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CLINICAL AND MORPHOLOGICAL FEATURES OF THE PLACENTA IN EXTREMELY AND DEEPLY PREMATURE INFANTS

Placenta is a connecting link between mother and fetus. The article is devoted to the problem of identifying pathological changes in the placenta for the diagnosis of various clinical conditions in a premature extremely immature child. The continuous sampling method examined 131 afterbirth (96 afterbirth of extremely premature infants with a gestational age of less than 28 full weeks and 35 afterbirth of premature infants from 28 to 32 weeks of gestation). A comparative analysis of the main morphometric parameters of the placenta was performed; the presence of inflammatory diseases of the placenta (chorioamnionitis; deciduitis; placentitis; funiculitis, villousitis, phlebitis of umbilical cord vessels); the presence of acute placental circulatory disorders, chronic decompensated placental insufficiency. The results obtained for each of the latter were entered into a common database and subjected to statistical processing. When comparing the main clinical and morphometric parameters of live and stillborn babies at gestation from 22 to 32 weeks, a significant difference was found in fetal weight, gestation period, placenta mass and umbilical cord mass. An intrauterine infection, manifested by villousitis and deciduitis, increases the probability of stillbirth by 3.3 times at 22 to 28 weeks of gestation. The presence of placental involution increases the risk of stillbirth by 17.3 times. Histological examination of the placenta is an important step in diagnosing the causes of stillbirth at 22 to 32 weeks of gestation.

Keywords: placenta, extreme immaturity, premature, stillbirth, intrauterine infection, involution

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Introduction. The placenta plays an important role in fetal development and function, being a link between the mother and the fetus, providing nutrition and gas exchange for the fetus, participating in the removal of metabolic products [10], determining fetal growth. Placental weight and neonatal body weight are highly correlated [13], changes in placental function can be biological predictors of the child's health. Gross morphological and histopathological features of the placenta are associated with adverse fetal outcomes, therefore, placental biomarkers can be used to predict outcomes due to the fact that the impact can be subclinical and invisible to the clinician, which is important for prognosis [7].

Many pregnancy complications are associated with abnormal placental development in the first trimester, the most dramatic are preeclampsia, fetal growth restriction, unexplained stillbirth, placental abruption and premature birth [14].

One of the important problems of perinatology is the infectious factor: thus, chorioamnionitis, confirmed histologically and clinically, or infection of the amniotic cavity are associated with a higher probability of early and late sepsis in premature infants [5, 9], is an independent risk factor for the development of IVH in premature infants [11]. The frequency of chorioamnionitis in premature infants aged 21 to 37 weeks of pregnancy was 18.7%, while in full-term infants it was only 3.9% [8].

Detection of pathological changes in the placenta may be important for the diagnosis of various clinical conditions in a premature extremely immature child [9].

The purpose of the study is to identify the clinical and morphological features of the placenta in liveborn and stillborn extremely and deeply premature infants.

Materials and methods. A continuous sampling method was used to study all placentas of premature babies born alive and stillborn in Khabarovsk from January 2020 to December 2023. A total of 131 placentas were studied (96 placentas of extremely premature babies with a gestational age of less than 28 completed weeks and 35 placentas of premature babies from 28 to 32 weeks of gestation).

Inclusion criteria are placentas of premature babies, gestational age less than 28 and more than 32 weeks, availability of complete primary medical records.

Exclusion criterion are congenital malformations incompatible with life leading to stillbirth.

The source of information was the data of medical documentation: N 097-1 / y-97 "History of the development of the newborn" and form N 003 / y "Medical record of a patient receiving medical care in inpatient settings, in a day hospital." The pathological examination was carried out according to a single protocol, within 24 hours from the moment of birth of the placenta, in the pathological department of the KGBUZ "Perinatal Center named after G.S. Postol", a morphological study of the placenta and an overview histological study were carried out. The mass of the placenta in grams was determined on the electronic scale "Sasha". Excision of pieces of tissue for an overview histological study was carried out in the central,

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paracentral, marginal and pathologically altered parts of the placenta, as well as the umbilical cord and extraplacental membranes. The obtained material was fixed in 10% neutral formalin after standard paraffin wiring. The overview histological examination was carried out in accordance with the methodological recommendations "Rules for conducting pathological and anatomical studies of the placenta" [3], which provide for an assessment of the maturity of the villous chorion, diagnosis of disorders of the uteroplacental and fetoplacental blood circulation, as well as an assessment of compensatory processes and a statement of placental insufficiency with clarification of the form and stage of the same. The morphofunctional assessment of the placenta was carried out by a pathologist according to the order (N82 of April 29, 1994) [4]. A macroscopic description of the placenta and a study of micropreparations (Leica TP1020, Germany) were carried out using a Nikoneclipse E200 light microscope (Japan), which included data on the mass, shape, size and structure of the placenta, characteristics of the umbilical cord, fetal membranes, a description of the structural components of the placenta, membranes, the presence of involutional-dystrophic changes, as well as the calculation of the placental-fetal coefficient (PFC). The nature of fetoplacental insufficiency was assessed by the duration of its course and the degree of compensation according to the classification adopted in obstetrics [1].

