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Morphological Characteristics of Placental Complex in Pregnant Women Without Complications in Pregnancy and in the Presence of Severe Preeclampsia

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ABSTRACT

According to the WHO data, preeclampsia develops during late pregnancy in 2-8% of women. Preeclampsia is a major cause of maternal and perinatal morbidity and mortality, therefore, the study of the morphological features of placental complex, taking into account gestational complications in postpartum women with severe preeclampsia is an important factor for finding the optimal treatment during pregnancy. The study was conducted on a placental complex (placenta, umbilical cord, fetal membranes) obtained from 24 pregnant women (10 pregnancies without complications, 14 with severe preeclampsia) of the first maternity home in Aktobe city. Paraffin histological sections were stained with hematoxylin - eosin and by using Van Gieson's stain. In the presence of severe preeclampsia, villi walls of separate blood vessels are sclerotic; sometimes vessels are dilated and filled with blood. Areas of eosinophilic accretions on the surface of the chorionic plate increased significantly, up to 15,9 ± 0,6%, areas of Langhans fibrinoid contacting terminal villi - up to 15,3 ± 1,2%. Rohr area on the basal lamina increased up to 21,1 ± 1,1%, along with increase in the number and area of decidual cells - up to 11,3 ± 1,14%. There was an increase in the number and area of terminal villi, up to 4,6 ± 0,45%. Arterial blood vessels of the umbilical cord lost annular invagination rolls into the lumen of the vessel. The study showed consolidation and infiltration of cellular elements of the fetal membranes. In response to strengthening of the destructive processes (inflammation, apoptosis), one could observe more pronounced compensatory and adaptive processes in the form of strengthening fibrinoid barriers aimed at eliminating defects of the fetoplacental barrier and at increasing the number of terminal villi, in the development of placental insufficiency.

KEYWORDS
Placental complex, Langhans fibrinoids, Rohr fibrinoid, Nitabuch fibrinoid, decidual cells

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Introduction

Preeclampsia presents a threatening complication of pregnancy. According to world literature and WHO data, preeclampsia develops in the second half of pregnancy in 2-8% of women (Dubova et al., 2013; Kolesnikov, Paraskun & Martynov, 1975). Taking into account the lack of common terminology, classification and criteria I the Russian statistics, assessment of severity varies by tens of times (0.3-30% in different regions of the country). The incidence of severe preeclampsia and eclampsia in Russia is 2-3 times higher as compared with the developed countries (Niyazyaeva et al., 2014).

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Preeclampsia and eclampsia as specific complications of pregnancy are diagnosed in the presence of high blood pressure (<140/90) and proteinuria, which exceeds 0.3 grams per day (Sidorova et al., 2015). Every year, 8.5 million cases of preeclampsia are registered in the world. In the developing countries, this complication of pregnancy is the leading cause of maternal mortality; in the developed economies, it takes second-third places in its structure (generally 15-20%) (Sidorova & Nikitina, 2014). Eclampsia develops in 2-3 cases per 10,000 births in Europe and in the United States; in the developing countries, the incidence is 10-30 times higher (Sidorova et al., 2015). In the presence of severe preeclampsia and eclampsia, practically all organs and systems are involved in the pathological process (Sidorova et al., 2014). Placental insufficiency is regarded as a non-specific syndrome characterized by the inability of placenta to maintain adequate exchange between the organism of mother and fetus. Its frequency varies from 20 to 50% depending on pregnancy complications. At the same time, it takes the 4th place in the structure of perinatal morbidity and mortality (Shchegolev et al., 2012). These authors believe that violation of utero-placental and / or placental - fetal circulation presents a major factor in the pathogenesis of placental insufficiency.

Thus, there was a need to study the morphology of the main target organs (placental complex) in the presence of preeclampsia.

