

ORCID and contributionship:

Dubivska S. S.: 0000-0003-0367-6279 ^{ABCDEF}

Viedienieva R. Y.: 0000-0002-3988-1912 ^{BC}

Hryhorov Yu. B.: 0000-0003-4185-8540 ^{BC}

Conflict of interest:

The authors declare no conflict of interest.

Corresponding author

Dubivska Svitlana Stanislavivna

Kharkiv National Medical University

Ukraine, 61022, Kharkiv, 4 Nauky av.

Tel: +380677879407

E-mail: Dubovskaya@ukr.net

A – Work concept and design, B – Data collection and analysis, C – Responsibility for statistical analysis, D – Writing the article, E – Critical review, F – Final approval of the article.

Received 16.03.2022

Accepted 14.09.2022

DOI 10.29254/2077-4214-2022-3-166-168-173

UDC 618.414.8:618.396]-076.1

Dubossarska Yu. O., Puziy Ye. O.

HISTOLOGICAL FEATURES OF THE INFECTIOUS AND INFLAMMATORY STATE OF THE PLACENTA IN WOMEN WITH PRETERM PREMATURE RUPTURE OF MEMBRANES DEPENDING ON THE DURATION OF THE INTERVAL BETWEEN MEMBRANE RUPTURE AND DELIVERY AND OTHER FACTORS

Dnipro State Medical University (Dnipro, Ukraine)

obgyn.pg@dmu.edu.ua

A study was conducted to histologically evaluate the infectious and inflammatory state of the placenta in women with preterm premature rupture of membranes (pPROM) and its relationship with the duration of the interval between membrane rupture and delivery, the level of expression of antimicrobial peptides (β -2-defensins) and other factors of the course of pregnancy and labour.

There were examined 56 women of the main group, whose pregnancy was complicated by pPROM at 23-36 weeks of pregnancy and 20 pregnant women of the control group with intact fetal membranes, who subsequently gave birth to full-term babies. The study included anamnesis, study of the course of pregnancy, labour and postpartum period, clinical and laboratory parameters of the mother, including the level of expression of antimicrobial peptides (β -2-defensins) in the blood serum, functional status of the newborn, histological examination of the placenta.

It was found that in the morphological study of placentas in women with pregnancy complicated by pPROM, in most cases (85.7%) signs of placental insufficiency were found, of which in a quarter of cases (25.0%) the insufficiency was acute, which was closely associated with perinatal mortality. The frequency of lesions of various elements and structures of the placenta, membranes and umbilical cord of infectious and inflammatory nature significantly depended on the duration of the interval between membrane rupture and delivery. The average level of expression of β -2-defensins in the blood of pregnant women with pPROM was reduced by 1.4 times compared to healthy pregnant women and inversely correlated with both the acute course of placental insufficiency and funiculitis and simultaneous damage to several elements and structures of the placenta.

Key words: preterm premature rupture of membranes, histological examination of placenta, interval between membrane rupture and delivery, expression of beta-2-defensins.

The connection of the publication with planned research works. This work is a fragment of the planned research of Dnipro State Medical University «Diagnosis and Preventive Treatment of Obstetric and Gynecological Diseases in Extragenital Pathology», № state registration 0120U101467.

Introduction. Preterm premature rupture of membranes (pPROM) occurs in 3% of pregnancies and is the cause of 30% of preterm births [1]. Despite the urgency of the problem, the issues of pathogenesis and possible prognosis of pPROM are not fully understood. Inflammatory changes of membranes are one of the leading

causes of pPROM [2, 3]. On the other hand, waiting tactics for pPROM is associated with the risk of developing infectious complications; in particular, it is an independent prognostic factor for the development of choriodecidualitis and chorioamnionitis [4], which directly correlates with the duration of the interval between membrane rupture and delivery. The gold standard for confirming the presence of an infectious and inflammatory process in the fetoplacental complex is the data of histological examination of the placenta [5].

Changes in the expression of defensins, antimicrobial peptides with a broad spectrum of anti-infective

properties in amniotic fluid, mucous membrane of the reproductive tract of women, have been reported in a number of clinical studies, which indicate that dysregulation of defensins may affect the prognosis of pregnancy, labour and diseases in women [6]. However, there is a lack of studies on the level of defensins expression in the blood of the expectant mother and its relationship with the course of pregnancy, labour and placental infection.

