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ULTRASTRUCTURAL AND MORPHOMETRIC CHARACTERISTICS OF THE PLACENTA IN PREECLAMPSIA OF VARYING SEVERITY

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Abstract. *Preeclampsia remains one of the most complex and clinically significant issues in contemporary obstetrics. Globally, this condition complicates approximately 2.8% of pregnancies and is among the leading contributors to maternal and perinatal morbidity and mortality. The incidence of preterm delivery in preeclamptic pregnancies may reach 15%, while neonatal morbidity is observed in 64–78% of cases. Perinatal mortality ranges from 18% to 30%. According to numerous studies, these high complication rates are closely associated with morphofunctional disturbances in the fetoplacental system. The application of modern ultrastructural imaging techniques allows for a more detailed understanding of the underlying pathological mechanisms within the maternal–placental–fetal unit.*

Keywords: *preeclampsia, placental villi, elements in the vessels of the placental chorionic villi, endothelial cells, thrombi.*

Introduction. Preeclampsia (PE) remains one of the most severe and clinically significant gestational complications, exerting a profound negative influence on maternal and fetal health during the antenatal, intrapartum, and postpartum periods. On a global scale, PE affects approximately 2.8% of pregnancies and is among the leading etiological factors contributing to maternal and neonatal morbidity and mortality. The incidence of preterm delivery in pregnancies complicated by PE may reach 15%. According to multiple studies, neonatal morbidity in this context ranges from 64% to 78%, while perinatal mortality is estimated at 18–30% [1,5].

The placenta plays a central role in the pathogenesis of PE, as the condition is exclusively associated with the presence of placental tissue and typically resolves following its delivery. Moreover, the clinical manifestations of fetal and neonatal compromise in PE are directly linked to the structural and functional integrity of the placenta.

Current research indicates that placental-derived antiangiogenic factors, upon entering the maternal circulation, induce endothelial dysfunction, which contributes to the development of hallmark features of PE such as arterial hypertension, proteinuria, glomerular endotheliosis, the HELLP syndrome, and systemic manifestations of preeclampsia [10,13]. The placenta is a uniquely transient organ that undergoes continuous development and differentiation, significantly influencing both fetal growth and maternal physiology throughout gestation. While normal pregnancy is characterized by a degree of systemic inflammation, oxidative stress, and modulation of angiogenic factor levels and vascular reactivity [2,3,7], these physiological adaptations become pathologically intensified in PE due to the failure of compensatory mechanisms. This ultimately results in placental insufficiency and vascular dysfunction [4,9,11,12].

Preeclampsia is commonly associated with the development of chronic placental insufficiency (PI), which stems from early disruptions in the formation of the functional maternal–placental–fetal unit. Histopathological examinations of placental tissues from PE patients often reveal morphological signs consistent with varying degrees of PI. These include delayed maturation of the villous tree,

obliterative angiopathy, stromal sclerosis of the villi, areas of non-functioning tissue, and ischemic infarction. Additionally, inflammatory alterations are frequently observed within the placental parenchyma [14,15].

Aim of the Study. To identify the general morphological and ultrastructural features of the fetoplacental system in various degrees of PE that affect the functioning of the system and the condition of the fetus.

Materials and Methods. The research materials included placentas from 32 pregnant women with moderate PE (Group 1) and 24 women with severe PE (Group 2). The control group consisted of samples from 20 women with uncomplicated pregnancies. In all groups, clinical and laboratory examinations were conducted, and the data were compared with morphological changes in the placenta. All placentas were examined at both macroscopic and microscopic levels. Tissues for morphological examination were obtained during vaginal deliveries in 31 women (55.3%) or cesarean sections in 25 women (44.7%) at gestational ages ranging from 34 to 39 weeks.