The following parameters were compared: placenta weight, length, width and thickness; umbilical cord weight, thickness and number of vessels; fetal membrane weight; placental-fetal coefficient (PFC); membranous-placental coefficient (MPC); child's body weight; gestational age; presence of inflammatory placental diseases (chorioamnionitis; deciduitis; placentitis; funiculitis, villusitis, phlebitis of umbilical cord vessels); presence of acute placental circulatory disorder, chronic decompensated placental insufficiency. The fetal-placental coefficient (PPC) serves as an objective morphological indicator of the circulatory-metabolic balance of the fetoplacental system and, under conditions of normal pregnancy, fluctuates within the range of 0.11–0.14. Exceeding this indicator indicates compensatory hyperplasia of placental tissue, which is typical for the compensated stage of chronic placental insufficiency. A decrease in the IPC is associated with chronic subcompensated and decompensated placental insufficiency, the development of intrauterine hypoxia, intrauterine growth retardation, and a high risk of intrauterine fetal death.

IPC is an integral indicator of the drainage function of the placenta, which largely corrects the volume and composition of the amniotic fluid. The normal level of IPC is 0.10–0.13 and increases as the filtration properties of the fetal membranes deteriorate, reaching maximum values (0.18–0.22) in severe forms of ascending bacterial infection of the placenta, occurring with exudative choriodeciduititis [2].

The results obtained for each placenta were entered into a common database and subjected to statistical processing. The description of quantitative indicators is performed indicating the median (Me), minimum and maximum values (min; max). Comparison of quantitative indicators in the comparison groups was performed using the Mann-Whitney test and Fisher's point test. Correlation analysis was performed using the Spearman rank correlation method. To assess the relationship between the studied factors and outcomes in the comparison groups, the odds ratio (OR) with the calculation of the confidence interval (95% CI) was used. Statistical analysis of the study results was performed using the statistical programs STATISTICA, version 12.0 (StatSoft Inc., USA), IBM SPSS Statistics 20. The level of statistical significance when testing the null hypothesis was considered to be p <0.05. The study was approved by the local ethics committee at the Far Eastern State Medical Univer-

Table 1

Comparative clinical and morphological characteristics of the study groups

Indicators	Gestation period up to 28 weeks, n=96	Gestation period 28-32 weeks, n=35	r
Live births, abs, %	67 (69.8)	30 (85.7)	-
Stillbirths, abs, %	29 (30.2)	5 (14.3)	-
Placenta weight, g Me (min ; max)	191.5 (90.0-616.0)	240.0 (80.0-655.0)	p<0.05
Placenta length, cm Me (min ; max)	14.0 (10.0-24.0)	15.0 (10.0-23.0)	p>0.05
Placenta width, cm Me (min; ma x)	12.0 (6.0-18.0)	12.0 (7.5-18.0)	p>0.05
Placenta thickness, cm Me (min ; ma x)	1.5 (0.4-5.0)	1.5 (0.8-2.5)	p>0.05
Baby's weight at birth, g Me (min; max)	710 (370-1490)	1120 (430-1640)	p<0.01
Gestation period, Me (min; max)	25 нед. (22 нед. - 27 нед. 6 дн.)	28 нед. (28 нед. - 32 нед.)	p<0.01
Umbilical cord weight, g Me (min; max)	19.0 (4.7-76.0)	28.0 (8.0-59.0)	p<0.05
Thickness of the umbilical cord, cm	1.5 (0.5-2.0)	1.3 (0.7-2.0)	p>0.05
Number of umbilical vessels Me (min; max)	3 (3-3)	3 (3-3)	p>0.05
Shell weight, g Me (min; max)	20.0 (2.0-80.0)	27.0 (8.0-66.0)	p>0.05
Placental-fetal coefficient, conventional unit Me (min; max)	0.31 (0.1-1.05)	0.21 (0.13-0.47)	p>0.05
Membranous-placental coefficient, conventional unit Me (min; max)	0.11 (0.02-0.61)	0.12 (0.03-0.39)	p>0.05