Thus, the high risk of developing perinatal infections and purulent-septic complications in the mother against the background of pPROM limits the spread of the tactics of long-term prolongation of pregnancy, requires adequate and timely assessment of risk factors, including the level of antimicrobial peptides (human β -2-defensins), which will expand scientific knowledge about the pathogenesis of pPROM and predict complications in the mother and newborn.

The aim of the study. To evaluate the histological features of the placenta in women with pregnancy complicated by preterm premature rupture of membranes and their relationship with the duration of the interval between membrane rupture and delivery, the level of expression of antimicrobial peptides (β -2-defensins) and other factors of the course of pregnancy and labour.

Object and methods of research. The study was carried out at the clinical base of the Department of Obstetrics, Gynecology and Perinatology of the Faculty of Postgraduate Education of the Dnipro State Medical University in the obstetric departments of the Municipal Enterprise "Dnipropetrovs'k Regional Perinatal Center" of the Dnipropetrovs'k Regional Council, Dnipro.

The study included 56 women aged 19 to 52 years (median – 31 years) with singleton pregnancy complicated by pPROM at 23-36 weeks of gestation (median – 30.5 weeks). The duration of the latent period during the waiting tactics of labor management with the informed consent of the woman ranged from 2.5 to 1400 hours, with an average (Me (IQR)) of 92.7 (25.5; 295.7) hours. Depending on the duration of the interval between membrane rupture and delivery (DI), all women were divided into 3 groups: Group I – 20 pregnant women with a DI up to 48 hours (mean duration – 15.3 (6.1; 28.6) hours), Group II – 19 women with a DI from 48 to 168 hours (mean – 99.1 (76.5; 133.0) hours), Group III – 17 women with a DI of 168 hours or more (mean – 345.3 (312.0; 493.8) hours). The selected groups were statistically homogeneous in terms of gestational age at the time of delivery: Group I – 32.5 (29.5; 34.5) weeks, Group II – 31.0 (26.0; 34.0) weeks, Group III – 30.0 (29.0; 34.0) weeks ($p=0.618$ by criterion H).

At 24-34 weeks of pregnancy, 40 (71.4%) women received prophylaxis of respiratory distress syndrome of the newborn, of which 29 (51.8%) received dexamethasone and 11 (19.6%) betamethasone in appropriate doses of 24 mg. Nifedipine tocolysis was performed in 35 (62.5%) cases. In order to prevent intrauterine infection, all pregnant women received antibacterial medications in medium therapeutic doses.

To compare the level of expression of β -2-defensins, a control group of 20 pregnant women, aged 17 to 38 years (median – 27 years), with intact fetal membranes, who subsequently gave birth to full-term babies, was formed.

The study included anamnesis, study of the course of pregnancy, childbirth and postpartum period, clinical and laboratory parameters of the mother, including the level of expression of antimicrobial peptides (β -2-defensins) in the blood serum, functional status of the newborn, histological examination of the placenta. The study of general clinical blood parameters was performed using the MicroCC-20Plus analyzer, the expression of β -2-defensins was determined by enzyme-linked immunosorbent assay (Elabscience human DEF β 2/DEFB2 (Defensin Beta 2) ELISA Kit). Newborns' condition was assessed on the 1st and 5th minute after birth using the Apgar scale, Downes score and during the child's stay in the hospital. Histological examination of the placenta was carried out after sequential preparation of the material with fixation in 10% formalin, treatment with ethyl alcohol solution 90°, paraffin embedding of sections and staining with hematoxylin and eosin using a LEICA CME microscope. Signs of infection and inflammation, placental insufficiency, the presence of compensatory and adaptive reactions were determined.

Statistical processing of the survey data was carried out using the licensed software package Statistica v. 6.1 (Statsoft Inc., USA, № AGAR909E415822FA). The data are presented as arithmetic mean (M) with standard deviation (SD), 95% confidence interval for the mean (95% CI), median (Me) and interquartile range (IQR – 25th; 75th percentiles). The Mann-Whitney test (U) was used to compare the mean values between the two groups, the nonparametric Kruskal-Wallis test (H) was used for multiple comparisons, the two-sided Fisher exact test (FET) and Pearson's Chi-square test (χ^2) were used for relative indicators; Spearman rank correlation coefficients (r) were used to assess the relationship between the characteristics. The results were considered statistically significant at $p<0.05$.

