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THE ROLE OF UMBILICAL CORD PATHOLOGY IN PERINATAL MORTALITY AND MORBIDITY

321.15 – OBSTETRICS AND GYNECOLOGY

Abstract of the PhD thesis in medical sciences

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The thesis was developed within the Department of Obstetrics and Gynecology, Obstetrics and Gynecology Discipline, at *Nicolae Testemitanu* State University of Medicine and Pharmacy.

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INTRODUCTION

Relevance and importance of the addressed problem.

Pathology of the umbilical cord (UC) is a medical and social problem within the contemporary disciplines of obstetrics and perinatology, determined by its place in the structure of causes of perinatal morbidity and mortality [9]. According to the opinion of various authors, the frequency of UC pathology in singleton pregnancies ranges from 4.8% to 38.4% [6, 21, 23, 29, 30], which represents for approximately 40% of neonatal morbidity [5], 50% of perinatal mortality, 70-80% of early neonatal mortality, and over 65-75% of mortality observed during infancy.

Despite the fact that various aspects of this major problem have been studied for a long time, methods are still being continuously sought worldwide to reduce increased perinatal indicators, as there are no clear answers to many questions. According to an analysis by the World Health Organization (2012), prevention of pathological perinatal outcomes was possible in 1.1 million cases through early detection, monitoring, and timely resolution of pregnancy [27]. Thus, the fetal condition and the health of the newborn are determined both by the conditions of intrauterine growth and development, as well as the character of interrelationships with the maternal body [33], which occur through the fetoplacental complex.

Specialized literature [6] reports that scientists, since ancient times, have been interested in the pathology of fetoplacental complex. The interest lies in the study of the UC, which constitutes the unique connection between the fetus and the placenta, containing two arteries and a vein covered with Wharton's jelly with a spiral disposition, ensuring the fetal nutrition, necessary for his development. Umbilical cord pathology includes abnormalities in length, diameter, insertion, vascular anomalies, knots, Wharton's jelly pathology, location pathology, infection, or trauma [14, 26, 29, 30]. Jessop F. and coaut. (2014) presented the link between umbilical anomalies and possible perinatal outcomes based on literature reviews [18]. Thus, UC pathology determines perinatal morbidity and mortality in 21-65% of cases, the most important pathologies being: fetal growth restriction, fetal distress, asphyxia, intrauterine death, and fetal congenital anomalies. In this context, an important moment in UC pathology is a meticulous diagnosis aimed to improving perinatal indicators.

The contemporary technologies, such as ultrasound, Doppler velocimetry, cardiotocography, has improved the possibilities for prenatal diagnosis of placental complex [3, 19, 20, 32, 34]. Doppler velocimetry is a non-invasive method for assessing fetal functional status, which allows to determine the origine of hemodynamic disorders in proper time. Although the implementation of new technologies has offered the possibility of intrauterine diagnosis of various fetal conditions. This si an important fact because until now, UC pathology has been poorly studied, containing many unknown components being determined in one in third birth, causing ante- and intranatal deaths in 1.7-4.3% of cases and neonatal deaths in 1.5-1.6% of cases [10, 15, 28].

It should be noted that contemporary diagnostic methods are widely used nowadays, but routine examinations, such as histological examination of fetal annexes, remain important and current. In recent years, the morphological and functional characteristics of the placenta in various pregnancy complications have became the subject of in-depth research [17, 25]. However, scientific studies in the field of UC physiology and pathology and placental chorionic plaque (PCP) have a limited character and are largely focused on the diagnosis of developmental

anomalies and specific inflammatory reactions [4, 11]. The segmental and mesenchymal interactions of the UC are less examined, taking into account the presence and severity of placental insufficiency and its effect on perinatal outcomes [16, 24]. It is known that current morphometric research and organometry of the UC only aim to assess its length and mass [8, 22, 31]. Considering that the UC is directly involved in fetal and placental circulation, it is also necessary to evaluate its blood flow [12]. Each UC has its own morphological and functional characteristics, therefore, a proper assessment and the results implementation in dayly practice is recommended. Thus, it is of particular interest to establish the relationship between morphological changes in the epithelial-stromal-vascular components of the UC and PCP and perinatal pathology, which reflects its etiopathogenesis.

Given the above, it can be mentioned that UC pathology represents an important problem in obstetrics, in terms of perinatal morbidity and mortality [1, 2, 7, 28]. Detecting structural changes in the UC during early gestation provides the opportunity to develop optimal obstetric management, which can contribute to improving perinatal outcomes by allowing the future prediction and prevention of consequences for the newborn health [13, 30].

The complex aspects and issues related to UC pathology have led us to conduct the current study, defining its purpose and research objectives.

The aim of the study.

The purpose of the study was to investigate the role of umbilical cord pathology in the manifestation of perinatal outcomes (mortality and morbidity), in order to optimize obstetric management, improve maternal-fetal prognosis, and statistical indicators.

Objectives of the study: 1. To determine the clinical and evolutionary peculiarities of pregnancies and deliveries in patients with umbilical cord pathology. 2. To identify the risk factors of umbilical cord pathology and the prognostic criteria for perinatal outcomes. 3. To characterize the morbidity and mortality of newborns with umbilical cord pathology. 4. To evaluate the structural and functional peculiarities of the umbilical cord and placental chorionic plaque in different umbilical and to study their effect on perinatal outcomes. 5. To develop diagnostic criteria for umbilical cord pathology to optimazing clinical management and improving perinatal outcomes.

The general methodology of the research. The research was carried out based on the Department of Obstetrics and Gynecology of the *Nicolae Testemitanu* State University of Medicine and Pharmacy, in the obstetric wards (units) nr. 1, 2, 3 of the Perinatal Center within the *Gheorghe Paladi* Municipal Clinical Hospital (MCH) and in the Pathology and Cytology Department of the Institute of Mother and Child (IMC) in the Republic of Moldova, during the period of 2016-2022. A informed consent of the medical institutions was obtained. The research project was approved by the Research Ethics Committee of the *Nicolae Testemitanu* State University of Medicine and Pharmacy (minutes no. 95/110 of 21.06.2017) and by the Bioethics Committee of the MCH nr. 1 (minutes no. 3-A of 08.11.2017).