Background Paper

Gestosis presents a syndrome of multiple organ failure, pathogenically associated with pregnancy, characterized by generalized vascular spasm and perfusion abnormalities in vital organs and in placenta. Currently clinical practice is based on the following classification of gestosis: mild, medium, severe gestosis, preeclampsia and eclampsia. All types of gestosis are characterized by the presence of the three most evident symptoms (Zangemeister's triad): hypertension, edema of pregnant women, proteinuria. At that, hypertension plays a key role in the gestosis triad (Medvedev, 2008); according to WHO data (2011), hypertensive disorders are registered in 10% of pregnant women and present one of the leading causes of maternal and perinatal morbidity and mortality worldwide (World Health Organization, 2011).

The problem of studying preeclampsia development during pregnancy is associated with high levels of maternal and infant morbidity and mortality of this complication of placental insufficiency, which, coupled with the severity of preeclampsia symptoms leads to early delivery (Belotserkovtseva, Kasparova & Kovalenko, 2013). Chronic hypertension and renal failure are often formed in women who had preeclampsia, (Davison, Homuth & Jeuabalan, 2004); pathology of the central nervous system, hypertension and heart failure are often observed in children born under fetoplacental insufficiency (FPI) (Strizhakov & Ignatko, 2007).

Practically all organs and systems are involved in the pathological process in the presence of severe preeclampsia and eclampsia (Sidorova et al., 2014).

Today, most researchers consider preeclampsia an inflammatory disease, associated with immune and endothelial dysfunction (Klimov, 2008). Several studies indicate that in the presence of preeclampsia during pregnancy, against the backdrop of angiogenesis disorders, neutrophils cause dysfunction of vascular cells and the development of oxidative stress in the early gestation

stages (Matthiesen, 2005). However, it is believed that in the presence of preeclampsia, trophoblast invasion is sufficient in the early stages of pregnancy, albeit under surface placentation, which leads to incomplete transformation of arteries. At that, one can observe oxidative stress and decrease in vascular caliber that contribute to blood flow discontinuity and to the development of gestation pathologies (Cindrova-Davies, 2007). The impact of pathological factor in the early stages along with the development of angiogenesis disorders cause FPI and pregnancy complications (Orazmuradov, Apresian & Radzinsky, 2009). In this regard, comprehensive assessment of the course of pregnancy, including morphological examination of the placenta, provides the possibility to understand pathophysiological processes of the pathology and to assess their impact on the fetus and health of newborns (Kasparova, 2013).

The important factors of pathogenesis include violation of trophoblast invasion and the formation of the placental tree, which main component is presented by the terminal villi (Ghulmiyyah & Sibai, 2012). Since terminal villi play a leading role in the exchange of blood between mother and fetus, violation of their structure can cause various complications during pregnancy threatening health of newborns (Dubova et al., 2013).

The main task of traditional pathological studies of retained products is to identify pathological changes and signs of compensatory processes that determine the pathogenesis of violations in the mother-placenta-fetus system as well as a number of diseases in newborns.

Thus, preeclampsia is a major cause of maternal and perinatal morbidity and mortality (Klimov, 2008). To date, the cause of preeclampsia has not been established, but its development is associated with placental ischemia due to violation of trophoblast invasion of spiral arteries in the myometrium. Placental hypoxia leads to the development of systemic endothelial dysfunction, inflammatory response, and multiple organ failure (Serov & Sukhikh, 2014). Therefore, the study of specific features of placental changes in the presence of preeclampsia provides the possibility expand knowledge of pathogenetic mechanisms related to the development and growth of preeclampsia severity.

Research Purpose

The purpose of this research is to study morphological features of placental complex, taking into account gestational complications in postpartum women with severe preeclampsia.

Research questions

What are the morphological characteristics of pregnant women without complications in pregnancy and in women with severe preeclampsia?