Results of the study and their discussion. In the study of anamnestic and clinical data in women with pPROM, it was found that the course of pregnancy in most of them – 44 (78.6%) was accompanied by the threat of spontaneous abortion or premature birth – in 20 (35.7%), anemia – in 26 (46.4%), the development of such complications of the gestational period as premature placental abruption – in 7 (12.5%), fetal distress – in 3 (5.4%), gestational diabetes mellitus – in 6 (10.7%), preeclampsia – in 3 (5.4%), isthmio-cervical insufficiency (ICI) – in 6 (10.7%). Bacterial vaginosis was noted in half of the pregnant women – 31 (55.4%), asymptomatic bacteriuria – in 25 (44.6%), kidney pathology (mainly chronic pyelonephritis, cystitis) had 16 (28.6%) women. At the time of hospitalization, anemia was registered in 24 (42.9%) women with pPROM. Vaginal delivery occurred in 41 (73.2%) women, caesarean section was performed in 15 (26.8%) patients. Chorioamnionitis was detected in 8 (14.3%) cases. Complications of childbirth were noted in 14 (25.0%) women, among which the most common was the retention of parts of the placenta – 10 (17.9%) cases.

Indicators of pregnancy outcomes and the condition of newborns depending on the DI are shown in **table 1**. It should be noted that the course of pregnancy complicated by pPROM resulted in a high incidence of perinatal losses – stillbirth was 14.3% (8 cases out of 56), including 4 cases of antenatal fetal death, in the other 4 cases – intrapartum (3 cases during vaginal delivery, 1

Table 1 – Evaluation of pregnancy outcomes and the condition of newborns depending on the duration of the interval between membrane rupture and delivery

Indicator	Total (n ₁ =56, n ₂ =48)	Groups by DI		
		I group (DI<48 hours) (n ₁ =20, n ₂ =17)	II group (DI 48-168 hours) (n ₁ =19, n ₂ =15)	III group (DI>168 hours) (n ₁ =17, n ₂ =16)
Stillbirth rate, n/%:	8/ 14,3	3/ 15,0	4/ 21,1	1/ 5,9
- antenatal	4/ 7,1	2/ 10,0	2/ 10,5	-
- intrapartum	4/ 7,1	1/ 5,0	2/ 10,5	1/ 5,9
<i>Condition of live birth children</i>				
Gender: male/female, n	24/ 24	10/ 7	6/ 9	8/ 8
Apgar 1 min, Me (IQR)	5,0 (4,0; 7,0)	6,0 (4,0; 7,0)	5,0 (3,0; 7,0)	5,0 (4,0; 6,5)
Apgar 5 min, Me (IQR)	6,0 (5,0; 7,0)	6,0 (5,0; 7,0)	6,0 (4,0; 7,0)	6,0 (6,0; 7,0)
Body weight at birth, g, Me (IQR)	1830 (1240;2350)	1900 (1260; 2350)	1470 (1100; 2470)	1780 (1300; 2325)
- low weight, n/%	23/ 47,9	11/ 64,7	5/ 33,3	7/ 43,8
-very small weight, n/%	13/ 27,1	4/ 23,5	5/ 33,3	4/ 25,0
-extremely low body weight, n/%	7/ 14,6	1/ 5,9	3/ 20,0	3/ 18,8
Intrauterine fetal infection, n/%	2/ 4,2	-	1/ 6,7	1/ 6,3
Neonatal respiratory distress syndrome, n/%	21/ 43,8	5/ 29,4	7/ 46,7	9/ 56,3
Lesions of the nervous system, n/%	37/ 77,1	15/ 88,2	11/ 73,3	11/ 68,8
Neonatal jaundice, n/%	22/ 45,8	8/ 47,1	7/ 46,7	7/ 43,8

Notes: n₁ – total number of observations; n₂ – number of live births; differences between groups are not significant (p>0.05 for all comparisons).

case – during cesarean section). In 6 out of 8 cases, the fetus had an extremely low weight (from 500 to 900 g), and the gestational age did not exceed 27 weeks (median – 24 weeks).

