

Tiulienieva Olena, Davydenko Igor, Tiulienieva Viallanta, Marchuk Olena, Shelest Tetiana, Volkov Oleksandr. Features of violation of maturation of the chorionic tree of the placenta at immaturity of the placental bed of the uterus on the background of iron deficiency anemia in pregnant women in terms of chronic insufficiency of manure. *Journal of Education, Health and Sport*. 2021;11(03): 258-265. eISSN 2391-8306. DOI <http://dx.doi.org/10.12775/JEHS.2021.11.03.025>  
<https://apcz.umk.pl/czasopisma/index.php/JEHS/article/view/JEHS.2021.11.03.025>  
<https://zenodo.org/record/5136587>

The journal has had 5 points in Ministry of Science and Higher Education parametric evaluation. § 8. 2) and § 12. 1. 2) 22.02.2019.

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The authors declare that there is no conflict of interests regarding the publication of this paper.

Received: 15.02.2021. Revised: 26.02.2021. Accepted: 31.03.2021.

## **Features of violation of maturation of the chorionic tree of the placenta at immaturity of the placental bed of the uterus on the background of iron deficiency anemia in pregnant women in terms of chronic insufficiency of manure**

**Olena Tiulienieva<sup>1</sup>, Igor Davydenko<sup>1</sup>, Viallanta Tiulienieva<sup>1</sup>, Olena Marchuk<sup>1</sup>,  
Tetiana Shelest<sup>2</sup>, Oleksandr Volkov<sup>3</sup>**

**<sup>1</sup>Bukovinian State Medical University, Chernivtsi, Ukraine**

**<sup>2</sup>International Humanities University, Odesa, Ukraine**

**<sup>3</sup>Ushinsky Pedagogical University, Odesa, Ukraine**

**Address for correspondence** Olena Tiulienieva, Department of the Pathological Anatomy, Bukovinian State Medical University, Teatralnaya Square, 2, Chernivtsi, Ukraine  
e-mail: [tuleneva@bsmu.edu.ua](mailto:tuleneva@bsmu.edu.ua), phone: +380502400144

Olena Tiulienieva <https://orcid.org/0000-0003-2961-4076>

Igor Davydenko <https://orcid.org/0000-0002-8395-6651>

### **Abstract**

The authors of the article investigated the quantitative parameters of the placental chorion tree during physiological pregnancy and gestation against the background of iron deficiency anemia. It has been established that iron deficiency anemia in pregnant women inhibits the development of the placental chorionic tree, which is explained by the formation of chorionic villi (through trophoblastic and free processes) and violation of the transition of terminal villi to terminal "specialized" villi. The diagnosis of chronic placental insufficiency during pregnancy on the background of iron deficiency anemia can be verified morphologically based on quantitative indicators of assessment of the structure of the

placental chorionic tree - the percentage of terminal villi should be higher than 43% and the percentage of terminal "specialized" villi lower than 15%.

**Key words:** chorionic tree maturation disorders; placental immaturity; iron deficiency anemia in pregnant women; chronic placental insufficiency.

**Introduction.** The uterine-placental area (UPA) or placental bed of the uterus is the focus of gestational endometrium at the site of attachment of the ovum to the uterine wall [1-3]. In our previous studies it was shown that against the background of iron deficiency anemia in pregnant women (IDA), the placental bed of the uterus morphologically almost always has signs of gestational immaturity, the severity of which depends on the degree of iron deficiency [4, 5]. Insufficiency of cytotrophoblastic invasion in the structure of UPA, lack of adequate gestational changes of the spiral arteries, venous insufficiency and signs of venous stasis in the projection of placental attachment are a prerequisite for the development of chronic insufficiency of manure [2].

To understand the morphogenesis of pathology in the mother-placenta-fetus system, it is extremely important to study the processes of proliferation and differentiation of trophoblast of the chorionic villi of the placenta in conditions of limited cell proliferative potential against the background of iron deficiency and immaturity of the uterine placenta. [4].

Immunohistochemical methods of studying the processes of cell number regulation (proliferation and apoptosis) we have shown that in the placenta at IDA develop prerequisites for impaired maturation of the chorionic tree [5, 6]. The relevance of such studies is unquestionable for the reason that the violation of the maturation of the chorionic tree is one of the most important causes of chronic placental insufficiency (CPI).

**The purpose of the study:** to establish the features of disorders of maturation of the chorionic tree of the placenta in immaturity of the placental bed of the uterus on the background of iron deficiency anemia in pregnant women in terms of chronic defecation of the placenta.

