

## Histopathological Alterations in Placentas of Severe and Non-Severe Preeclamptic Patients

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### Abstract

Preeclampsia is a significant pregnancy complication associated with vascular lesions and trophoblastic invasion, leading to substantial maternal and fetal risks. This study compares histopathological changes in placental structures among severe and non-severe preeclamptic patients. Placental tissues were analyzed, revealing that preeclampsia groups showed notable villous degeneration, increased fibrin deposition, vascular dilatation, congestion, and syncytial node formation. Severe preeclampsia further exhibited intensified hemorrhage and leukocyte infiltration. These findings underscore the link between preeclampsia severity and placental dysfunction, providing insights into the pathological mechanisms affecting perinatal outcomes.

**Keywords:** placenta, preeclampsia, HELLP, histology

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## INTRODUCTION

Preeclampsia, also known as pregnancy poisoning, is a condition characterized by symptoms such as high blood pressure (hypertension), proteinuria, and damage to the kidneys or other organs during pregnancy. It is seen in approximately 3-5% of pregnancies. Preeclampsia usually occurs after the 20th week of pregnancy. In cases where preeclampsia is severe, there may be red blood cell destruction, low blood platelet count, liver dysfunction, swelling and dysfunction in the kidneys, shortness of breath or visual disturbances due to fluid in the lungs <sup>1-3</sup>. Preeclampsia can result in premature birth and even have undesirable and fatal consequences for both the mother and the fetus <sup>4</sup>. If left untreated, it can cause seizures known as eclampsia <sup>5</sup>. The placenta is a complex structure that develops in the uterus during pregnancy and connects the mother's uterus to the umbilical cord, transmits nutrients and oxygen to the fetus, carbon dioxide and waste products to the mother. The placenta, a fetal organ, develops shortly after pregnancy and plays a critical role in fetal development by connecting to the baby via the umbilical cord <sup>6</sup>. The

functions of the placenta include providing oxygen and nutrients to the fetus, removing harmful wastes and carbon dioxide from the fetus, playing a role in the production of hormones that help the fetus grow, passing the mother's immunity to the baby, and helping the fetus develop and protect <sup>7</sup>. In this study, we aimed to show different pathologies in placentas of women with severe and nonsevere preeclamptic patients by histochemical staining.

## MATERIALS AND METHOD

### Tissue preparation procedure

The ethical approval for the study was obtained from the Dicle University Faculty of Medicine Non-Interventional Clinical Research Ethics Committee (date: 28/02/2023 and protocol number: 74). The placentas used in the study were obtained from patients hospitalized in the Dicle University Faculty of Medicine, Gynecology and Obstetrics Clinic. During the collection of placentas, after interviews with the patients after delivery, the placentas washed with physiological serum from each patient were taken in 10% buffered neutral formalin under

appropriate conditions in the operating room for tissue tracking and sent to the Dicle University Faculty of Medicine, Histology and Embryology Department Laboratory. After the fixation process, the tissue pieces were kept under running tap water for 12 hours to remove the formalin solution. Then, the tissue pieces were kept in 50%, 70%, 80%, 90% and 96% alcohols for a total of 8 hours for dehydration. In the last stage of dehydration, the tissues were kept in 99.9% absolute alcohol for 2x20 minutes and completely dried. In order to remove the alcohol, the tissues were kept in xylene for 2x15 minutes and the transparency process was performed. The infiltration stage was carried out by keeping the tissue pieces in paraffin for 2x1 hour in an oven set at 58 °C. Then, the tissue pieces were embedded in paraffin blocks. After this embedding process, 5 µm thick sections were taken from each paraffin block using a fully automatic rotary microtome (Leica RM2265, Germany)<sup>8</sup>.

### Hematoxylin-Eosin Staining

Placental tissue sections obtained from paraffin blocks were placed in a bain-marie at 37 °C for histological examination. In order to melt the excess paraffin on the sections, they were kept in a 58-62 °C oven for 6 hours. Then, the sections were deparaffinized in xylene for 15 minutes three times. After deparaffinization, the sections were kept in decreasing alcohol series containing 100%, 96%, 90%, 70% and 50% ethyl alcohol for 10 minutes

and finally transferred to distilled water and kept for 5 minutes. For histological examination, the sections were stained with hematoxylin-eosin (H&E) dyes. After the staining process was completed, the sections were quickly dipped in increasing alcohol series (80%, 90%, 96% ethyl alcohol) and then kept in absolute alcohol for 2 minutes. Finally, the sections were kept in xylene for 15 minutes three times to become completely transparent. The tissue samples were covered with coverslips by dropping mounting medium. These procedures made the sections ready for examination under the microscope and allowed a detailed analysis of histological structures<sup>9</sup>.