We did not find a significant relationship between the condition of newborns and the DI; the indicators generally corresponded to the estimates characteristic of preterm infants and correlated with the gestational age of the child. However, given the high risks of developing infectious and inflammatory complications in preterm infants who were born to women with pPROM, in the postpartum period, special attention was paid to the diagnosis of adaptation disorders and pathological conditions in newborns (**table 1**). Intrauterine fetal infection (IUFI) was noted in 2 cases (male sex, gestational age – 27 weeks, DI – 163 hours and 493.8 hours, body weight – 980 g and 970 g, Apgar score 1 min/5 min – 4/5 points). Neonatal respiratory distress syndrome (NRDS) was registered in 43.8% of children, mainly 2-3 degree of respiratory failure (37.5%), with a tendency

Table 2 – Results of histological examination of placenta depending on the duration of interval between membrane rupture and delivery, n/%

Indicator	Total (n=56)	Groups by DI		
		I group (DI < 48 hours) (n=20)	II group (DI 48-168 hours) (n=19)	III group (DI > 168 hours) (n=17)
Placental insufficiency, including:	48/ 85,7	19/ 95,0	16/ 84,2	13/ 76,5
- acute course	14/ 25,0	7/ 35,0	3/ 15,8	4/ 23,5
- chronic course	39/ 69,6	15/ 75,0	15/ 78,9	9/ 52,9
Chorio-decidualitis	10/ 17,9	3/ 15,0	4/ 21,1	3/ 17,6
Chorioamnionitis	1/ 1,8	1/ 5,0	-	-
Membranitis	32/ 57,1	6/ 30,0	14/73,7 *	12/70,6 *
Intervillitis	20/ 35,7	3/ 15,0	6/ 31,6	11/64,7 **
Funiculitis	22/ 39,3	5/ 25,0	7/ 36,8	10/58,8 *
Including combined damage to various elements of the placenta	28/ 50,0	6/ 30,0	10/ 52,6	12/ 70,6 *

Notes: * – p<0.05 compared to group I; ^ – p<0.05 compared to group II (criterion χ^2 or FET)

to increase the frequency of its development with the DI more than 7 days (from 29.4% in group I to 56.3% in group III, p=0.12 by χ^2). Intraventricular hemorrhage (IVH) of 1-3 degrees was observed in 11 (22.9%) newborns, which closely correlated with early gestation (r=-0.53; p<0.001), very low birth weight (r=-0.45; p<0.001) and led to CNS damage (r=0.57; p<0.001). Various nosological forms of nervous system damage were noted in the majority of newborns – 37 (77.1%), including neonatal cerebral depression – in 20 (41.7%) children, neonatal cerebral agitation – in 2 (4.2%), perinatal hypoxic-ischemic damage of CNS (PHID CNS) – in 15 (31.2%). Congenital malformations of newborns are represented by heart defects in the form of atrial and/or ventricular septal defect (6.3%) and open foramen ovale (8.3%). Hypoxic disorders of acute and delayed onset are represented respectively by pulmonary atelectasis (2.1%) and necrotizing enterocolitis (12.5%).

The general assessment of pathomorphological changes in the placenta and membranes was carried out according to the existing classification of placental insufficiency in Ukraine and generally accepted by practicing obstetricians and gynecologists and pediatric pathologists. Placental insufficiency is associated with metabolic disorders not only in the placenta itself, but also in the membranes, and can occur even in the absence of signs of inflammation in the placenta, in the presence of vaginitis, immunological changes or dysplastic process in the smooth chorion. The degree of compensation of placental insufficiency was carried out taking into account the weight of the fetus and placenta, the maturity of the villous chorion according to gestational age. This term is not reflected in the latest version of the Amsterdam classification of placental lesions in 2015, pathomorphological changes in the placentas studied by us and indicated in the pathomorphological findings correlate with the specified pathological processes in the Amsterdam classification. The results of the histological examination of the placenta preparations showed that the morphological signs of placental insufficiency (PI), as a comprehensive assessment of the severity of disorders of compensatory and adaptive mechanisms, circulatory and involutonal-dystrophic process-