The average age of the women studied was 28.6 ± 4.2 years. In the analysis of the obstetric and gynecological history of the patients with preeclampsia, the following were identified: menstrual cycle disorders (in 25%), infertility (8.3%), benign cervical diseases (37.5%), chronic inflammatory diseases of the genital organs (29.2%), uterine fibroids (25%), spontaneous early miscarriages (20.8%), missed miscarriages (12.5%), perinatal fetal death (4.2%), birth trauma to the child (4.2%), and preterm birth occurred in 16.6% of the women.

In the history of 6 patients with moderate PE and 8 women with severe PE, previous pregnancies were already complicated by hypertensive syndrome. Among the studied women, 21% were primigravida (first pregnancy), and 79% were multigravida, of which 38% were admitted for their fourth or more delivery. The most common extragenital pathologies among patients with PE were chronic pyelonephritis, grade 1–2 obesity, thyroid diseases (mainly nodular, diffuse, and mixed goiter with euthyroid state, and in two cases – autoimmune thyroiditis with euthyroid state), and eye disease – myopia of grade 1 or 2. Mild to moderate anemia was identified in nearly all PE patients, with 18% showing signs of severe anemia.

Standard clinical, laboratory, and functional methods accepted in obstetric practice were used in the examination. To monitor the condition of the fetus, national protocol-approved methods were applied, including ultrasound examination using the “Aloka” device (Japan), and Doppler ultrasound using the Aloka 5500 system from the 28th week of pregnancy every two weeks or more frequently, if indicated, to assess the state of the fetoplacental system. A qualitative analysis of blood flow velocity waveforms in the uterine arteries and umbilical artery was conducted, with the resistance index being evaluated. From the 28th week of pregnancy, indirect cardiotocography was performed weekly (or more frequently if necessary) to monitor the intrauterine condition of the fetus. Cardiotocography was conducted using a Corometrics Fetal Monitor.

Objective. The present study aims to determine the common morphological and ultrastructural alterations in the fetoplacental system across varying severities of preeclampsia and to assess their impact on placental function and fetal condition.

Study Design. This was an open-label, independent, prospective study.

Materials and Methods. Placental specimens were obtained from 32 patients diagnosed with moderate preeclampsia (Group 1) and 24 patients with severe preeclampsia (Group 2). A control group included placentas from 20 women with physiologically normal pregnancies. Standard obstetric diagnostic tools, including clinical, laboratory, and functional methods, were employed. Macroscopic examination and histological analysis were conducted. Histological sections were stained using hematoxylin and eosin and examined under a “TOPIC–T” CETI light microscope.

For ultrastructural analysis, scanning electron microscopy (SEM) was conducted on samples fixed in glutaraldehyde using “FE Quanta 200 3D” and “FEI Quanta 600 FEG” (Netherlands). Atomic force microscopy (AFM) was performed in constant and intermittent contact modes using the “Ntegra-Aura” system (NT-MDT, Zelenograd, Russia). Imaging and data analysis were conducted using “NOVA” and “ImageAnalysis” software.

Results. Preeclampsia was associated with a notable increase in areas of placental infarction—both chronic (white) and acute (red)—as well as hematomas, extensive intervillous thrombi, non-functional zones, cavitations, and calcifications. Marked circulatory abnormalities were evident, including congestion, thrombosis, hemorrhages, stromal edema, and destructive lesions culminating in focal necrosis.

In cases of severe preeclampsia and prolonged moderate forms, a significant reduction in vascular density was observed. In 20.0 ± 2.5% of structural components, thrombosis occurred in the context of cellular sludging, syncytiotrophoblast desquamation, endothelial atrophy, and vascular sclerosis.

Conclusion. Innovative morphometric and ultrastructural methods revealed profound disruptions in placental function—including the hemoplacental barrier, gas exchange, nutritional transport, and excretory processes—beyond what conventional techniques have previously identified. These findings underscore the need for clinicians to account for such placental impairments when managing pregnancies complicated by preeclampsia, to optimize outcomes for both fetus and neonate.