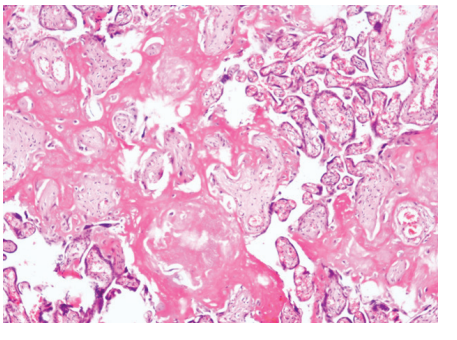

Fig. 1. Placenta x 10. Fibrinoid necrosis of chorionic villi - histological picture of chronic decompensated insufficiency

sity of the Ministry of Health of the Russian Federation (protocol No. 2 dated 16/05/2024).

In the first group of premature infants born in very early preterm labor at a gestation period of less than 28 weeks, 67 children (69.8%) were born alive; 29 fetuses (30.2%) were stillborn. In the second group, represented by children with a gestation period of 28-32 weeks, the majority (30 children) were born alive (85.7%), 5 children (14.3%) were stillborn.

The median placenta weight in the first group was 191.5 grams, in the second group, naturally, the median was higher and amounted to 240.0 grams. A statistically significant difference was found between the placenta weight, the umbilical cord weight, the gestational age and the body weight of the child (Table 1).

When comparing live and stillborn children born at 22-28 weeks of gestation, a significant difference was noted only in fetal body weight: in live births, the IBW was 800 grams, while the IBW in stillborns was 497 grams ($p<0.05$). In the group of live and stillborn children with a gestation period of 28-32 weeks, statistically significant differences in the analyzed characteristics were not found ($p>0.05$).

There are no significant differences between stillborn and live births at 22-28 weeks, as well as live and stillborn children at 28-32 weeks of gestation in either acute placental circulatory disorder or chronic decompensated placental insufficiency (Figure 1).

When analyzing the correlation relationships between stillbirths and the analyzed characteristics, a direct relationship of medium strength was established between stillbirths and the value of the AUC ($r = 0.51$; $p < 0.05$); the frequency of implantation failure ($r = 0.55$; $p < 0.05$) and placental involution ($r = 0.60$; $p < 0.05$) in stillbirths born at 22 to 28 weeks of gestation. No other significant relationships of medium and high strength were found with this method of statistical processing (Table 2).

When determining the odds ratio (Table 3), there is an increased relationship between placental involution and stillbirth at 22-28 weeks of gestation (OR 17.26 (1.97-150.70)). There is a relationship between deciduitis OR 3.95 (1.43-10.93) and willusitis OR 2.52 (1.03-6.14) with stillbirth of children up to 28 weeks of gestation (Figure 2).

The simultaneous presence of deciduitis and villousitis increased the incidence of stillbirth by 3 times (OR = 3.24, 95% CI (1.28 - 8.18)). However, many inflammatory diseases of the placenta (placentitis, chorioamnionitis) were equally characteristic of both live and stillbirths at 22-32 weeks of gestation (Figure 3).

R.K. Kersonsky and co-authors found that in extremely premature stillbirths, delayed maturation of the villi and a decrease in the number of nucleated erythrocytes were observed, indicating a lesser role of hypoxia as a cause of death in this group [6].

Disruption of blood circulation between the fetus and the mother is a common cause of stillbirth. The fetal vascular lesions observed in the placenta likely result from impaired fetal blood flow, which may be caused by fetal heart failure, umbilical cord occlusion, or hypercoagulability leading to venous congestion and venous thrombosis [12]. Previously referred to as uteroplacental insufficiency, maternal vascular perfusion is a consequence of inadequate extravillous trophoblast invasion and spiral artery remodeling

