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# Pathomorphological and Ultrastructural Placental Changes in Women with a High Risk of Placental Insufficiency

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**Abstract**
**Background:** Placental insufficiency is one of the most common clinical problems in obstetrics. The PI problem based on violations of compensatory-adaptive mechanisms, is still relevant, due to its negative impact on the fetus, numerous complications of childbirth, and high perinatal mortality.
**Methodology:** We have examined placentas of women with a high risk of placental insufficiency development based on three risk factors: iron deficiency anemia, gestational pyelonephritis, or chronic pyelonephritis and preeclampsia.
**Results:**The most pronounced was placental insufficiency in women with preeclampsia: placental mass was significantly reduced, and the morphological picture corresponded to decompensation. Less pronounced placental insufficiency was in women with infectious diseases of the urinary tract: the weight of the placenta was slightly increased, and the morphological picture corresponded to full compensation. In women with iron deficiency anemia, placental insufficiency was the least pronounced.
**Conclusions:** The morphological changes of placentas reflect the tendency to the development of compensatory-adaptive reactions with their subsequent exhaustion. The weight of placentas is dependent on accompanying pathologies. The main impact on placental dysfunction has preeclampsia. Can be concluded, high incidence of placental insufficiency in pregnant women with risk factors such as anemia, late preeclampsia, and inflammatory kidney disease.

**Keywords:** placenta, insufficiency, iron deficiency anemia, preeclampsia, inflammation.

## Introduction

The placenta is the largest fetal organ during antenatal life. It plays a central role in the health of both the fetus and its mother and has a lifelong impact on their future wellbeing [1]. Indeed, disordered placental development is the primary defect in major diseases of pregnancy, such as pre-eclampsia, fetal growth restriction, recurrent miscarriage, and stillbirth [2].

Placental insufficiency (PI) or placental dysfunction is considered to be one of the most important problems of modern obstetrics and perinatology and is one of the leading causes of perinatal morbidity and mortality [3-5]. Placental insufficiency affects ~8% of all pregnancies and commonly begins early in pregnancy for a multitude of reasons, including maternal chronic disease (chronic hypertension, pregnancy-induced hypertension, and other vascular disorders),placental disorders (preeclampsia, abruption, infarcts), inflammation diseases, different

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types of anemia and idiopathic causes [6].According to modern studies, 20-60% of perinatal mortality is directly connected with placental pathology [7-9].

The PI problem based on violations of compensatory-adaptive mechanisms, is still relevant, due to its negative impact on the fetus, numerous complications of childbirth, and high perinatal mortality. Also, different severity of placental dysfunction can lead to the presence of numerous changes in the child's body during the first years of life including neuropsychiatric disorders, as well as an increase in somatic and infectious diseases [10]. There is a strict connection between in utero environment and susceptibility to chronic disease in adults [11].

PI is a relatively common condition.It is found in 3-4% of healthy women with an uncomplicated pregnancy, and in the case of various perinatal pathologies, its frequency ranges from 24 to 46%.The most common causes of PI are extragenital and obstetric pathology of the mother during pregnancy, which leads to disorders of uteroplacental and later fetoplacental circulation.Due to these changes, irreversible morphological processes develop and the basic functions of the placenta are disrupted [12-15].

One of the most important risk factors for the development of PI is chronic salpingo-oophoritis, iron deficiency anemia, and late preeclampsia during pregnancy.Recently, there has been a growing scientific interest in the influence of risk factors on the state of the fetoplacental complex, which causes disorders of uteroplacental hemodynamics as a key link in the pathogenesis of PI. In special attention, we have to take care about cardiovascular pathologies, especially it a case of difficult them diagnostic because of non-vivid symptoms what is common in woman, especially in pregnancy condition [26].

***The main aim*** of our study is estimating the morphological features of placentas in parturients from the group of the high risk of placental insufficiency.

