhead: syncytial node, star: intervillous area, fb: fibrin, bd: connective tissue, asterisk: capillary, Hematoxylin Eosin Staining, Bar: 50 µm, Magnification: 20X

Hematoxylin-Eosin Findings of PROM+Preeclampsia group

In the PROM+preeclampsia group, degeneration in the villi, pyknosis and apoptosis in the trophoblastic layer cells were observed. Vascular dilatation and congestion were detected in the villi, while hyperplasia was

observed in the endothelial cells. There was intense hemorrhage and immune cell accumulation in the intervillous area. While fibrin accumulation increased, numerous Hoffbauer cells were detected in the villous stroma. Decidual cell degeneration was clearly observed in areas close to the maternal plate (Figure 3 and Figure 4).

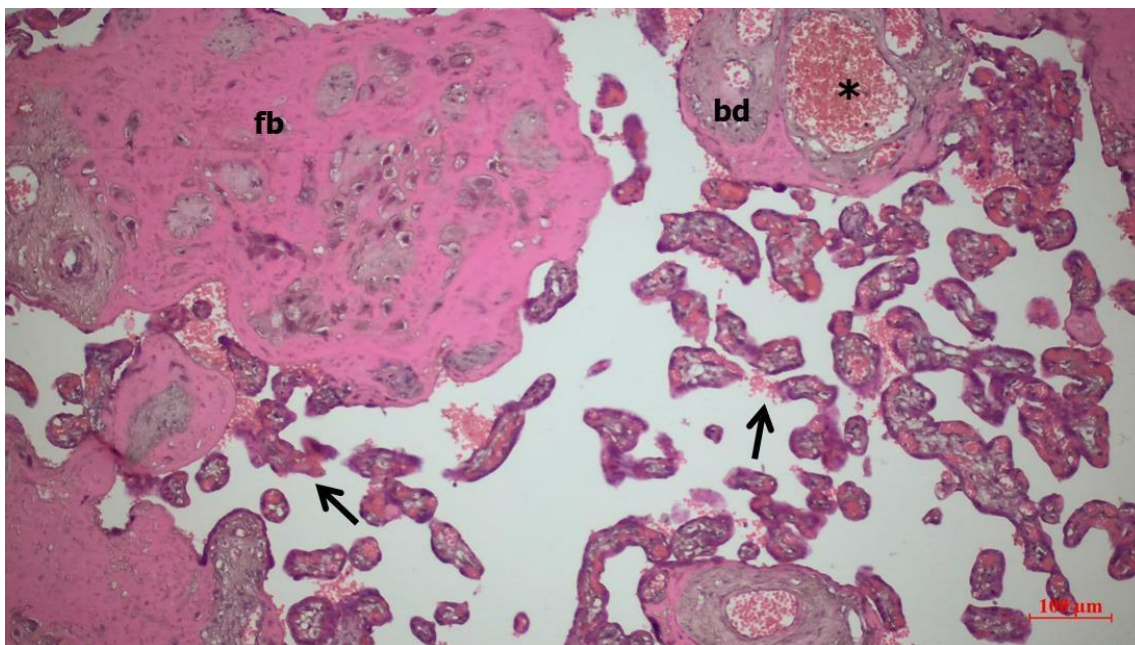


Figure 3: Placental section of PROM+preeclampsia group. Arrow: villus, fb: fibrin, asterisk: capillary, bd: connective tissue, Hematoxylin Eosin Staining, Bar: 10 μm, Magnification: 10X