The scientific novelty and originality of the obtained results. For the first time in the Republic of Moldova, the conducted study appreciated the particularities of pregnancy, childbirth (delivery), and postpartum period evolution in patients with UC pathologies. The determinant factors in the development of those conditions were identified. The study investigated the types of abnormal umbilical cords and their role in perinatal morbidity and mortality.

In patients with UC pathology, the function of the fetoplacental complex, the evolution of fetal intrauterine status during pregnancy, and early neonatal results were estimated.

The structural and functional morphological and histological changes of the and the placental chorioamnionic plaque in different pathological UC cases were studied.

Diagnostic criteria for UC pathology were developed to optimize clinical management and improve perinatal outcomes.

The theoretical significance of the thesis. The present scientific study has contributed to the determination and assessment of new aspects in the development of UC pathology, based on clinical, paraclinical, organometric, morphological, histological, and statistical studies, with practical and theoretical and scientific relevance.

The practical value of this study. The research carried out highlights new evolutionary features of pregnancy in cases of pathological UC, which facilitates understanding of the physiological and pathological mechanisms involved in the fetoplacental complex in cases of umbilical abnormalities. This is an important factor in developing optimal clinical management for pregnant women with UC pathology. The role of determinant factors in the development of UC pathology has been identified. Based on the study, two standardized clinical protocols have been developed and implemented in obstetrical and morphopathological practice at the *Gheorghe Paladi* Municipal Clinical Hospital and the Institute of Mother and Child. This will contribute to optimizing the management of complicated pregnancy and childbirth with UC pathologies and improving perinatal indicators. The main results of the study are applied in the teaching process of the Obstetrics and Gynecology discipline at the *Nicolae Testemitanu* State University of Medicine and Pharmacy and in the activity of the Department of Morphopathology and Cytopathology at the Institute of Mother and Child.

Approval of the scientific results. The basic principles of the present study have been reported and discussed at various national and international scientific forums:

- Conferința științifică anuală consacrată aniversării a 90 de ani de la nașterea ilustrului medic și savant Nicolae Testemițanu. Chișinău, 16-20 octombrie 2017.
- Conferința *Zilele Universității de Stat de Medicină și Farmacie „Nicolae Testemițanu”*. Chișinău, 15-19 octombrie 2018.
- The 7th International Medical Congress for Students and Young Doctors. *MedEspera*. Chisinau, May 3-5, 2018.
- The 15th International Congress for Medical Students and Young Doctors. Romania, Iasi, May 3-6, 2018.
- Congresul consacrat aniversării a 75 de ani de la fondarea Universității de Stat de Medicină și Farmacie *Nicolae Testemiţanu*. Chișinău, 21-23 octombrie 2020.
- The 8th International Medical Congress for Students and Young Doctors *MedEspera*. Chisinau, September 24-26, 2020.
- IV Международный междисциплинарный Евразийский Саммит *Женское здоровье*. Москва, 25-27 мая, 2020.
- XXI Всероссийский научно-образовательный форум *Мать и дитя*. Красногорск, 28-30 сентября, 2020.
- BIRTH Congress. 6th edition Clinical Challenges in Labor and Delivery. A virtual experience (online), October 1-3, 2020.
- Міждисциплінарна науково-практична конференція з міжнароднім участем *Сучасні напрямки перинатальної та репродуктивної медицини: від теорії інноваційного пошуку до практики*, присвяченої пам’яті вчителя, професора Олександра Олексійовича Зелінського. Одеса, 16-17 квітня, 2021.

- ECPM 2021: XXVII European Congress of Perinatal Medicine. Live online congress. Lisbon, 14-17 July, 2021.

Publications. Based on the research 35 works were published, including 4 articles in national journals, 3 articles in international journals, 3 articles without a co-author, 8 abstracts in national and international scientific conference proceedings, 4 innovator certificates, 3 certificates for registering copyright and related rights, 5 communications in international and 2 national scientific forums, 3 international and 1 national posters, and 2 standardized clinical protocols.

Volume and structure of the thesis. The thesis is presented in 224 typed pages and consists of an introduction, literature review (Chapter 1), material and methods of research (Chapter 2), two chapters of original results (Chapters 3, 4), synthesis of the obtained results, general conclusions, practical recommendations, a bibliography with 270 sources, and 10 appendices. The work contains 20 tables and 81 figures.

Keywords: umbilical cord, chorioamnionic plaque, pathology, anomaly, morbidity, mortality, perinatal period

CONTENT OF THE THESIS

1. UMBILICAL CORD PATHOLOGY – A CURRENT ISSUE IN CONTEMPORARY OBSTETRICS

This chapter is a synthesis of bibliographic data related to the issue of UC pathology in general, aspects related to etiopathogenesis, classification criteria, modern concepts in diagnosis, management of pregnancy and childbirth in patients with UC pathology, and its influence on perinatal outcomes.

Pathological conditions of the UC can cause restrictions in blood circulation, leading to a decrease in oxygen and nutrient supply to the fetus, resulting in subsequent impairment. Determining umbilical cord pathology requires the use of several diagnostic methods (CTG, USG, Doppler velocimetry), which allow obtaining maximum information about the presence of UC changes. A meticulous antenatal examination of the UC ensures the proper and timely diagnosis, thereby providing opportunities to improve pre- and intranatal obstetric management. Morphohistology allows for certain postnatal diagnosis of UC pathology. The results of macroscopic examination methods of the cord, which include organometry and macroscopy, with determination of the anatomical characteristics of the cord, often correlate with the morphopathological changes detected in the epithelial-stromal-vascular structure of the cord and the chorioamnionic plaque. In consequence, postnatal macroscopic examination of the cord can argue the cause of fetal distress, establishing a prognosis for the newborn.