**Material and methods.** Morphological studies were conducted at the Department of Pathological Anatomy of Bukovynian State Medical University (Chernivtsi, Ukraine) in compliance with the basic bioethical provisions of the Council of Europe Convention on Human Rights and Biomedicine (04.04.1997), Helsinki Declaration of the World Medical Association on ethical principles of scientific medical research with human participation (1964–2008), as well as the order of the Ministry of Health of Ukraine № 690 dated

23.09.2009. 140 placentas of physiological pregnancy and gestation observations on the background of IDA I, II and III degrees of severity were studied. The term of childbirth is 37-40 weeks. IDA is a chronic pathology, so the study took only cases of complete clinical development of the disease. The criterion for the severity of IDA on the basis of medical records was the concentration of hemoglobin in the blood of the pregnant woman: In all cases, the anemia was hypochromic. According to a set of clinical data during pregnancy, the diagnosis of "Chronic placental insufficiency syndrome" was made or rejected, which was specified in the pathomorphological examination of manure. The number of observations in specific study groups is given in table 1.

For histological examination, the material was fixed in a 10% aqueous solution of neutral buffered formalin, dehydrated in an ascending ethanol battery and poured into paraffin wax. Histological sections with a thickness of 5  $\mu$ m were stained for review with hematoxylin-eosin, and for visualization of fibrin and fibrous component of connective tissue - chromotrope - water blue by the method of NZ Slinchenko. According to the Shapiro-Wilk criterion for each group of studies, the hypothesis of a normal distribution in the samples was accepted, so the arithmetic means and their errors were calculated, the differences between the sample values were estimated using the odd two-tailed Student's test (computer program PAST 3.06, free license, O.Hammer, 2015) [7].

**Results of research and discussion.** The percentage of different types of chorionic villi, as well as trophoblastic and free processes (which are the direct precursors of true chorionic villi) of the placenta during physiological pregnancy and gestation on the background of IDA in terms of chronic placental insufficiency are given in table 1.

A typical histological picture of the chorionic tree of the placenta of observations with the physiological course of pregnancy and on the background of IDA in the aspect of CRF is shown in Figure 1.

In all groups of study of placentas at IDA in comparison with placentas at physiological course of pregnancy we found signs of inhibition of development of a chorion tree which is shown by the big percent of gestational less mature chorionic villi, namely: trunk "early", mesenchymal, embryonic, non-embryonic, pro and free processes. A sign of inhibition of the development of the chorionic tree is also a violation of the transitions of the terminal villi in the terminal "specialized" forms. In the morphogenesis of placental pathology, inhibition of the development of the chorionic tree must inevitably lead to the development of chronic insufficiency of manure.

**The percentage of different types of free formations of the chorionic tree of the placenta at 37-40 weeks of gestation during physiological pregnancy and IDA ( $X \pm s_x$ )**

Types of free formations	Comparison groups				The main groups		
	Physiological pregnancy (n=20)	CPI without IDA(n=20)	IDA without CPI (n=38)		CPI with IDA I st (n=22)	CPI with IDA II st (n=24)	CPI with IDA III st (n=16)
			I st (n=20)	II st (n=18)			
Stem "early" villi	0,1±0,01	1,4±0,04	0,2±0,01	0,2±0,03	1,6±0,03	1,9±0,02	2,4±0,16
Stem "late" villi	4,0±0,21	2,8±0,12	4,8±0,12	4,9±0,12	3,2±0,12	4,2±0,18	5,5±0,38
Trophoblastic and free processes	1,1±0,04	2,5±0,11	2,0±0,10	2,6±0,11	2,9±0,12	3,0±0,14	3,1±0,20
Mesenchymal villi	0,4±0,02	1,3±0,04	0,4±0,03	0,4±0,02	1,3±0,04	0,9±0,05	0,6±0,05
Embryonic villi	0,6±0,05	1,6±0,05	1,2±0,12	1,2±0,14	1,6±0,06	1,5±0,07	1,4±0,12
Intermediate immature villi	3,0±0,14	9,3±0,16	3,1±0,18	4,7±0,17	9,0±0,17	9,3±0,14	9,6±0,49
Intermediate mature villi	14,9±0,82	20,8±0,95	20,4±0,96	22,4±0,94	25,8±0,93	34,4±0,91	37,6±1,16
Terminal villi	38,4±1,23	32,4±1,01	58,8±1,96	56,5±1,95	33,7±1,04	35,4±1,01	36,0±1,22
Terminal "specialized" villi	37,5±1,16	27,9±1,22	9,1±0,43	7,1±0,42	20,9±1,26	9,4±1,19	3,8±0,14

It should be noted that according to the data of table 1, in the placentas of observations of pregnancy on the background of IDA without signs of CPI also found similar phenomena of impaired maturation of the chorionic tree. This fact means that this group of cases refers to the compensated form of CPI (without deficiency of fetal weight, newborn), ie morphological changes (impaired maturation of the chorionic tree) did not lead to placental insufficiency due to the development of sufficient compensatory changes.