Method

The study was conducted on a placental complex (placenta, umbilical cord, fetal membranes) obtained from 24 pregnant women (10 pregnancies without complications, 14 with severe preeclampsia) from the first maternity home located in Aktobe city. All manipulations with human placental organs were carried out upon the resolution of the ethical committee of Marat Ospanov West Kazakhstan State Medical University (Protocol No.1 dated 25 December 2009). Materials were fixed in 10% neutral formalin. In two cases, prior to fixation in

formalin (Anderson et al., 2012), fresh placental material was stored in the refrigerator for 48 hours at + 4 ° C, as changes in the content of metabolites and in the structures of intracellular organelles occur within 5-20 minutes after birth. After histological treatment, pieces of organs were stored in paraffin. Histological sections were stained with hematoxylin - eosin, by using Van Gieson's stain. The authors studied the placenta, umbilical cord and fetal membranes. Structural formations in placenta were counted by using a morphometric grid (256 pixels). Statistical × 200 and × 400 processing of research results was carried out by using Statistica 10 software. Analysis of the results was performed using the arithmetic mean, mean error, and Student's t-test. Differences were considered significant between the averages, $P \leq 0.05$.

Data, Analysis, and Results

Histological study of specimens of the fetal part of placenta taken from women of the control group revealed that it was formed by chorionic plate and covered with a flat-amniotic partially exfoliated epithelium. The plate basis contained loose connective tissue having a typical structure. The plate contained vessels of the umbilical cord, rather large, blood-filled arteries with well-developed muscle wall and veins with a thin muscular layer.

Using histological placenta specimens stained with hematoxylin and eosin taken from the control group, the authors found matching of villous tree maturation and gestational age, as well as moderately expressed compensatory - adaptive processes (the presence of syncytium - capillary membranes) and involution - degenerative processes (accretion of intervillous and peri-villous fibrinoid, calcification pieces).

The authors observed stem, intermediate and terminal villi of different size and shape, however, dominated by round and oval villi. The villi contained terminal vessels of the fetus. The villi were covered by cyto- and syncytiotrophoblast. Connective tissue of the villi included small capillaries and larger vessels. In some villi, trophoblast becomes thinner being replaced by a thicker syncytiotrophoblast. The villi were covered by Langhans fibrinoid (Figure 1a), being in contact with the fibers, mainly terminal; the Nitabuch fibrinoid was observed in the fetal part of the placenta, covering 8,1 ± 0,4% of the chorionic plate surface. The maternal part of placenta was formed by basal lamina, characterized by dystrophic changes and accretion in 11,2 ± 0,9% (Figure 2). The decidual capping revealed capillaries, small blood vessels and decidual cells having oval, round or polygonal shape (Figure 3). The area of decidual cells made 4,3 ± 0,4%.

In the presence of severe preeclampsia, walls of individual vessels in the fetal part of placenta were hardened (4a, b), the blood vessels of the villi were significantly expanded and filled with blood. The villi volume was increased. Fibrin accretion beneath the villi epithelium increased (Figure 1b). Fibrin was often found on the villi surface. Some villi were partially destroyed and "walled up" in fibrin. In certain villi, blood vessels were expanded and filled with blood, stroma decreases and the epithelium undergoes degeneration. In the maternal part of the placenta, destructive processes reinforce a compensatory self-healing in the form of greater accretion of Rohr's fibrinoids (2b), one could observe increase in the number and thickening of collagen fibers, expansion of vessels and their over-filling with blood accompanied by an increase the number of

decidual cells (Figure 3b). The authors also observed cytoplasm vacuolization, and hyperchromatic nuclei with pycnosis.

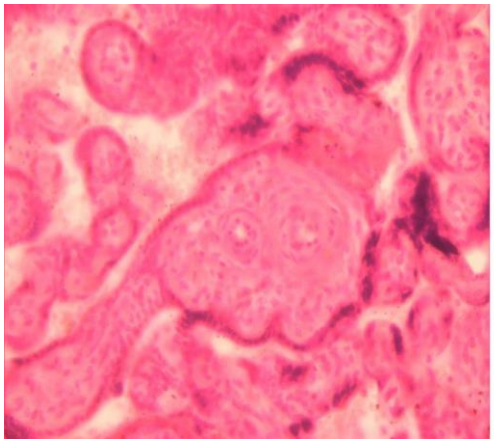


Figure 1a. Langhans fibrinoids around villi in the control group (stained with hematoxylin – eosin, x 400).