UC pathology represents a current issue in contemporary obstetrics, leading to further research aimed to minimizing the occurrence of complications in the fetus and newborn, and reducing perinatal morbidity and mortality as a consequence.

2. MATERIAL AND METHODS OF RESEARCH

The research was carried out based on the Department of Obstetrics and Gynecology of the *Nicolae Testemitanu* State University of Medicine and Pharmacy, in the obstetric units nr. 1, 2, 3 of the Perinatal Center within the *Gheorghe Paladi* Municipal Clinical Hospital and the Morphopathology and Cytopathology department of the Institute of Mother and Child in the Republic of Moldova, with the permission of the administration of above-mentioned institutions for data collection and processing, during the period of 2016-2022.

A prospective cohort study was planned and conducted in four stages, during which cases of UC pathology were examined according to the designed protocol (Figure 1).

The required number of research units was estimated based on formula (1):

$$n = \frac{1}{(1-f)} \times \frac{2(Z_\alpha + Z_\beta)^2 xP(1-P)}{(P_o - P_1)^2} \quad (1)$$

Thus, the optimal volume of a research group, with a representative value, is no less than 92 patients. In the study, a total of 210 women were selected and after all inclusion and refusal criteria, we arrived at the representative number of 190 patients, which were divided into two groups with a ratio of 1:1, as follows: the research group (L_1) included 95 respondents with UC pathology and 95 of their newborns; the control group (L_0) included 95 respondents without UC pathology and 95 of their newborns. The following inclusion and exclusion criteria were applied to select patients.

Inclusion criteria for the research:

1. Gestational age between 37^{+0} and 41^{+6} weeks;
2. Spontaneously occurred pregnancy;
3. Singleton pregnancy;
4. Patient age ≥ 18 years old;
5. Informed consent, in written form, for participation in the research.

Exclusion criteria from the research:

1. Gestational age below 36^{+6} and above 42^{+0} weeks;
2. Pregnancy resulted from assisted reproductive technologies;
3. Multiple pregnancy;
4. Patient age ≤ 18 years old;
5. Presence of fetal malformations;
6. Patient severe somatic condition;
7. Absence informed consent to participate in the research.

The study project was approved by the Research Ethics Committee of the *Nicolae Testemitanu* State University of Medicine and Pharmacy (minutes no. 95/110 of 21.06.2017) and the Bioethics Committee of the Municipal Clinical Hospital nr. 1 (minutes no. 3-A of 08.11.2017). The consent to participate in the research was obtained directly from the participants (informed consent forms).

Following the study and extraction of data from the medical records (perinatal record, patient medical record, newborn's record), a comprehensive examination of the patient and newborn was performed, which included both clinical and paraclinical aspects. The clinical examination involved gathering anamnestic and clinical data through standardized interviewing,

determining the general objective and obstetric and gynecologic status of the patient, assessing anthropometric data, gestational age, and the newborn's condition at birth (Apgar score). The paraclinical examination was performed using cardiotocography, ultrasound examination, Doppler velocimetry, and morphopathological examination of the UC and the chorioamnionic plaque. The obtained results were included in a special questionnaire developed and applicable for both groups, which contained nine compartments and 161 questions (Annexe 1). The complex and multi-aspect morphopathological examination of the UC and villous chorion was carried out based on a unique *Protocol for examining the structural and functional characteristics of the UC and chorioamnionic plaque,* developed by the researchers (Annexe 2). All 190 placental complexes after birth underwent morphological explorations.