to increase the frequency of its development with the DI more than 7 days (from 29.4% in group I to 56.3% in group III, p=0.12 by χ^2). Intraventricular hemorrhage (IVH) of 1-3 degrees was observed in 11 (22.9%) newborns, which closely correlated with early gestation (r=-0.53; p<0.001), very low birth weight (r=-0.45; p<0.001) and led to CNS damage (r=0.57; p<0.001). Various nosological forms of nervous system damage were noted in the majority of newborns – 37 (77.1%), including neonatal cerebral depression – in 20 (41.7%) children, neonatal cerebral agitation – in 2 (4.2%), perinatal hypoxic-ischemic damage of CNS (PHID CNS) – in 15 (31.2%). Congenital malformations of newborns are represented by heart defects in the form of atrial and/or ventricular septal defect (6.3%) and open foramen ovale (8.3%). Hypoxic disorders of acute and delayed onset are represented respectively by pulmonary atelectasis (2.1%) and necrotizing enterocolitis (12.5%).

es, were determined in most cases – 48 (85.7%), and mainly had a chronic nature – 39 (69.6%) cases. According to the degree of compensation of chronic PI, the subcompensated stage prevailed – 27 cases out of 39 (69.2%); compensated stage occurred in 8 (20.5%) cases, uncompensated stage – in 4 (10.3%). Most often hyperplastic form of chronic PI was determined – in 24 (61.5%) observations, infarct form was observed in 7 (17.9%) cases. Signs of acute PI were detected in 14 (25.0%) samples, which were mainly due to premature placental abruption, infarct changes in placental tissue and signs of acute umbilical cord circulation disorders.

Analysis of the localization of infectious and inflammatory changes in the placentas of women with pPROM showed a high frequency of membranous lesions, as evidenced by the detection of signs of purulent necrotic membranitis in more than half of the observations – 32 (57.1%), especially with increasing of the DI (more than 70% of cases) (table 2).

Inflammatory process in some elements of the membranes, in particular, parietal choriodecidualitis, was detected in 10 (17.9%) cases. Inflammation in the intervillous space of the placenta (intervillitis – the second maternal stage of infection) occurred in every third case – 20 (35.7%), and the frequency of lesions increased directly proportionally with the prolongation of DI: from 15.0% in DI < 48 hours to 31.6% in DI 48-168 hours and up to 64.7% in prolongation of pregnancy after pPROM for more than 7 days (p<0.05). Umbilical cord inflammation (funiculitis – a fetus inflammatory reaction) was detected in 22 (39.3 %) cases and also significantly depended on the DI (table 2). Combined inflammatory lesions of the membranes, placenta and umbilical cord structures were observed in half of the cases (50.0%), and the prevalence of this process significantly correlated with the duration of latency period (r=0.33; p<0.05).

In order to search for new diagnostic and prognostic markers of perinatal infections and purulent-septic complications in the newborn and mother, we studied the level of expression of antimicrobial peptides (β-2-defensins) in the serum of pregnant women with pPROM. A significant decrease (by 1.4 times) of these indicators in the examined pregnant women of the main group compared to healthy pregnant women of the control group was found – 76.7 (21.1) pg/ml against 107.4 (11.4) pg/ml (p<0.001).

According to the results of the correlation and comparative analysis of the expression levels of β-2-defensins in the blood of the expectant mother and the histological characteristics of the placenta of infectious and inflammatory nature, inverse relationships between these indicators were established. Thus, the acute PI in the mother was as-

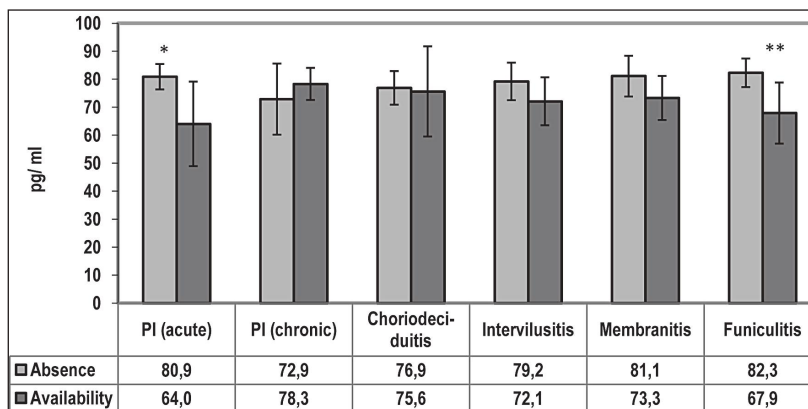


Figure – Mean levels of expression of β-2-defensins in the blood of pregnant women with pPROM depending on the histological characteristics of the placenta.