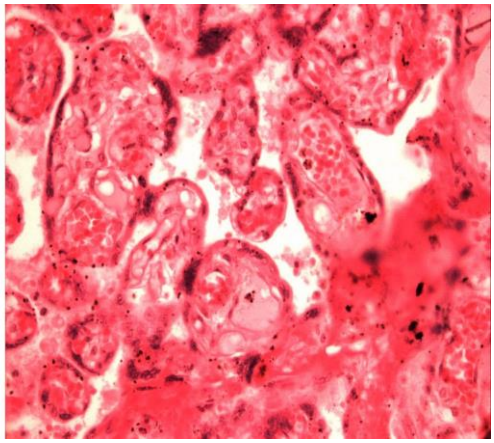


Figure 1b. Langhans fibrinoids around villi in the presence of severe preeclampsia (stained with hematoxylin – eosin, x400)

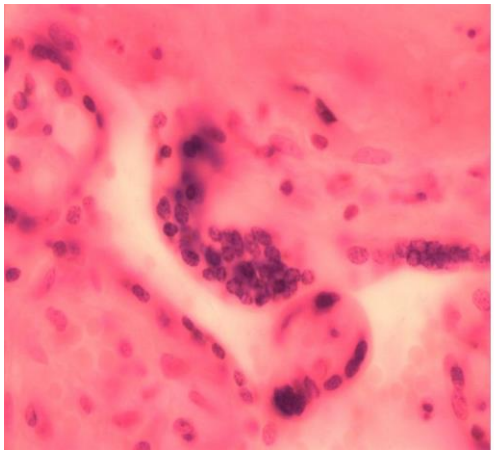


Figure 2a. Basal plate with Rohr's fibrinoid in the control group (stained with hematoxylin – eosin, x1000)

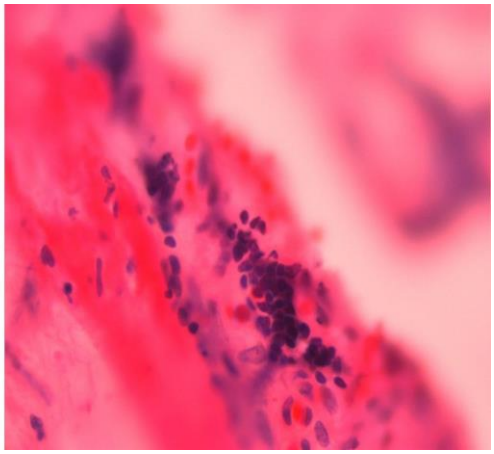


Figure 2b. Basal plate with Rohr's fibrinoid in the presence of severe preeclampsia (stained with hematoxylin – eosin, x1000

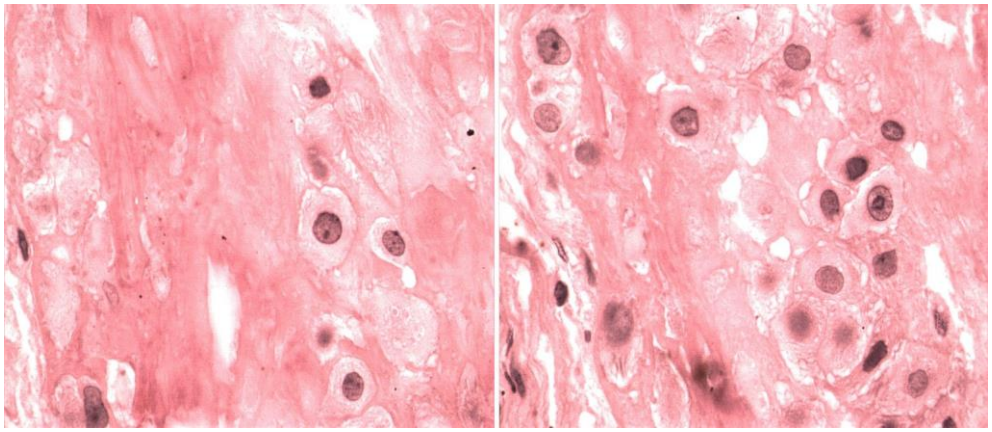
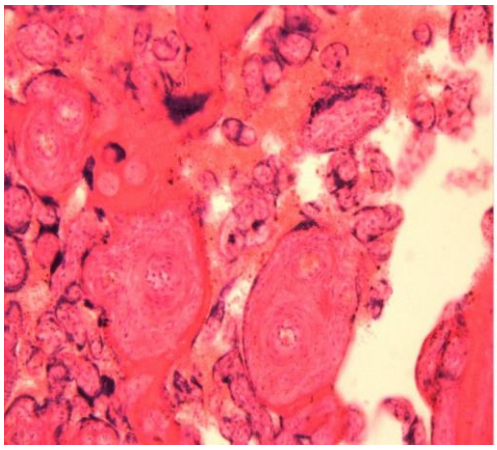