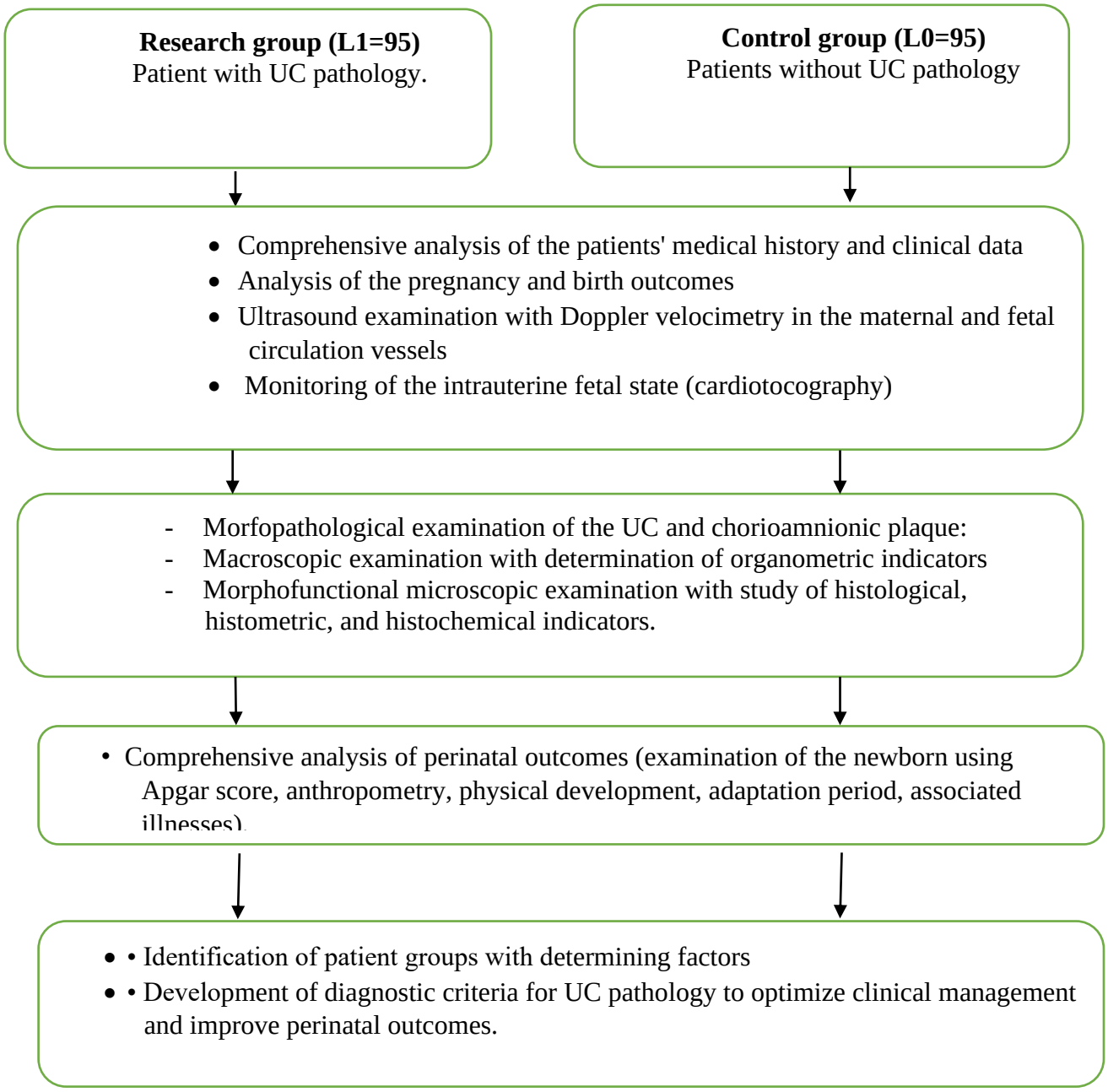

Figure 1. **Study design**

The macroscopic examination of placental complex included: organoscopy and organometry of the UC (length, weight, diameter, volume, Unit of Linear Mass (ULM), Unit of Volumetric Mass (UVM), Standard Mass Indicator (SMI)), macroscopy of the UC and chorioamnionic plaque, and the microscopic examination included histological examination with determination of the morphological epithelial-stromal-vascular criteria of the umbilical-chorioamniotic placental component.

The data were processed using modern mathematical and statistical methods in SPSS 23.0 (Statistical Package for Social Sciences), SAS 9.4 (Statistical Analysis System), and Microsoft Office Excel 2016, which provided the possibility to calculate rates, mean values, proportion indicators, and to determine the statistical significance of the results obtained at 95.0%. The normal distribution was determined using Kramer-von Mises, Kolmogorov-Smirnov, Shapiro-Wilk, and Anderson-Darling tests, with the application of the Student (t) criterion or ANOVA dispersion analysis, Kruskal-Wallis with the Wilcoxon degree of marking, the U criterion - Mann-Whitney test, the Van der Waerden test, and the median criterion (median analysis). The Fisher test was used to compare relative values. Pearson and Spearman correlation coefficients were used to determine the correlation of the indices obtained in the study for two variables with linear progression, and the Pearson chi-square criterion ($\chi 2$) was used for discrete variables. Odds ratios (OR) were calculated, indicating confidence intervals (CI). The logistic regression method was used to assess the relative risk of developing UC pathology cases (ROC curve, Sp, Se). All results obtained were reflected in tables, graphs, and diagrams.

3. CLINICAL AND ANAMNESTIC CHARACTERISTICS AND THE COURSE OF THE PERINATAL PERIOD IN UMBILICAL CORD PATHOLOGY

3.1. The anamnestic and clinical-evolutive peculiarities of pregnancy, childbirth, and the postnatal period in the pregnant women included in the study

We found that in both groups, the majority of women – 79 (83.1%) versus 88 (92.7%) – were aged between 20 and 34 years (mean 29.09±4.85 years vs. 27.86±4.36 years, $p>0.05$), with a coefficient of variation of 15.66% for L0 and 16.66% for L1, indicating absolute homogeneity of the groups based on this criterion. In the study groups, the respondents were mostly from urban areas with $\chi^2=1.01$, $p=0.31$ [OR=1.5075; CI 95% 0.6767-3.3584]. Examination of the social and economic status (marital status, educational level, place of work), compared to the data between groups, did not establish statistically significant differences ($p>0.05$). The evaluation of harmful factors at the workplace of the patients in L1 found that these factors were more frequently recorded, but only psychoemotional overloads were correlated with UC pathology with $\chi^2_{1df}=5.9047$, V Cramer=0.21; $p=0.01$ and [OR=2.5536; 95% CI 1.1861-5.4976; $p=0.01$]. The analysis of behavioral risk factors found a high incidence of harmful habits in patients with UC pathology, smoking being a determining factor with $\chi^2_{1df}=4.0461$, V Cramer=0.2; $p=0.04$. In terms of parity, the samples were heterogeneous, primiparity being a determining factor, which correlated with the risk of UC pathology with $\chi^2_{2df}=10.2928$, V Cramer=0.23; $p=0.005$. In the patients included in the study, the obstetrical history was complicated by medical and spontaneous abortions (at 2-17 weeks of gestation), pregnancies interrupted in development (at 4-15 weeks of gestation), ectopic pregnancies, cesarean sections (C-section), premature births, as well as the presence of UC pathology in previous pregnancies ($\chi^2_{2df}=18.8479$, V Cramer=0.4; $p<0.0001$). Thus, a higher number of perinatal complications

were found in patients with UC pathology. Analyzing the correlation between the number of spontaneous abortions in the history and the number of umbilical vessels on antenatal ultrasound examination, an indirect Pearson correlation was established in the baseline sample (rxy= -0.33; p=0.001), which indicates that as the number of spontaneous abortions increases, the number of umbilical vessels decreases, with the risk of vascular anomalies. From all gynecological pathologies noticed in the patients in L_1, only infertility was identified as a determining factor for UC pathology, with statistically significant data with χ^2_{2df}=7.1556, V Cramer=0.2; p=0.02. In most cases, the evolution of pregnancy was compromised by 2 or 3 medical conditions. Among all somatic diseases diagnosed in the study groups, urinary tract disorders (chronic pyelonephritis, bacteriuria, chronic cystitis, hydronephrosis, nephroptosis, renal colic, pyelonephritis, nephrolithiasis, duplicated kidney) were more frequently recorded in the extragenital pathology structure of the patients, with a rate of 40 (42.11%) cases in L_1 compared to 25 (26.32%) cases in L_0 (χ^2_{1df} = 5.2615, V Cramer = 0.2; p = 0.02 [OR = 1.2727; 95% CI 1.0323-1.5692; p = 0.02]).