Notes: Data are presented as M (95% CI); significant differences between groups: * – p<0.05; ** – p<0.01 (Mann-Whitney test).

sociated with a 1.3-fold lower level of expression of β-2-defensins (r= -0.26; p<0.05), which averaged 64.0 (31.2) pg/ml in the development of the acute PI against 80.9 (14.6) pg/ml in other cases (p<0.05) (fig.).

Against the background of a reduced level of expression of β-2-defensins in the blood, the frequency of involvement in the inflammatory process of blood vessels and stroma of the umbilical cord (r= -0.37; p<0.01) and other elements of the placenta (r= -0.28; p<0.05) significantly increased (Table 3). The average level of expression of β-2-defensins in the blood of mothers with funiculitis in histological preparations of the placenta was 67.9 (5.5) pg/ml, while in the absence of inflammation in the umbilical cord the index was 1.2 times higher – 82.3 (2.6) pg/ml (p<0.01).

Among the indicators of peripheral blood in the examined patients, which were significantly associated with infectious and inflammatory changes in the placenta, an increased level of erythrocyte sedimentation rate (ESR) was identified.

The results of the correlation analysis of the relationships between the histological characteristics of the afterbirth and the main clinical, anamnestic, laboratory factors of mothers and their newborns, shown in table 3, allowed to outline the factors that can serve as predictors of high risk of fetal infection, perinatal mortality

Table 3 – Relationship between histological characteristics of placenta and various factors

Histological characteristics of the placenta	DI, hours	Anemia during hospitalization	Bacterial vaginosis	Level of expression of β-2-defensins	ESR, mm/hour	Stillbirth	Chorioamnionitis	Apgar 1min./5 min.	IUFI	NRDS	Weight of the child, g	PHID CNS
PI (acute)	-	-	-	-0,26*	0,27*	0,35**	-	-0,47/-0,45^	-	0,44**	-	0,34*
Membranitis	0,35**	-	-	-	-	-	0,26*	-0,28/-0,26*	-	0,31*	-0,28*	-
Intervillitis	0,41**	0,34**	-	-	0,36**	-	0,55^	-	0,29*	-	-0,26*	-
Funiculitis	0,28*	-	-	-0,37**	0,30*	-	0,30*	-0,34/-0,27*	0,26*	-	-0,30*	-
Combined damage to placenta elements	0,33*	-	-	-0,28*	0,32*	-	0,41**	-0,28*/-0,22	-	0,27*	-0,28*	-

Notes: Significant Spearman correlation coefficients are given: * – p<0.05; ** – p<0.01; ^ – p<0.001; «-» – no statistically significant relationship (p>0.05)

and the development of various complications in newborns.

In particular, the combined lesion of the inflammatory nature of the membranes, placenta and umbilical cord structures inversely correlated with the fetal Apgar score at 1 minute ($r = -0.28$; $p < 0.05$) and weight of the newborn ($r = -0.28$; $p < 0.05$), and was directly associated with the development of chorioamnionitis ($r = 0.41$; $p < 0.01$) and NRDS ($r = 0.27$; $p < 0.05$).

Conclusions. In the morphological study of placentas in women with pregnancy complicated by pPROM, signs of PI were detected in most cases (85.7%), of which in a quarter of cases (25.0%) the failure had an acute course, which was closely associated with perinatal mortality ($r = 0.35$; $p < 0.01$). The frequency of lesions of various elements and structures of the placenta, membranes and umbilical cord of infectious and inflammatory nature

significantly depended on the duration of the interval between membrane rupture and delivery: the correlation coefficient with membranitis was $r = 0.35$; $p < 0.01$, with intervillitis – $r = 0.41$; $p < 0.01$, with funiculitis – $r = 0.28$; $p < 0.05$, with widespread inflammatory process – $r = 0.33$; $p < 0.05$. The average level of β -2-defensins expression in the blood of pregnant women with pPROM was reduced by 1.4 times compared to healthy pregnant women ($p < 0.001$) and inversely correlated both with the acute PI ($r = -0.26$; $p < 0.05$) and with funiculitis ($r = -0.37$; $p < 0.01$) and combined damage to several elements and structures of the placenta ($r = -0.28$; $p < 0.05$).