Table 2

Correlations between the studied factors and stillbirth

Indicators	Stillbirth Gestation period up to 28 weeks	Stillbirth Gestation period 28-32 weeks
Weight placenta, g	0.14 p<0.05	0.32 p<0.05
Length placenta, cm	0.23 p<0.05	0.29 p<0.05
Width of the placenta, cm	0.05 p<0.05	0.28 p<0.05
Thickness placenta, cm	0.35 p<0.05	0.33 p<0.05
Baby's weight at birth, g	-0.056 p>0.05	0.30 p<0.05
Term gestation	-0.04 p<0.05	-0.615 p<0.05
Weight umbilical cords, gr	0.06 p<0.05	0.15 p<0.05
Thickness umbilical cord, cm	0.13 p<0.05	0.16 p<0.05
Weight shells, gr	0.08 p>0.05	0.33 p<0.05
Placental-fetal coefficient, conventional unit	0.51 p<0.05	0.31 p<0.05
Membranous-placental coefficient, conventional unit	0.165 p<0.05	0.25 p<0.05
Swelling Vartanova well	0.38 p<0.05	-0.54 p>0.05
Deciduitis	0.46 p<0.05	0.36 p<0.05
Funiculitis	0.41 p<0.05	-0.40 p>0.05
Placentitis	0.05 p<0.05	-0.48 p>0.05
Chorioamnionitis	0.23 p<0.05	0.10 p<0.05
Villusite	0.40 p<0.05	0.60 p>0.05
Phlebitis vessels umbilical cord	0.49 p<0.05	0.45 p<0.05
Hypoplasia placenta	0.36 p<0.05	0.55 p>0.05
Involution placenta	0.60 p<0.05	0.23 p>0.05
Spicy violation placental blood circulation	0.38 p<0.05	0.54 p>0.05
Violation implantation	0.55 p<0.05	0.59 p>0.05

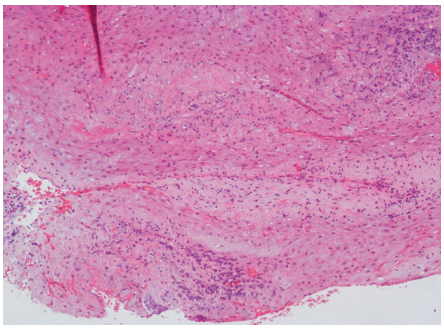

Fig. 2. Placenta x 10. Lymphocytic necrotic deciduitis

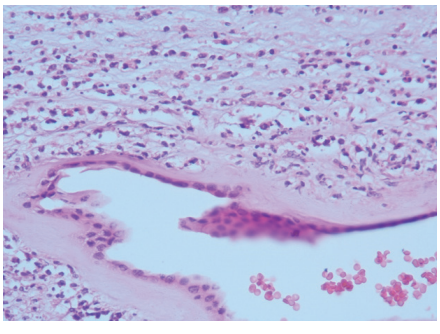

Fig. 3. Placenta x 40. Lymphocytic amnionitis

[15]. Inflammatory and molecular changes in the placenta have also been found in pregnancies complicated by stillbirth. Dysregulation of maternal immune function is also a consequence of impaired extravillous trophoblast invasion [15].

Conclusions. When comparing the main clinical and morphometric parameters of the placentas of live and stillborn babies at a gestation period of 22 to 32 weeks, a reliable difference was found only in fetal weight, gestation period, placental weight, and umbilical cord weight.

A high level of inflammatory diseases of the placenta is noted in both stillborn and liveborn babies; intrauterine infection, manifested by villusitis and deciduitis, increases the likelihood of stillbirth by 3.3 times at a gestation period of 22 to 28 weeks.

Correlation analysis revealed a moderate-strength relationship between the placentas, the frequency of implantation failure, and placental involution in stillborn babies in the period from 22 to 28 weeks of gestation: the presence of placental involution increases the risk of stillbirth by 17.3 times.

Thus, histological examination of the placenta is an important stage in the diagnosis of the causes of stillbirth at a gestation period of 22 to 32 weeks and can serve as the basis for the development of preventive measures for the prevention of extreme prematurity and stillbirth.

Table 2

Odds ratio between stillbirth and the factors studied

Indicators	Gestation period up to 28 weeks	Gestation period 28-32 weeks
Deciduit	3.95 (1.43-10.93)	0.75 (0.13-4.25)
Funiculitis	1.46 (0.5-4.19)	-
Placentitis	0.24 (0.09-0.67)	-
Chorioamnionitis	0.74 (0.30-1.81)	-
Villusit	2.52 (1.03-6.14)	6.0 (0.93-38.5)
Phlebitis vessels umbilical cord	0.30 (0.04-2.60)	-
Hypoplasia placenta	1.32 (0.49-3.58)	0.50 (0.05-4.83)
Involution placenta	17.26 (1.97-150.70)	-
Spicy violation placental blood circulation	1.174 (0.393-3.50)	-
Chronic decompensated placental insufficiency	1.25 (0.5-3.1)	-
Violation implantation	1.47 (0.13-6.33)	1.20 (0.11-12.53)

The authors declare no conflict of interest.

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