The study examined the evolution, clinical management, and complications of the current pregnancy, finding that each third to fourth woman from the study group experienced at least one episode of threatened abortion, which was more frequently recorded at the 27-28 weeks of gestation (p<0.05). In the control group, polyhydramnios was detected ten times more frequently than in the study group, confirming once again that there is a correlation between polyhydramnios and UC pathology (p<0.05). The study's results showed that fetal growth restriction (FGR) was recorded only in patients from the study group (χ^2_{1df}=5.1351, V Cramer=0.2; p=0.02), with great changes in the fetoplacental complex causing fetal distress.

To evaluate the particularities of the birth evolution in the women from the research groups, we studied and analyzed the term, modality and duration of delivery, the incidence and structure of cesarean operations, as well as the complications that occurred during labor. In all study groups, vaginal delivery prevailed: 81 (85.26%) cases in L_0 vs 71 (74.73%) in L_1, while the C-section was performed more frequently in the study group – 24 (25.26%) cases vs 14 (14.74%) in L_0 (χ^2_{1df}=2.1934, V Cramer=0.1; p=0.01), urgent C-section being more frecquent: 11 (11.58%) vs 2 (2.11%) in L_0 (χ^2_{1df} =3.9100, V Cramer = 0.32; p=0.04 and [OR=5.0769; CI 95% 1.9287-27.7546]). UC pathology did not represent its self an indication for C-section, but all patients were diagnosed with UC pathology. Analyzing the complications that occurred during the labor, we can conclude that patients with UC pathology have a higher risk of dynamic dystocia [OR=4.26; CI 95% 1.14-15.90; p<0.05]. Following the evaluation of cases with ruptured membranes, it was found that in patients with umbilical pathology, it was prolonged – up to 109 hours and 45 minutes, with a mean of 9.17±17.76 (95% CI 5.11-13.23), while in L_0 it ranged from 5 minutes to 18 hours and 15 minutes, with a mean of 3.69±3.65 (95% CI 2.88-4.49) and p<0.05 (figure 2). Examination of the color of the amniotic fluid (AF) showed that in the group of patients with UC pathology, meconium fluid, thick meconium, and hemorrhagic AF were more frecquent, compared to the control group, in which the AF was predominantly transparent (χ^2_{3df} =7.4889, V Cramer = 0.2; p=0.03). The fetal distress required the acceleration of the birth by applying obstetric forceps in patients with UC pathology in 12 (12.63%) cases vs. one case in L_0 (χ^2_{1df} =11.1143, V Cramer = 0.26; p=0.0009). Postpartum uterine hemorrhage (> 500 ml) was more prevalent in patients with UC pathology: 31 (32.55%) cases compared to 16 (16.80%) cases with normal UC (p<0.05).

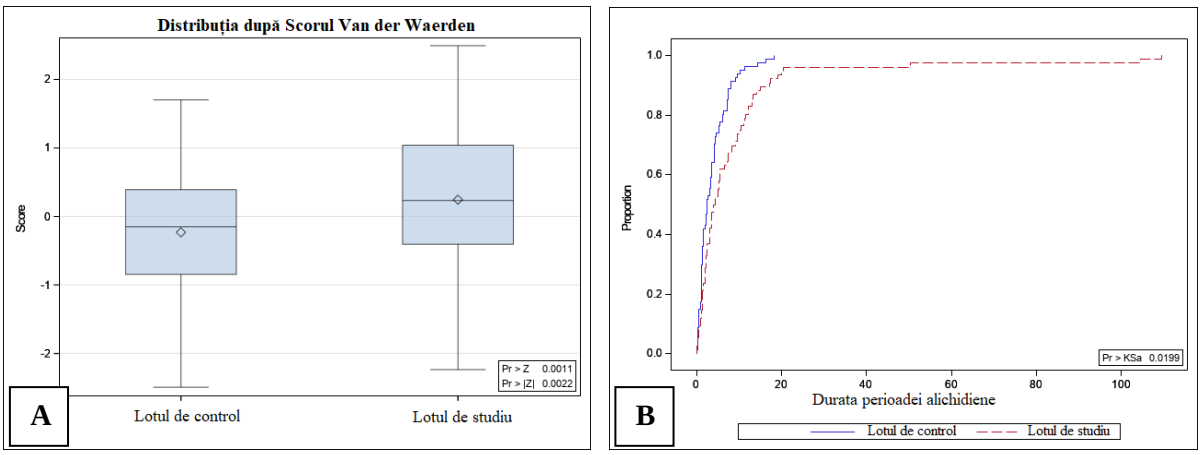

Figure 2. **Distribution of study groups based on the duration of the ruptured membranes (hours/minutes)**

Therefore, the analysis of the anamnestic and clinical peculiarities of the perinatal period in patients with UC pathology, compared to pregnant women without this pathology, allowed us to confirm that this commonly encountered obstetric condition represents a considerable risk factor for perinatal complications, with repercussions on the fetus and affecting the newborn's condition, which must be taken into account in clinical management, surveillance and conduct of pregnancy, delivery, and newborn care.

3.2. Characteristics of newborns, evaluation of perinatal morbidity and mortality structure

The impact of UC pathology on perinatal outcomes is significant, which is why the study also assessed the condition of infants born with various umbilical anomalies. The number of live newborns in the study group was 92 (96.84%), while the number of stillbirths was 3 (3.16%), while in the control group, all children were alive – 95 (100%) cases ($p < 0.05$). The obtained data showed that all cases of perinatal mortality occurred during the antenatal period in the presence of combined UC pathologies, such as: long cord ($p<0.0001$), vascular abnormalities (varices, hematoma) ($p<0.0001$), Wharton's jelly constriction ($p=0.01$), and torsion ($p=0.02$). In terms of the sex, the number of children from both study groups was the same ($p = 0.46$). The newborn state was assessed according to the Apgar score (Table 1).