Prospects for further research. In further studies, it is planned to create prognostic models for the development of complications of pregnancy, childbirth and postpartum in women with pPROM based on the expression of antimicrobial peptides (β -2-defensins).

References

1. Kayem G, Girard G. Prenatal management of the risk of maternal infection in cases of pPROM. Arch Pediatr. 2015;22(10):1056-1063.
2. Elovitz MA, Gajer P, Riis V, Brown AG, Humphrys MS, Holm JB, et al. Cervicovaginal microbiota and local immune response modulate the risk of spontaneous preterm delivery. Nat Commun. 2019;10:1305.
3. Etyang AK, Omuse G, Mukaindo AM, Temmerman M. Maternal inflammatory markers for chorioamnionitis in preterm prelabour rupture of membranes: a systematic review and meta-analysis of diagnostic test accuracy studies. Systematic reviews. 2020;9(1):141.
4. Park CW, Park JS, Norwitz ER. Timing of histologic progression from chorio-decidualitis to chorio-deciduo-amnionitis in the setting of preterm labor and preterm premature rupture of membranes with sterile amniotic fluid PLoS One. 2015;10(11):e0143023.
5. Nijman TA, van Vliet EO, Benders MJ, Mol BW, Franx A, Nikkels PG. Placental histology in spontaneous and indicated preterm birth: A case control study. Placenta. 2016;48:56-62.
6. Varrey A, Romero R, Panaitescu B, Miller D, Chaiworapongsa T, Patwardhan M, et al. Human β -defensin-1: A natural antimicrobial peptide present in amniotic fluid that is increased in spontaneous preterm labor with intra-amniotic infection. American journal of reproductive immunology (New York, N.Y.: 1989). 2018;80(4):e13031.

ГІСТОЛОГІЧНІ ОСОБЛИВОСТІ ІНФЕКЦІЙНО-ЗАПАЛЬНОГО СТАНУ ПОСЛІДУ У ЖІНОК з передчасним розривом плодових оболонок В ЗАЛЕЖНОСТІ ВІД ТРИВАЛОСТІ БЕЗВОДНОГО ПРОМІЖКУ ТА ІНШИХ ФАКТОРІВ Дубоссарська Ю. О., Пузій Є. О.

Резюме. Мета дослідження – оцінити гістологічні особливості посліду у жінок з недоношеною вагітністю, ускладненою передчасним розривом плодових оболонок, та їх зв'язки з тривалістю безводного проміжку, рівнем експресії антимікробних пептидів (β -2-дефензинів) та іншими факторами перебігу вагітності та пологів.

Об'єкт і методи дослідження. Обстежено 56 жінок основної групи, у яких вагітність ускладнилася передчасним розривом плодових оболонок (ПРПО) на 23-36 тижні вагітності та 20 вагітних жінок контрольної групи з цілим плодовим міхуром, які згодом народили доношених дітей. Дослідження включало збір анамнезу, вивчення перебігу вагітності, пологів та післяпологового періоду, клініко-лабораторні показники матері, в тому числі рівень експресії антимікробних пептидів (β -2-дефензинів) у сироватці крові, функціональний стан новонародженої дитини, гістологічне дослідження посліду. При гістологічному дослідженні посліду визначали ознаки інфікування та запалення, плацентарної недостатності, наявність компенсаторно-приспосувальних реакцій.

Результати. Перебіг недоношеної вагітності, ускладнений ПРПО, обумовив високу частоту перинатальних втрат. Не виявлено достовірного зв'язку між станом новонароджених дітей та тривалістю безводного проміжку; показники в цілому відповідали оцінкам, характерним для недоношених дітей і корелювали з гестаційним віком дитини.

Аналіз локалізацій інфекційно-запальних змін у послідах жінок з ПРПО показав високу частоту ураження плодових оболонок, про що свідчить виявлення ознак гнійно-некротичного мембраніту у понад половини спостережень 57,1 %, особливо при збільшенні тривалості безводного проміжку (понад 70 % випадків).