Given the fact that the histological picture of the chorionic tree showed signs of inhibiting the development of free structures, it was important to assess the aspect of CPI heteromorphism of the chorionic tree, because it is known that one of the morphological adaptive reactions of the placenta in chronic pathology is the intensification of new chorionic villi. in the marginal parts of the body [1, 6].

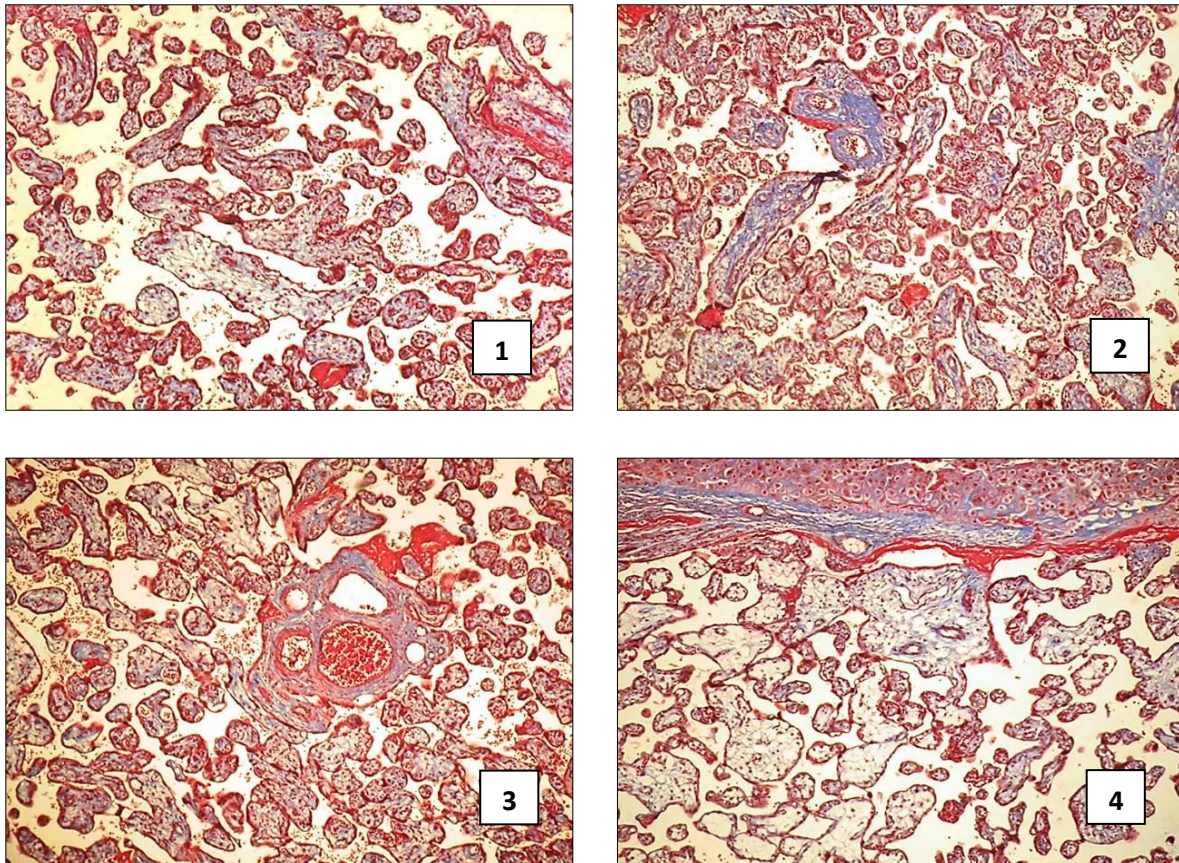


Fig. 1. Chorionic tree of placental observations with the physiological course of pregnancy and on the background of IDA in terms of chronic placental insufficiency: 1 – placenta with the physiological course of pregnancy, the structure of the chorionic tree corresponds to gestation; 2 – placenta on the background of IDA without signs of CPI, there are signs of inhibition of the development of the chorionic tree; 3 – placenta with clinical manifestations of chronic placental insufficiency without IDA, insufficient number of terminal and terminal "specialized" villi; 4 – placenta with clinical manifestations of chronic placental insufficiency on the background of IDA, a significant deficit of terminal and terminal "specialized" villi against the background of the predominance of gestational less mature types of chorionic villi. Chromotrope - water blue by NZ Slinchenko. Ob.3,5x, Ok.7x.