Table 1. **Distribution of newborns according to Apgar score in study groups (abs./%)**

Apgar score (points)	**Study group (n=95)**		**Control group (n=95)**		**p-value**
	1'	5'	1'	5'	
Severe asphyxia: 0-3 points	4 (4,2)	3 (3,15)	-	-	< 0,0001
Moderate asphyxia: 4-5 points	2 (2,1)	1 (1,05)	-	-	
Mild asphyxia: 6-7 points	23 (24,2)	13 (13,7)	4 (4,2)	-	
Apgar 8-10 points.	66 (69,5)	78 (82,1)	91 (95,8)	95 (100)	

The assessment of the frequency of asphyxia in newborns found that in the first minute of life, in the study group, the Apgar score was 0-3 points in 4 (4.2%) cases, 4-5 points in 2 (2.1%), 6-7 points in 23 (24.2%) cases, and 8-10 points in 66 (69.5%) cases, with a mean of 7.46±1.65 points (95% CI 7.12-7.80). In the control group, only 4 (4.2%) children were born with mild

asphyxia – 6-7 points, while the remaining 91 (95.8%) cases were recorded with 8-10 points, with a mean of 8.66±0.69 (95% CI 8.52-8.80) points.

In the fifth minute after birth, this ratio was: 0-3 points in 3 (3.15%) cases, 4-5 points in one case (1.05%), 6-7 points in 13 (13.7%) cases, and 8-10 points in 78 (82.1%) cases, with a mean of 8.01±1.7 (95% CI 7.66-8.35). The children's wellbeing included in the control group at five minutes of life was satisfactory in all cases, with an assessment of 8-10 points and a mean of 9.13±0.67 points (95% CI 8.99-9.27).

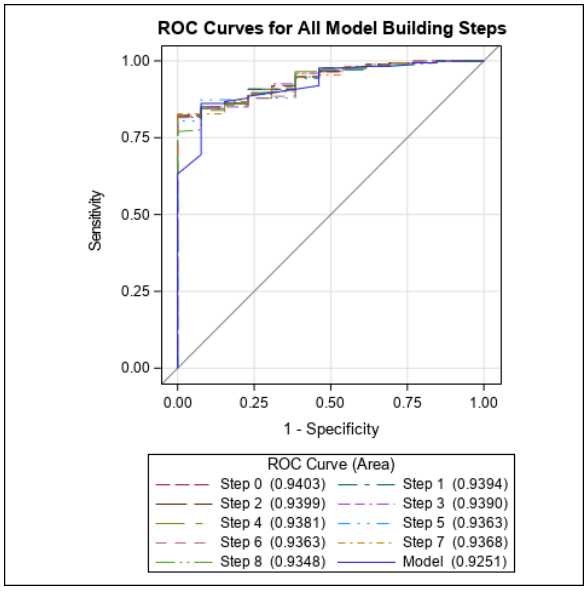

Figure 3. **ROC curve of the predictive model of the probability of admission to the Neonatal Intensive Care Unit (NICU) of newborns with pathology, based on the adaptation period.**

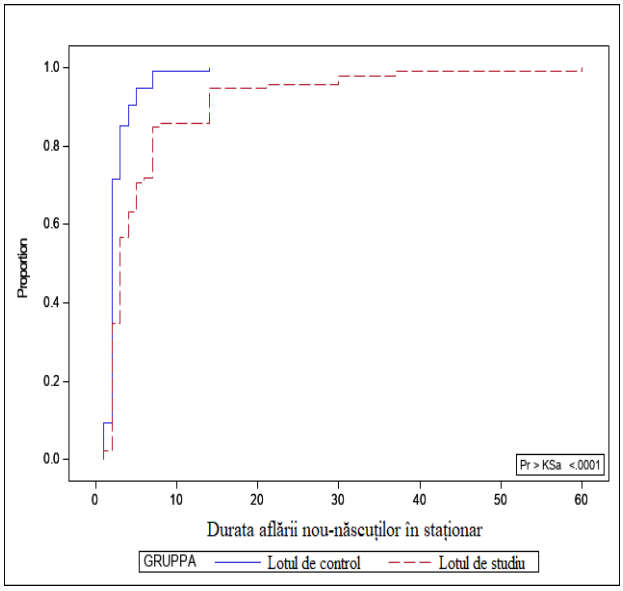

Figure 4. **Distribution of groups by admission duration of newborns (days/patient)**

A number of newborns with UC pathology whom suffered birth asphyxia required special care and were admitted to the neonatal intensive care unit (NICU) in 13 (14.13%) cases (figure 3). The adaptation status of newborns with normal UC was physiological in all cases, and they did not require additional care (χ^2_{1df} =14.42, V Cramer=0.3; p=0.0001).

The newborns from the study group developed multiple neonatal pathologies were diagnosed compared to the control group (χ^2_{1df}=28.18, V Cramer=0.38; p<0.0001 and [OR=1.18; CI 95% 1.1-1.35]): acute fetal hypoxia, intrauterine infection, congenital pneumonia, different level of respiratory distress syndrome, FGR, iron-deficiency anemia, hyperbilirubinemia, birth trauma (cephalohematoma, intracranial hemorrhage), and metabolic, respiratory, and circulatory disorders (Table 2, Figure 5).

Fetal growth restriction is a serious pathology, which in the present study was diagnosed during the pregnancy, resulting from the disruption of the supply of necessary nutrients for fetal growth and profound changes in the fetoplacental complex, causing to fetal distress. The obtained results showed that FGR was only recorded in patients from the study group, and it was absent in the control group, with χ^2_{1df}=5.1351, V Cramer=0.2, p=0.02. The predictive model had an AUC (Area Under the Curve) of 0.8679 (Figure 6).