Morphological Methods of Investigation. A comprehensive study of the placenta was carried out through macroscopic (weighing and measuring dimensions, analyzing its shape, color, umbilical cord attachment, structural abnormalities, presence of white and red infarctions, caverns, intervillous thrombi, calcifications, hematomas) and microscopic examinations.

Immediately after delivery, tissue fragments were taken from the placenta for light microscopy and atomic force microscopy (three fragments up to 0.5 ± 0.1 cm each), as well as for scanning electron microscopy, and were fixed in appropriate media. For scanning electron microscopy, the selected pieces were immediately placed in a 0.85% isotonic sodium chloride solution at 37°C. Several 0.5 cm^3 sections were cut underwater and rinsed in 2–3 batches of freshly prepared isotonic sodium chloride solution. In the final portion, the samples were kept for 2–3 hours at room temperature. Then, the samples were placed into a fixative solution at 37°C: 2% glutaraldehyde in 0.15 M phosphate buffer with a pH of 7.2–7.4. The samples were kept in the fixative in a refrigerator for 2 days to 1 month.

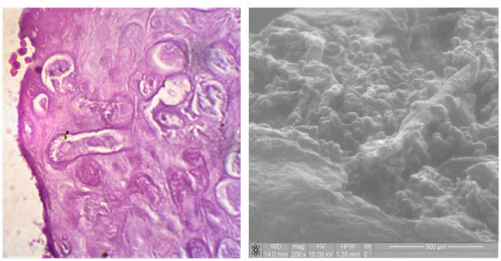

Fig. 1. Pregnant woman No. 3, 35 weeks of gestation. Severe preeclampsia. Placental tissue.
Fig. A (x400): Light microscopy. Hematoxylin and eosin staining.
Fig. B (x200): Scanning electron microscopy.
Infarct fragments (A, B). Non-functional zones with pathological approximation of villi (B).

Upon examining the maternal and fetal surfaces, we identified progressive pathological changes in the following areas: impaired circulation with the presence of congestion, thrombus formation,

hemorrhages; tissue edema; and degenerative processes, including focal areas of necrosis. These changes were directly dependent on the severity and duration of the disease. Sclerotic regions were also observed, including sclerosis in the walls of blood vessels (Figures 2 and 3).

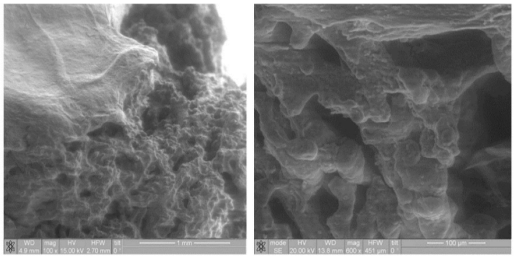

Figure 2. Pregnant woman No. 4, 39 weeks of gestation. Placental fragments in moderately expressed preeclampsia
Fig. B (x600): Fragment of **Fig. A (x100).**
Fetal surface and villous tree with predominance of stem and intermediate villi (A, B).

The villous tree plays a key role in the exchange, protective, and immune mechanisms of the placenta. Therefore, in our study of its microstructural features, primary focus was placed on this component. All morphological parts of the villous tree were examined: stem, intermediate, and terminal villi (Figures 4 and 5).

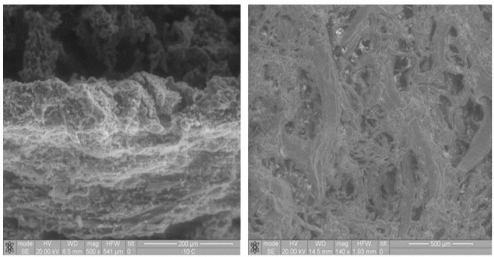

Fig. 3. Pregnant woman No. 4, 39 weeks of gestation. Placental fragments in moderate preeclampsia.
Fig. A (x500), Fig. B (x140): Scanning electron microscopy.
Maternal surface with edema and sclerosis (A).