## RESULTS

In the placental sections of the control group, it was observed that the chorionic villi were regular and their borders were distinct. No degeneration or irregularity was observed in the villi. Cytotrophoblasts and syncytiotrophoblasts were regularly located and structural integrity was observed in the fetal capillary and villous connective tissue. Fibrin accumulation was minimal. No specific cellular density was observed in the placental sections and a homogeneous trophoblastic cell distribution was seen. No congestion, dilatation or pathology was detected in the vessels. The number of syncytial nodes was also observed to be quite low (Figure 1).

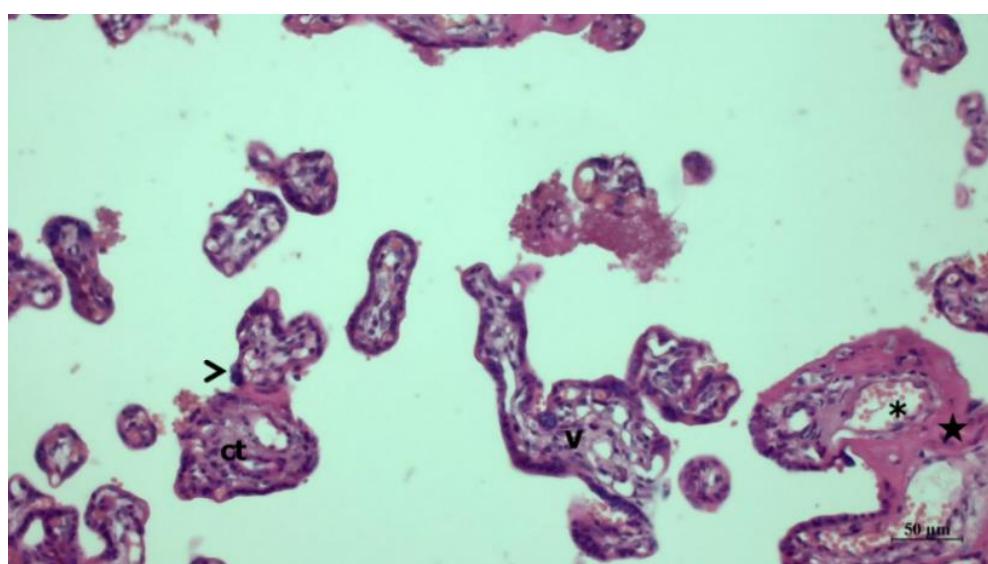


Figure 1: H-E stained placental section of the control group. V: villus, star: fibrin, \*: capillary, arrowhead: syncytial node, ct: connective tissue. Hematoxylin Eosin Staining, Bar: 50 µm, Magnification: 20X

When placental sections from the preeclampsia group were examined, it was observed that the placental villi were degenerated and had structural irregularities compared to the control group. Fibrin accumulation and a significant increase in the number of syncytial nodes

were detected. Congestion and dilatation in the vascular structures as well as lymphocyte infiltration were also recorded. Hemorrhage and leukocyte presence were detected in the intervillous area (Figure 2).

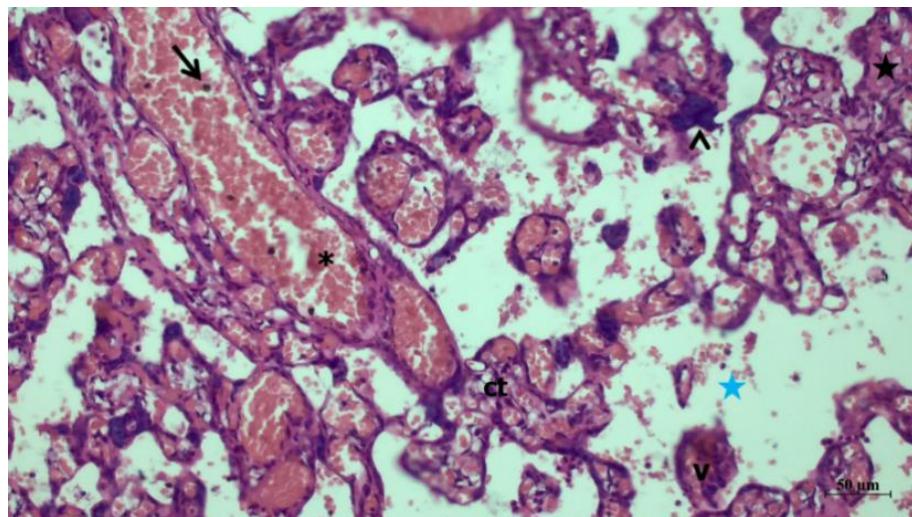


Figure 2: H-E stained placental section of the preeclampsia group. V: villus, black star: fibrin, blue star: leukocyte in the intervillous area, \*: dilatation/congestion, arrow: leukocyte, ct: connective tissue, Hematoxylin Eosin Staining, Bar: 50  $\mu$ m, Magnification: 20X