Table 2. **Neonatal morbidity structure in study groups (abs./%)**

Neonatal pathology	Study group (n=58)	Control group (n=21)	χ^2	p
Acute hypoxia	30 (32,26%)	1 (1,05%)	33,23	<0,0001
Fetal growth restriction	4 (6,9%)	0	1,52	<0,05
Intrauterine infection	5 (8,62%)	1 (4,76%)	0,33	<0,05
Congenital pneumonia	10 (17,24%)	1 (4,76%)	2,00	<0,05
Respiratory distress syndrome: - mild - moderate - severe	 1 (1,72%) 3 (5,17%) 5 (8,62%)	 1 (4,76%) 0 0	4,44	<0,05
Respiratory disorders (pneumopathy, transient tachypnea)	31 (53,45%)	6 (28,57%)	3,83	<0,05
Circulatory disorders (cardiac defects, thrombocytopenia)	8 (13,79%)	0	3,22	<0,05
Birth trauma (cephalhematoma, intracranial hemorrhage)	9 (15,52%)	1 (4,76%)	1,61	<0,05
Metabolic disorders (acidosis, hypoglycemia	8 (13,79%)	2 (9,52%)	0,25	<0,05
Neurological disorders (encephalopathy, convulsive syndrome)	6 (10,34%)	0	2,35	<0,05
Iron deficiency anemia	11 (18,97%)	7 (33,3%)	1,80	0,17
Hyperbilirubinemia (neonatal jaundice)	18 (31,03%)	10 (47,62%)	1,85	0,17

Note. Test statistic - χ^2 applied

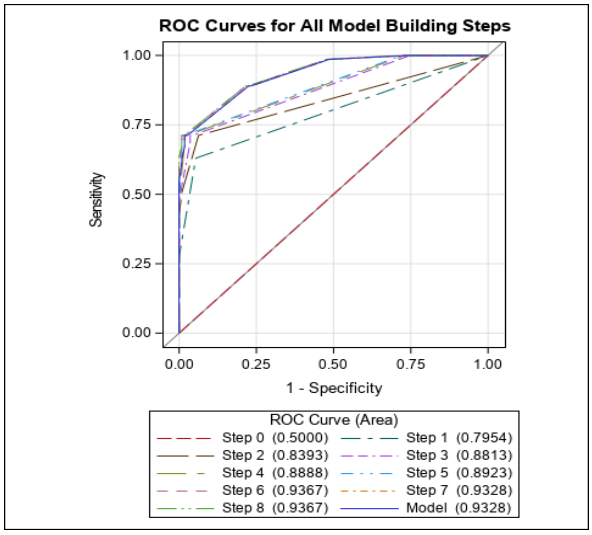

Figure 5. **ROC curve of the predictive model for the probability of morbidity in newborns with UC pathology**

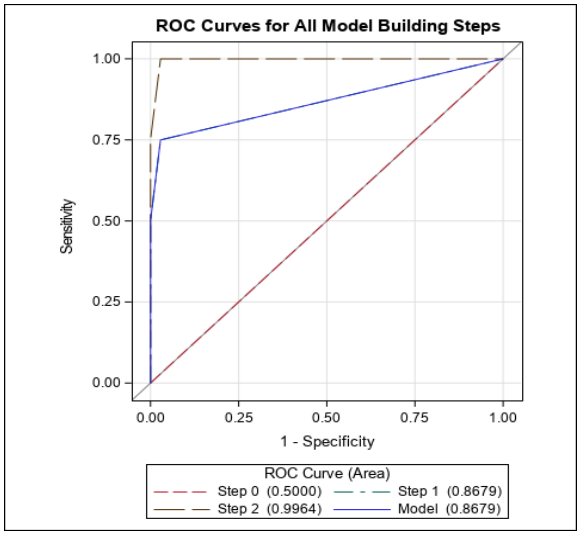

Figure 6. **ROC curve of the predictive model for the probability of developing FGR in case of UC pathology based on perinatal morbidity**

During the research, the hospital stay duration of the children in both groups was analyzed. Children with UC pathology were admitted in the hospital for a longer period, between 1 and 60 days/patient, with an average of 6.18±8.46 (95% CI 4.43–7.93), while in the control group, this indicator ranged between 1 and 14 days/patient, with an average of 2.61±1.74 (95% CI 2.25–

2.96; p<0.0001) (Figure 4), mostly due to early neonatal morbidity requiring additional postnatal care.

Therefore, significant differences were found between the study groups in term os newborns characteristics (p<0.0001). UC pathology had a negative impact on the newborn's condition, which led itself to an increased incidence of perinatal morbidity and mortality.

3.3. The peculiarities of the perinatal period evolution according to the type of umbilical anomaly.

Assesing the prevalence of UC abnormalities in the study group (L_1), they were divided into subgroups according to the classification, which included: length anomalies: long – 24 (25.26%), short – 21 (22.11%); diameter anomalies: thin – 24 (25.26%), thick – 16 (16.84%); insertion anomalies: marginal – 39 (41.05%), velamentous – 8 (8.42%); vascular anomalies: single umbilical artery (SUA) – one case (1.05%), supernumerary vessels – 7 (7.37%), varices – 28 (29.47%), hematoma – 1 (1.05%); knots: true – 8 (8.42%), false – 24 (25.26%); Wharton's jelly pathology: cysts – 4 (4.21%), pseudocysts – 7 (7.37%), coarctation – 4 (4.21%); pathologies based on the coiling index: hypocoiling – 34 (35.79%), hypercoiling – 7 (7.37%), torsion – 6 (6.32%); location: circular – 63 (66.32%); infection (funisitis) – 3 (3.16%) cases.

This subchapter presents the main pathologies of the UC, with the exposition of the anamnestic, clinical characteristics of pregnancy and delivery, and the perinatal results of the patients included in the study, reflected in tables.