Висновки. Встановлено, що при морфологічному дослідженні плацент у жінок з недоношеною вагітністю, ускладненою передчасним розривом плодових оболонок, в більшості випадків (85,7%) виявлено ознаки плацентарної недостатності, з яких в чверті випадків (25,0%) недостатність мала гострий перебіг, що тісно асоціювалось з перинатальною смертністю. Частота ураження різних елементів і структур плаценти, плодових оболонок і пуповини інфекційно-запального характеру достовірно залежала від тривалості безводного проміжку. Середній рівень експресії β -2-дефензинів у крові вагітних з передчасним розривом плодових оболонок був зниженим в 1,4 рази порівняно зі здоровими вагітними та зворотно корелював як з гострим перебігом плацентарної недостатності, так і з фунікулітом та одночасним ураженням кількох елементів та структур посліду.

Ключові слова: передчасний розрив плодових оболонок, гістологічне дослідження посліду, безводний проміжок, експресія бета-2-дефензинів.

HISTOLOGICAL FEATURES OF THE INFECTIOUS AND INFLAMMATORY STATE OF THE PLACENTA IN WOMEN WITH PRETERM PREMATURE RUPTURE OF MEMBRANES DEPENDING ON THE DURATION OF THE INTERVAL BETWEEN MEMBRANE RUPTURE AND DELIVERY AND OTHER FACTORS

Dubossarska Yu. O., Puziy Ye. O.

Abstract. *The purpose of the study* is to evaluate the histological features of the placenta in women with pregnancy complicated by preterm premature rupture of membranes (pPROM) and their relationship with the duration of the interval between membrane rupture and delivery, the level of expression of antimicrobial peptides (β -2-defensins) and other factors of pregnancy and labour.

Methods. We examined 56 women of the main group, whose pregnancy was complicated by pPROM at 23-36 weeks of pregnancy and 20 pregnant women of the control group with intact fetal membranes, who subsequently gave birth to full-term babies. The study included anamnesis, study of the course of pregnancy, labour and postpartum period, clinical and laboratory parameters of the mother, including the level of expression of antimicrobial peptides (β -2-defensins) in the blood serum, functional status of the newborn, histological examination of the placenta. In the histological examination of the placenta, signs of infection and inflammation, placental insufficiency, the presence of compensatory and adaptive reactions were determined.

Results. The course of pregnancy, complicated by pPROM, caused a high incidence of perinatal losses. No significant relationship between the condition of newborns and the duration of the interval between membrane rupture and delivery was found; the indicators generally corresponded to the estimates characteristic of premature infants and correlated with the gestational age of the child.

Analysis of the localization of infectious and inflammatory changes in the placentas of women with pPROM showed a high incidence of membranous lesions, as evidenced by the detection of signs of purulent necrotic membranitis in more than half of the observations (57.1%), especially with an increase in the duration of the interval between membrane rupture and delivery (more than 70% of cases).

Conclusions. It was found that the morphological examination of placentas in women with pregnancy complicated by pPROM in most cases (85.7%) revealed signs of placental insufficiency, of which in a quarter of cases (25.0%) the insufficiency had an acute course, which was closely associated with perinatal mortality. The frequency of lesions of various elements and structures of the placenta, membranes and umbilical cord of infectious and inflammatory nature significantly depended on the duration of the interval between membrane rupture and delivery. The average level of expression of β -2-defensins in the blood of pregnant women with pPROM was reduced by 1.4 times compared to healthy pregnant women and inversely correlated with both the acute course of placental insufficiency and funiculitis and combined damage to several elements and structures of the placenta.

Key words: preterm premature rupture of membranes, histological examination of the placenta, interval between membrane rupture and delivery, expression of beta-2-defensins.

ORCID and contributionship:

Dubossarska Yu. O.: 0000-0002-4040-227X^{AEF}

Puziy Ye. O.: 0000-0003-2608-1892^{BCD}

Conflict of interest:

The authors of the article have no conflict of interest.

Corresponding author

Dubossarska Yulianna Oleksandrivna

Dnipro State Medical University

Ukraine, 49044, Dnipro, 9 Vernadsky str.

Tel: +380667323365.

E-mail: obgyn.pg@dmu.edu.ua

A – Work concept and design, B – Data collection and analysis, C – Responsibility for statistical analysis, D – Writing the article, E – Critical review, F – Final approval of the article.

Received 12.03.2022

Accepted 15.09.2022