In the severe preeclampsia group, similar findings were obtained in the preeclampsia group. Degeneration and structural irregularities were observed in the villous structures. Degeneration was observed in the connective tissue areas. Compared to the preeclampsia group,

vascular structure deterioration, dilatation and congestion, thickening of the vascular wall and hemorrhage in the intervillous area were observed more intensely in this group. Increased fibrin accumulation and leukocyte infiltration were also detected (Figure 3).

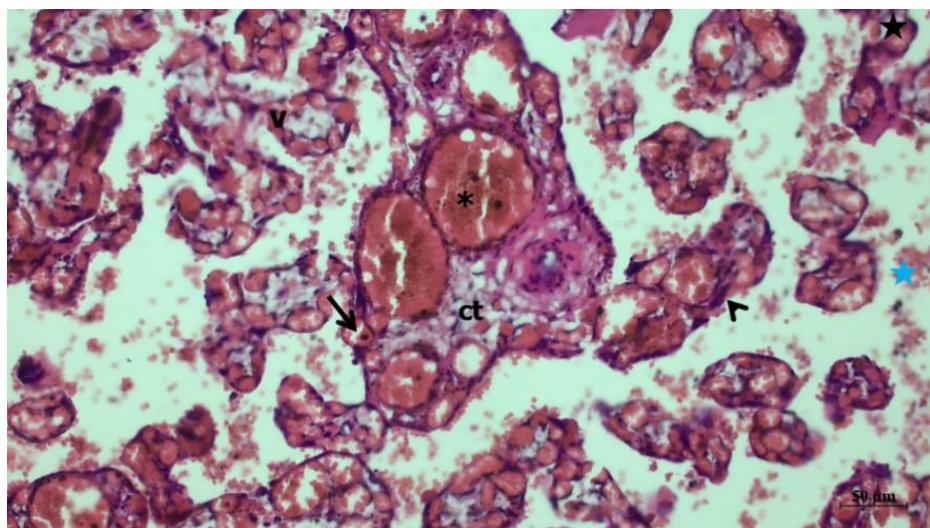


Figure 3: H-E-stained placental section of the severe preeclampsia group. V: villus, black star: fibrin, blue star: leukocyte in the intervillous area, \*: dilatation/congestion, arrow: leukocyte, ct: connective tissue, Hematoxylin Eosin Staining, Bar: 50  $\mu$ m, Magnification: 20X

## DISCUSSION

Preeclampsia is a common complication during pregnancy, increasing the risks of maternal and perinatal mortality and morbidity. Hypertensive effects, especially those that occur after the 20th week of pregnancy, can lead to both maternal, fetal and placental dysfunction <sup>10</sup>. This condition has been reported to be due to changes in RNA regulation and cell signaling pathways. Preeclampsia is a condition associated with vascular placental lesions and trophoblastic invasion, which causes significant damage in terms of histopathology. Studies show that syncytial degeneration, an increase in syncytial nodes and bridges, and congestion in blood

vessels develop depending on the severity of preeclampsia in trophoblast invasion. These findings reveal the effects of preeclampsia on structural and functional changes in the placenta <sup>11-15</sup>.

In our study, it was determined that placental structures in the preeclampsia and severe preeclampsia groups showed significant deterioration compared to the control group. In the control group, regular and well-defined placental villi, minimal fibrin accumulation and low syncytial node count support healthy placental structure and functions. The absence of any congestion, dilatation or pathology in vascular structures indicates that the control group maintained healthy circulation

and normal placental functions. In the preeclampsia group, degeneration of placental villi, increased syncytial nodes and fibrin accumulation indicate that placental circulation is impaired and an inflammatory response develops. In addition, congestion and dilatation in vascular structures as well as leukocyte infiltration indicate that preeclampsia is associated with inflammatory components and vascular dysfunction. These findings became more pronounced in the severe preeclampsia group, and vascular wall thickening and hemorrhage in the intervillous area suggest that impaired blood flow and insufficient oxygenation are more severe.

## CONCLUSION

In our study, significant structural changes were detected in placental structures in preeclampsia and severe preeclampsia groups. Placental villus degeneration, syncytial node increase, fibrin deposition and vascular pathologies associated with preeclampsia indicate that placental functions are impaired and this may have adverse effects on perinatal outcomes. Especially in severe preeclampsia, these impairments reach more serious levels and increase the risks threatening the health of the mother and the fetus.

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