## Materials and Methods

The study involved 40 placentas of women in the group at high risk of developing placental insufficiency: 10 placentas of women whose pregnancy was complicated by iron deficiency anemia (Group I), 10 placentas of women who suffered during pregnancy from inflammatory kidney disease: gestational pyelonephritis or chronic pyelonephritis exacerbation (group II), 10 placentas of women whose pregnancy occurred on the late preeclampsia background (group III). The comparing group included a study of 10 women placentas with uncomplicated pregnancies (control group).

To assess the condition of women placentas from the high-risk group of placental insufficiency, a histological examination was performed according to the guidelines of T.D. Zadorozhnaya for light microscopy[16].Placental tissues were stained with hematoxylin and eosin by the method of Van Gieson's (picrofuxin).Ultrastructural analysis was performed by a light microscope with a built-in digital camera "OLYMPUS" (Japan) with standard magnifications: x40, x100, x200, x400.

All the procedures used in the work (manipulations, operating aids) were following the ethical standards of the responsible committee on human experiments (institutional) and the 1975 Helsinki Declaration, revised in 2000. All patients agreed to participate in the experiment and did not deny the results of the experiment, which will be presented in the given research paper.

## Results andDiscussion

During the macroscopic examination of the placentas, an average placental weight of every group was measured (**Table 1**).

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**Table 1**. Average placentas weight for each examined group

| Name of group (Each group N=10) | Average placentas weight (p> 0.05 ) |
|---|---|
| Control group | 610 ± 21.05 g |
| Group 1 (iron deficiency anemia) | 609 ± 19.24 g |
| Group 2 (inflammatory kidney disease) | 725,72±24,84 g |
| Group 3 (preeclampsia) | 430,35±13,67 g |

***Iron deficiency anemia vs placental dysfunction***

It was determined that the average weight of women placentas whose pregnancies were complicated by iron deficiency anemia, had no significant difference compared with the control group: 609 ± 19.24 g vs. 610 ± 21.05 g (p> 0.05).

The histological placentas picture of women suffering from anemia during pregnancy had some differences.Thus, areas of fetal villi vessels uneven plethora (40.0%) and intervillous space hemorrhage (56.0%) were detected.In some places, the villi vessels were full-blooded with stasis.Such foci were local, although they were identified in most placentas of group 1 (56.0%).A small number of placentas (6.0%) showed a variant of intermediate immature villi, the stroma of these villi contained Hofbauer cells. In 8.0% of placentas, uneven maturation of villi was detected, in 4.0% – foci of glued villi (non-functional zones).At the same time, the intervillous space significantly decreased due to the convergence of the villi.In these areas, there was a significant increase in syncytial nodules number. Foci of hypervascularization were observed in all sections, especially in the terminal villi.In some sections, small hemorrhages were found in the basal plate area.These changes can be considered as compensatory-adaptive reactions of the placenta.

According to our study, the placentas of women whose pregnancies were complicated by anemia did not have significant pathological changes. However compensatory reactions due to local hypoxia prevailed. Still, sideropenic anemia increases placental maturity, which could be a possible cause of earlier spontaneous delivery among anemic women[17].

Maternal anemia was not associated with reduced placental volume and uterine arterial Doppler wave form at 11-13 weeks' gestation [18].

***Inflammatory kidney disease vs placental dysfunction***

The placentas of women with gestational pyelonephritis or chronic pyelonephritis exacerbation during pregnancy had a significantly increased weight compared to the placentas of healthy women: 725.72 ± 24.84 g (p <0.05).This indicates placental hyperplasia in the vast majority of women in group 2.

The morphological placentas features of this group of women were mainly inflammatory.Thus, stem villi endovasculitis was observed in 56.0% of cases, which is significantly more than in the control group - 16.0% (p <0.05).On the outer surface of the chorionic plate, the accumulation of polymorphonuclear leukocytes was observed (12% placentas of group 2), which indicates the presence of exudative inflammation and the development of placental chorioamnionitis.In the subchorionic region, the accumulation of polymorphonuclear leukocytes, the loss of fibrin threads, which is characteristic of subchorionic placental intervillositis (10% placentas of group 2). Inflammatory changes of the basal plate in the form of basal deciduitis were observed in 52.0% of cases.Compensatory-adaptive processes in the placentas of the second group were manifested in the form of the formation of a large number of syncytial nodules and hypervascularization of the terminal villi.