Figure 3a. Decidual cells in the basal lamina in the control group (stained with hematoxylin – eosin, x 1000)

Figure 3b. Decidual cells in the basal lamina in the presence of severe preeclampsia (stained with hematoxylin – eosin, x 1000)



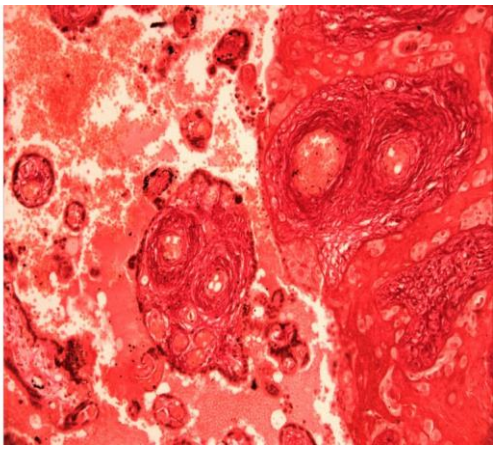


Figure 4a. Villous vessels in the control group; Van Gieson's stain, x 200.

Figure 4b. Villous vessels in the in the presence of severe preeclampsia; Van Gieson's stain, x 200.

Umbilical cord section has an oval - an elongated shape both in women from the control group and in women with severe preeclampsia. Outside, the umbilical cord was covered with a single layer of flat amniotic epithelium surrounding the mucous connective tissue with blood vessels (two umbilical arteries and one vein), as well as yolk sac and allantois vestiges. The cells of the connective tissue (Wharton's jelly) were stellate and spindle-shaped. They were located either alone or connected by appendages having different thicknesses and length. The artery wall was rather thick in women from the control group, pronounced annular protrusion of embankments could be easily seen in the lumen of the vessel, however, in the presence of preeclampsia they either were flattened or absent (Figure 5b). In the presence of severe preeclampsia, umbilical veins were significantly expanded, filled with blood, their walls were worn-out (Figures 6a, 6b).

Amniotic velum forms a wall of the reservoir with the fetus. It was covered mostly with flat epithelial cells. The connective tissue stroma of this velum includes basement membrane, a layer of dense fibrous connective tissue and a deep layer of loose fibrous connective tissue that connects the amnion and chorion. The velum was translucent in the control group. In the presence of preeclampsia, fibers in the connective tissue layer of the velum were significantly thicker, marked with cellular infiltration (Figure 7b), caused by inflammation.

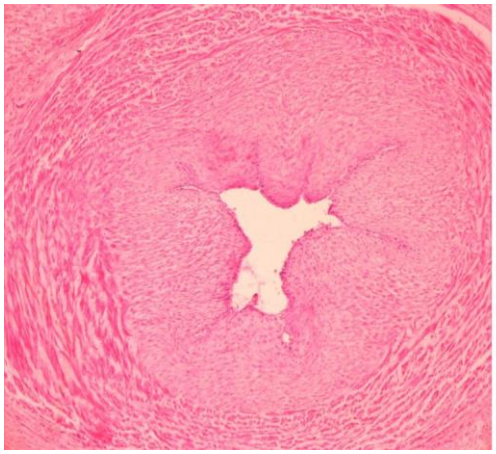


Figure 5a. Arterial vessel of the umbilical cord in the control group (stained with hematoxylin – eosin, x 100)