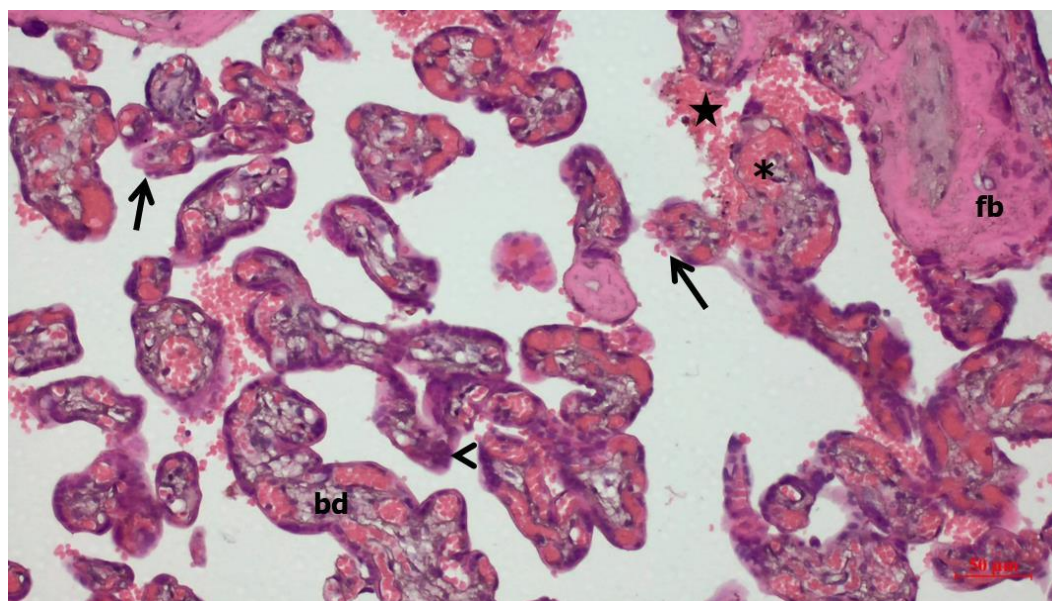


Figure 4: Close-up placental section of the PROM+preeclampsia group. Arrow: villus, arrowhead: syncytial node, star: intervillous area, fb: fibrin, bd: connective tissue, asterisk: capillary, Hematoxylin Eosin Staining, Bar: 50 μm, Magnification: 20X

DISCUSSION

Our study is the first to analyze histopathological changes in PE patients with PROM. In placenta studies, disruption of the controlled inflammatory response caused increased damage at the vascular and cellular levels.

Preeclampsia is a systemic disease that occurs in the second half of pregnancy, is characterized by hypertension and proteinuria, and can lead to serious complications for both the mother and the fetus. Although the etiopathogenesis of preeclampsia has not been fully explained, it is known that placental

insufficiency and endothelial dysfunction are among the basic mechanisms of the disease. Histopathological findings show how these mechanisms affect the placental structure throughout pregnancy⁷⁻¹¹

Histopathological changes commonly seen in preeclamptic placentas include placental ischemia, villous degeneration, limited trophoblast invasion, and fibrinoid necrosis. In normal pregnancy, as a result of the invasion of spiral arteries by trophoblasts, the vessel walls expand, forming a low-resistance system that supports uteroplacental circulation. However, in preeclampsia, this invasion is insufficient and the spiral arteries remain narrow and muscular. This reduces uteroplacental perfusion, causing hypoxia and oxidative stress. Oxidative stress triggers placental inflammation, leading to endothelial dysfunction and systemic inflammatory response¹²⁻¹⁴.

Histopathologically, significant fibrin deposition, intense inflammatory cell infiltration, increased Hoffbauer cells, and disruptions in chorionic villus structure are reported in preeclamptic placentas. In addition, findings such as increased apoptosis in trophoblastic cells, stromal edema, villous fibrosis, and perivascular degeneration are also common. In addition to endothelial cell hyperplasia and vascular dilatation, microthromboses are frequently observed in preeclampsia cases. These findings support the vascular dysfunction and inflammatory processes underlying preeclampsia^{15,16}.

The histopathological effects of preeclampsia can lead to complications such as fetal growth retardation (FGR) and intrauterine hypoxia due to placental insufficiency. Therefore, a better understanding of placental changes associated with preeclampsia is important for the development of early diagnosis and treatment strategies for the disease. Future studies may contribute to our better understanding of the pathophysiology of preeclampsia by examining the immunological and molecular mechanisms in more detail^{17,18}.

In our study, placental histopathological changes observed in the PROM+preclampsia group indicate that the placental structure may be seriously affected. The disruption of the controlled inflammatory response caused increased damage at the vascular and cellular levels. In terms of clinical significance, our findings underline the inflammatory and vascular processes in the placental microenvironment in pregnancies complicated by preeclampsia.

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Data Availability Statement: The data presented in this study are available on request from the corresponding author.

Ethical approval: This study was initiated with the approval of the Ethics Committee of Dicle University Faculty of Medicine dated 17.05.2023 and numbered 186.

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