The detected changes in the placenta of women with inflammatory kidney disease indicate the presence of compensated chronic placental insufficiency.

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***Late preeclapmsia vs placental dysfunction***

Gross pathological changes are most common with severe preeclampsia occurring preterm. The characteristicplacental changes of preeclampsia would be predicted to be those associated with placental ischemia. Consistent with this prediction, the placenta in preterm preeclampsia is small with several types of infarction. The gross placental changes with severe preeclampsia and FGR are quite similar. Histological changes in the placenta with preeclampsia and with FGR are also those of reduced perfusion. These can be found in the term but more commonly in preterm preeclampsia as well as with FGR and include accelerated villus branching, large and numerous syncytial knots, and small sclerotic villi. It is suggested that most of these findings are related to low oxygenation secondary to reduced perfusion[19-20].

The placentas of women with late preeclampsia had a significantly reduced weight compared to the placentas of healthy women: $430.35 \pm 13.67$ g ($p < 0.05$).

The placental surface was characterized by an uneven plethora (74.0%). In comparison with the control group, significant differences were found: foci of hemorrhage and thrombosis (30.0%), in 36.0% of placentas of group 3 small foci of infarction were found.In 92.0% of placentas, there was significant calcification on the placental maternal surface in the form of fine whitish inclusions.Histological examination of the placentas in women of group 3, revealed a dominant picture of pathological immaturity of the villous tree - the predominance of intermediate and chaotic, small villi with sclerosis on the background of terminal villi reduction.The morphological equivalent of local tissue hypoxia was a significant increase in syncytial nodules, most of which had involutive forms, which indicates the chronic nature of local hypoxia.Also, histological samples of placentas with preeclampsia showed groups of villi, walled up with fibrinoid - indicator of pseudoinfarctions.A special histological feature of the placentas of group 3 was the presence (46.0%) of small foci of true infarctions (46.0%).

Along with significant structural changes of the placental villous tree in women with late preeclampsia, minor compensatory-adaptive reactions were found.This was reflected in the presence of terminal villi that underwent hypertrophy, with a branched network of full-blooded capillaries in combination with a pronounced decrease of the intervillous space.Compensatory changes of terminal villi were more pronounced in the central and paracentral placental parts.In some cases, these changes were detected in the intermediate villi, and the number of terminal villi was significantly reduced, indicating early maturation of the placenta.

A common pathological feature of preeclampsia is the failure of the maternal arteries supplying the placenta to undergo the physiological adaptations of a normal pregnancy that facilitate adequate placental perfusion [21].

Hypoxia may not be a major feature of the abnormal vascular remodeling but rather the generation of reactive oxygen species. Also, there is a strict connection between preeclampsia and fetal growth restriction due to placental insufficiency development [22-25].

**Conclusion**

The morphological changes of placentas found by us in the examined women reflect the tendency to the development of compensatory-adaptive reactions with their subsequent exhaustion, which is a sign of placental insufficiency. We figured out that the weight of placentas in women with iron deficiency anemia does not differ from women without any pathology. A morphological picture of women whose pregnancies were complicated by anemia did not have significant pathological changes. Weight of placentas in women suffering from gestational pyelonephritis or chronic pyelonephritis exacerbation was significantly higher compared with control group women. Also, changes in the placenta of women with inflammatory kidney disease indicate the presence of compensated chronic placental insufficiency. The biggest impact on placental dysfunction has preeclampsia. The weight of the placentas from this group was significantly lower compared with women from the control group. The analysis of placentas of women with late preeclampsia demonstrates the combined nature of placental tissue damage and

indicates the presence of compensated, and in some cases decompensated chronic placental insufficiency. Our results suggest a high incidence of placental insufficiency in pregnant women with risk factors such as anemia, late preeclampsia, and inflammatory kidney disease.

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