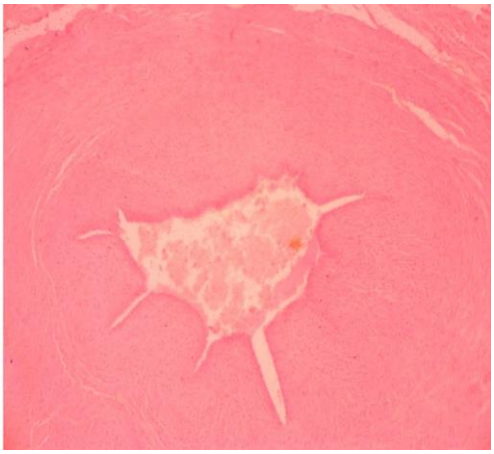


Figure 5b. Arterial vessel of the umbilical cord in the presence of severe preeclampsia (stained with hematoxylin – eosin, x 100)

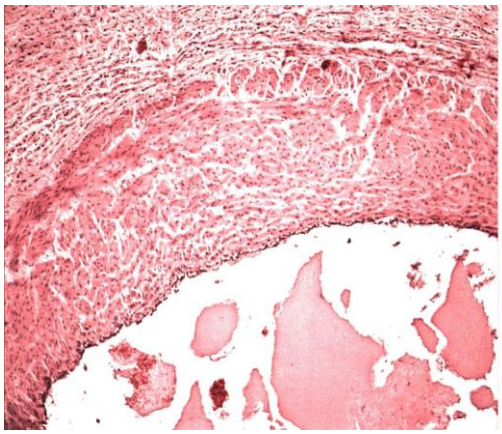


Figure 6a. Venous vessel of the umbilical cord in the control group (stained with hematoxylin – eosin, x100)

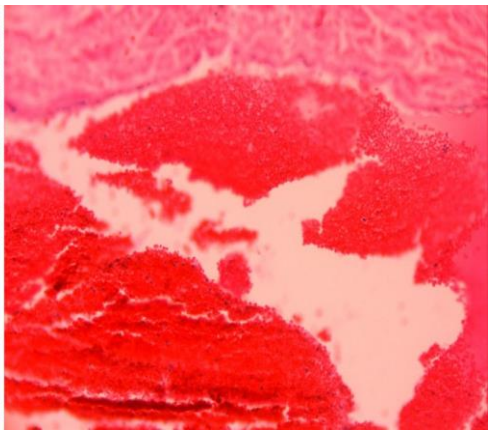


Figure 6b. Venous vessel of the umbilical cord in the presence of severe preeclampsia (stained with hematoxylin – eosin, x100)

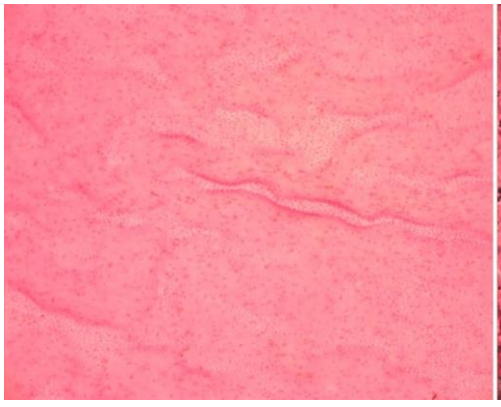


Figure 7a. Fetal integument in the control group (stained with hematoxylin – eosin,

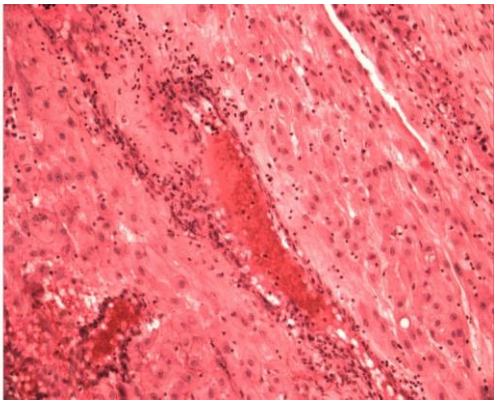


Figure 7b. Fetal integument in the in the presence of severe preeclampsia (stained

x100) with hematoxylin – eosin, x100)