In order to assess heteromorphism, the chorionic villi of 50 placentas of pregnancy observations on the background of IDA (main group) and 20 placentas during physiological pregnancy and childbirth (control group) were histologically examined. The percentage of different types of chorionic villi was determined according to the method described above.

Horizontal heteromorphism was defined as the integral difference between the cotyledons of the peripheral part and the rest of the cotyledons of the placenta, vertical heteromorphism was estimated as the integral difference between the area delineated by half the vertical distance from the chorionic plate down and the area delineated from the vertical. In order to determine the integral difference of the structure between these zones (measurement of heteromorphism), a special indicator was used, which is called the "integral

coefficient of difference of placental zones" (ICDPZ) [6]. It is calculated by the following formula:

$$IKVZP = \frac{K1 + K2 + \dots + Kn}{N}$$

where K is the ratio of a larger percentage of a certain type of chorionic villi in one area of the placenta to a smaller percentage in another area of the placenta. Calculated for each available type of chorionic villi separately (K1, K2, ... Kn), N - the number of types of villi.

It does not matter in which specific area the percentage of a certain type of chorionic villi is higher, because the main purpose of the IKVZP is to measure the relative difference first for each type of chorionic villi, and then - integrally, for all chorionic villi; N is the number of types of chorionic villi in a particular placenta. The value of the IKVZP cannot be less than one - one means the absolute similarity of the zones. The more the indicator differs from one - the greater the difference between the zones of the placenta, ie there is a greater heteromorphism.

In the control group, the rate of IKVZP in determining the horizontal heteromorphism was  $1.94 \pm 0.24$ . When passed the first century. and II st. according to this indicator there is a decrease in the difference between the zones of the placenta -  $1.89 \pm 0.13$ . This is due to an increase in the percentage of proliferating elements (trophoblastic and villous processes) and low-differentiated types of chorionic villi, which indicates the "inclusion" of placental reserves. The consequence of such changes is an increase in the area of the largest section of the placenta. In the placenta at IDA III st. the difference between the peripheral zone and the rest of the placental tissue is similar to the comparison groups, which is a reflection of the violation of the implementation of the reserve mechanism of the marginal zone of the placenta. The presented data on the features of placental heteromorphism can be used in the procedure of diagnosis of the placental form of CPI.

One of the possible manifestations of CPI may be excessive development of connective tissue fibers in the stroma of the chorionic villi with compaction of the latter (sclerosis). This is a direct morphological prerequisite for the deterioration of perfusion of substances from the mother's blood to the fetal blood and vice versa, and in addition, can cause disruption of the microcirculatory tract, which occurs during the transition of terminal villi to terminal "specialized". To evaluate the fibrous component, a method with a water-blue

chromotropic by NZ Slinchenko was chosen, which detects both collagen and reticular fibers in the chorionic villi.

As a result of placental studies in IDA both with clinical manifestations of CPI and without them (without a deficit of fetal weight, newborn), no sclerosis was detected in any type of chorionic villi (Fig. 1). This can be explained by the above-described violation of the maturation of the chorionic tree, because the immaturity of the chorionic villi is actually accompanied by a relatively low development of the fibrous component [6].

For the practical activities of placentologists on the basis of the results obtained in this study, we can propose the following specific criteria for the differential diagnosis of compensated forms of CPI with uncompensated forms (subcompensated and decompensated).

With compensated CPI, the range of the percentage of terminal villi (using two standard deviations) is 18-43%, ie if it is higher than 43%, it can be regarded as uncompensated CPI, at the same time it should be borne in mind that the percentage of terminal "specialized" villi at compensated CPI (without deficiency of fetal weight, newborn) is 15-41%, ie if it is below 15%, it can also be regarded as uncompensated CRF, and the latter criterion is even more important than the first.

### **Conclusions**

1. In placentas during gestation on the background of iron deficiency anemia is inhibition of the development of the chorionic tree, which is explained on the one hand by the formation of chorionic villi (through trophoblastic and free processes), and on the other - violation of the transition of terminal villi to terminal "specialized" villi, vertical and horizontal heteromorphism inherent in the placenta.

2. The diagnosis of chronic placental insufficiency in iron deficiency anemia can be morphologically determined on the basis of quantitative indicators - the percentage of terminal villi should be higher than 43%, and the percentage of terminal "specialized" villi - below 15%.

**Prospects for further research.** The prospects of this study are related to the establishment of mechanisms of violation of the maturation of the chorionic tree of the placenta in the immaturity of the placental bed of the uterus on the background of iron deficiency anemia.

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