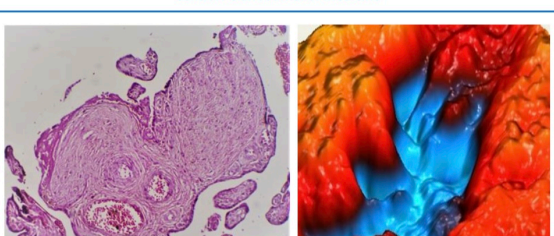

Fig. 4. Pregnant woman No. 3, 40 weeks of gestation. Placental fragments in moderately expressed preeclampsia.
Fig. A (x100): Light microscopy. Hematoxylin and eosin staining.
Fig. B (x1000): Atomic force microscopy, three-dimensional image.

Stem villi in certain cotyledons show sclerosis (A), including the vascular wall (A, B).The results of scanning electron microscopy indicate altered structure of the placental villi, vascular engorgement alternating with areas of reduced vascular channels.

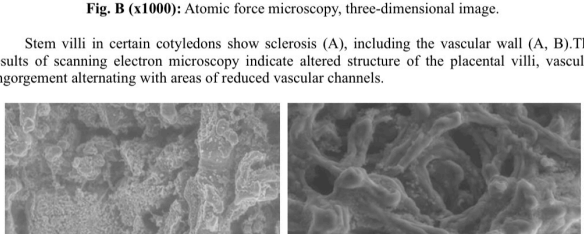

Fig. 5. Pregnant woman No. 3, 40 weeks of gestation. Placental fragments in moderately expressed preeclampsia.
Fig. A (x250), Fig. B (x500): Scanning electron microscopy.

In some cotyledons, the stem villi showed evidence of vascular congestion (Figure A), along with a significant rise in the proportion of intermediate villi (Figure B). To assess placental function accurately, it is essential to closely examine its tissue structure. For this purpose, we analyzed specific elements such as the relative area occupied by the villous tree and the number of syncytial knots

(considered indicators of regenerative activity), in relation to the fibrinoid-rich intervillous space. The results are presented in Table 1 and Figure 6.

Morphometric evaluation of placental samples from pregnancies affected by different severities of preeclampsia revealed a noticeable reduction in both the surface area of the villous tree and the number of syncytial knots, especially in the terminal villi (Table 1, Figures 7 and 8). At the same time, a compensatory widening of the intervillous space occurred, accompanied by an increased accumulation of fibrinoid material. These structural changes showed a significant association with the severity of preeclampsia ($p < 0.05$).

Table 1.

Morphometric Indicators of Placentas in Pregnant Women with Varying Degrees of Preeclampsia (%).

Observation group	Specific Area (%)			
	Villous Tree	Syncytial Knots	Intervillous Space	Intervillous Fibrinoid
Preeclampsia (moderately expressed)	55, 0±3,1*	2,1±0,2*	36,8±1,8*	6,1 ±0,9 *
Preeclampsia (severe)	50, 5±3,5* **	1,2±0,1* **	40,0±2,6* **	8,3 ±0,6* **
Control Group	62, 5±3,2	2,9±0,8	31,3±2,7	3,3 ±0,6

Appendix: ** $p < 0.05$ compared to the control group;*
*** $p < 0.05$ compared to groups with different degrees of preeclampsia.*

In studying the ratio of various types of pathologically altered villi in the placentas of pregnant women with different degrees of preeclampsia, we observed a shift in all types at the expense of unchanged ones. As the condition worsened, the proportion of unchanged and congested villi decreased, while the number of sclerotic, fibrinoid-altered, and edematous villi increased.

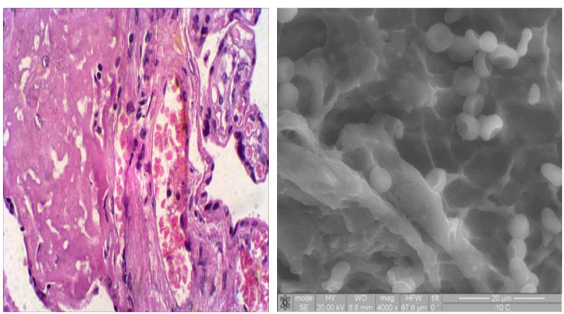

Fig. 7. Pregnant woman No. 4, 34 weeks of gestation. Placental fragments in severe preeclampsia.
Fig. A (x400): Light microscopy. Hematoxylin and eosin staining.
Fig. B (x4000): Scanning electron microscopy.