Thus, even during physiological pregnancy multiple morphological changes having both proliferative and destructive nature occur in placenta. Placenta formation on the one hand implies formation of blood vessels, and reproductive growth of epithelial cells of the connective tissue, on the other – destruction of endometrium. Destructive processes were observed in the control group in the form of trophoblast thinning and fetal integument destruction. Along with this, one could observe compensatory - adaptive processes in the form of fibrin precipitation in the defected villi, in the destroyed areas of basal lamina surface, and the appearance of decidual cells rich in glycogen in the basal layer of the connective tissue of the endometrium with a view to improve fetus trophism. The amorphous substance (Rohr fibrinoid) located on the surface of a basal lamina, chorionic villi, Langhans fibrinoid and Nitabuch fibrinoid being a product of plasma clotting around the villi, also play a significant role in the mother - fetus homeostasis (Ghulmiyyah & Sibai, 2012).

Significant increase in the eosinophilic accretion area in the presence of severe preeclampsia (Langhans fibrinoid) being in contact with the terminal villi up to 15 ± 1,2% (in the control group - 7,1 ± 0,5%), increase in the Rohr fibrinoid area up to 21,1 ± 1,1 % (in the control group -11,2 ± 0,9%), which occupies a significant part of the basal lamina surface, increase in the area of Nitabuch fibrinoid, accounting for 15,9 ± 0,6% surface of the chorionic plate (in the control group - 8,1 ± 0,4%) and increase in the number and area of decidual cells, rich in glycogen, glucose, lipids and vitamin C up to 11,3 ± 1,14% (in the control group - 4,3 ± 0,4%) suggests tense compensatory process. In addition, destruction of epithelial cells of the terminal villi and the basal lamina surface on the one hand worsens the metabolic processes; on the other - integrity of the hemochorial barrier is retained through replacement of decomposed chorionic villi of basal lamina (caused by epithelia involution) by fibrinoids. Development of placental insufficiency is naturally accompanied by the development of villous tree hypoxia, which manifests itself in the decreased size of terminal villi and in an increase in the number of their vessels (Murphy et al., 2015). This process is marked by the increase in the number of villi and the area of terminal villi up to 4,6 ± 0,45% (in the control group - 2,4 ± 0,21%), in the presence of severe preeclampsia.

Discussion and Conclusion

According to M. S. Murphy et al., preeclampsia is characterized by widespread endothelial dysfunction caused by anti - angiogenic, inflammatory and apoptotic processes (World Health Organization, 2011). All these processes were obvious in the case of severe preeclampsia.

In this study, the number of capillaries and their area increased in the presence of preeclampsia, whereas other authors indicate that the number of capillaries area decreased (Murphy et al., 2015). The authors of earlier studies described typical features – increase in vascularization of terminal villi, increase in the number of capillaries in the villi.

Physiological pregnancy is accompanied by proliferation, destructive changes (inflammation, apoptosis), compensatory and adaptive processes (fibrinoid transformation of trophoblast, formation of decidual cells) and by increase in the number of villi, more specifically, terminal villi.

Severe preeclampsia causes increase in: a) the development of fibrinoid substances (Langhans fibrinoids, Rohr fibrinoids and Nitabuch fibrinoids). b) the number of decidual cells. c) the number of small terminal villi along with an increased number of capillaries and their area.

Implications and Recommendations

The study showed that in response to the increase in destructive processes (inflammation, apoptosis) severe preeclampsia triggers more pronounced compensatory - adaptive processes in the form of "filling" fetoplacental barrier defects with fibrin, increase in the number of small terminal villi in response to the development of placental insufficiency. Research findings can be used in the development of treatment methods for pregnant women with severe preeclampsia.

Disclosure statement

No potential conflict of interest was reported by the authors.

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