Sclerosis of the villi (A, B) was observed, along with fibrinoid deposits on their surface—particularly in areas where the syncytiotrophoblast had detached (A, B)—as well as within the intervillous space (A, B), where intervillous thrombi were also present. Villi edema (A) was also noted. Fibrinoid accumulations were especially prominent in regions of syncytiotrophoblast shedding (A, B).

Electron microscopy revealed the presence of thin argyrophilic fibers and collagen fiber bundles surrounding fibroblasts and fibrocytes within the stroma. These cellular components were found in much greater numbers in preeclamptic samples than in the control group. Approximately one-third of the blood vessels showed signs of ischemia, with occasional erythrocytes—many undergoing hemolysis—visible in their lumens. Some vessels were congested, and thrombi were identified in about 20.0±2.5% of the examined structures. Many vessels also showed pronounced spasms along their entire length, averaging 1.2±0.5 µm in depth.

The vessel walls were often thickened and sclerotic, with structural degradation of their normal components. The endothelial lining appeared flattened and lacked its usual folded structure. Areas of necrosis were detected in some locations—these being the most common sites for thrombus formation. Endothelial cells were frequently atrophied. Fibrin threads often linked the stem villi together, significantly hindering maternal blood flow to the fetus and contributing to fetal hypoxia.

These conditions were associated with the clustering of villi, vascular congestion, and the development of stasis and cellular sludge (Figure 8).

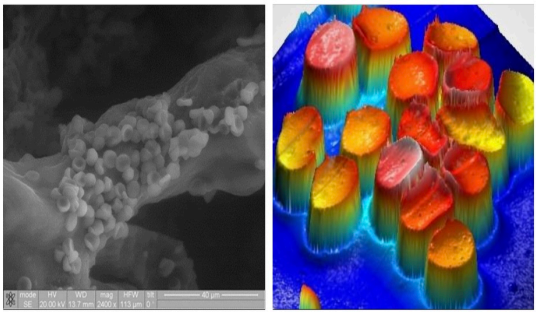

Fig. 8. Pregnant woman No. 3, 39 weeks of gestation. Placental fragment in moderately expressed preeclampsia.
Fig. A (x200): Scanning electron microscopy.
Fig. B (x15,000): Atomic force microscopy laboratory (three-dimensional image).

The vessels are congested. Stasis and cell sludging. Accumulation of erythrocytes in the intervillous space. Early stages of thrombosis formation. Erythrocytes in the capillaries and intervillous space are observed as normocytes, swollen discs, and complete or incomplete spheres.

Conclusion. Among the leading risk factors for preeclampsia, the most significant remain: a high number of pregnancies and births, chronic iron-deficiency anemia, and longstanding gynecological conditions linked to blood clotting abnormalities and endocrine disorders.

• Advanced morphological techniques—such as atomic force microscopy and scanning electron microscopy—allow researchers to explore the intricate mechanisms that contribute to placental insufficiency and fetal distress in pregnant women with hypertensive disorders.

• In cases of severe preeclampsia, as well as in prolonged moderate forms, areas with impaired blood flow become more prominent. Approximately 20.0±2.5% of the observed structures show thrombus formation, along with cellular sludge, shedding of the syncytiotrophoblast, endothelial cell degeneration, and vascular hardening.

• These placental changes reveal substantial functional impairment—including disruption of the hemoplacental barrier, as well as compromised respiratory, nutritional, and excretory roles. Such findings highlight more severe dysfunction than previously shown by conventional methods, underscoring the importance for clinicians to consider these factors in protecting fetal and newborn health.

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