Based on the obtained results, it was found that in cases of umbilical pathology, placental insufficiency, FGR developed later by fetal hypoxia during childbirth, the most difficult adaptation period of the newborn, as well as a higher level of morbidity in these children were more frequently observed (p <0.05).

4. FETOPLACENTAL STATUS AND STRUCTURAL-FUNCTIONAL PARTICULARITIES OF THE UMBILICAL CORD AND CHORIOAMNIOTIC PLAQUE IN DIFFERENT UMBILICAL PATHOLOGIES.

4.1. Prenatal examination of the placental complex and fetal status in pregnant women with UC abnormality.

Within the conducted study, in order to evaluate the fetal-placental system comprehensively, three research methods were used that complement each other: ultrasound examination (US), Doppler velocimetry, and cardiotocography (CTG). Information about the fetal state, placental insertion, size and structure, and UC characteristics were obtained through ultrasound examination with Doppler velocimetry. In pregnant women with UC abnormality, pathological changes in the placenta (p<0.05) were more frequently, which were associated with by placental circulatory insufficiency (χ^2_{1df} = 10.5556, V Cramer = 0.23; p=0.001) with the development of FGR (Figure 6, 7). The UC pathologies in which circulatory insufficiency was determined are as follows: velamentous insertion (p=0.04), single umbilical artery (p=0.0004), varices (p=0.0004), thin cord due to the absence of Wharton's jelly (p=0.02), thick cord (p=0.0005), hypocoiling or torsion cord (p=0.0009), and funisitis (p=0.02).

Correlational analysis, conducted to determine a relationship between the number of umbilical vessels on ultrasound and the degree of FGR (weeks of gestation), established a strong indirect Pearson linear correlation in L_1 (rxy= -0.88; p=0.04), demonstrating that these criteria

correlate in opposite directions: the smaller is number of umbilical vessels, the greater is degree of fetal restriction, and vice versa.

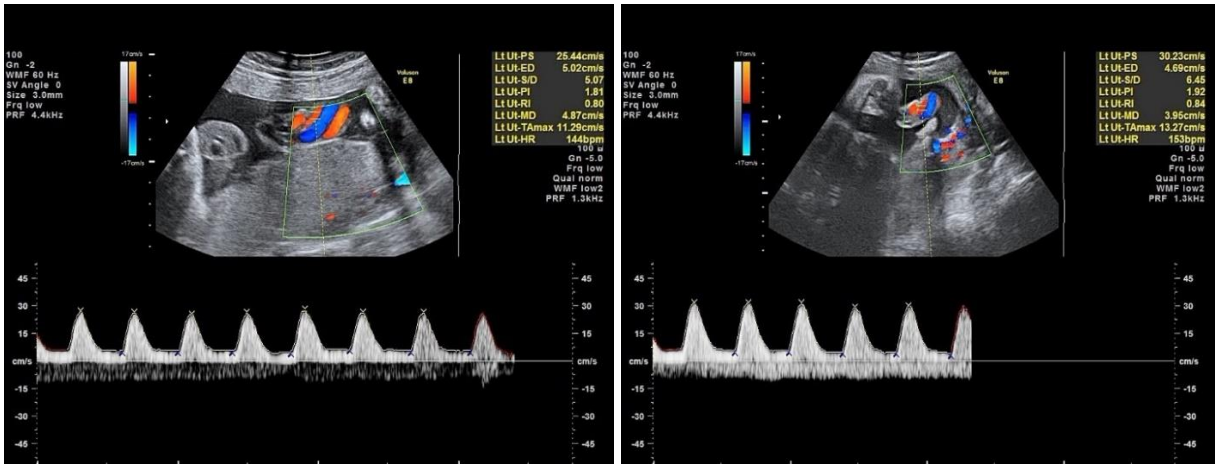

Figure 6. **Doppler velocimetry with decreased telediastolic flow in the umbilical artery due to pathologically increased resistance in the placental territory; cerebroplacental ratio of 1.26, corresponding to the 3rd percentile: severe symmetric FGR**

CTG was used to diagnose the disruption of umbilical blood flow, incipient signs of intrauterine hypoxia, or a reflex cardiac reaction to UC irritation. In the study group, the cardiotocographic trace was identified more frequently as suspect and pathological compared to the control group (χ^2_{2df}=54.45, V Cramer=0.54; p<0.0001). An abnormal baseline rhythm (<100 bpm or >160 bpm), modified variability (reduced, increased, or sinusoidal trace), and decelerations (sporadic or repetitive) revealed a suspect and pathological CTG.

To assess the importance and informativeness of fetal CTG examination in patients with UC pathology, we compared (NICE 2017) with the newborn's Apgar score (Table 3). These data determined that children born with UC pathology more frequently had different level of asphyxia and were assessed with a significantly lower Apgar score than children in the control group (p<0.0001).

Table 3. **Cardiotocographic tracings according to the newborns' condition**

Study groups	**Cardiotocographic tracing**			**Apgar score at 1 minute**			**p**
	Character	**abs.**	**%**	**8-10 points**	**6-7 points**	**3-5 points**	
L_1	Normal	42	45,65	40 (43,48%)	2 (2,17%)	-	< 0,0001
	Suspicious	31	33,7	20 (21,74%)	11 (11,95%)	-	
	Pathologic	19	20,65	7 (7,61%)	9 (9,78%)	3 (3,26%)	
L_0	Normal	90	94,74	90 (94,74%)	-	-	
	Suspicious	4	4,21	3 (3,16%)	1 (1,05%)	-	
	Pathologic	1	1,05	-	1 (1,05%)	-	

Thus, we can once again observe the importance of intrauterine monitoring of the fetus in pregnancies with increased risk, and CTG seemed to represent as one of the simplest, modern, non-invasive, and reliable methods for assessing fetal status, which fully meets current requirements, provided that it is correctly recorded and interpreted.

4.2. Morphological and morphometric characteristics of UC and CAP in the patients included in the study.

Morphological examination of UC and chorioamnionic plaque (CAP) is one of the most reliable postnatal diagnostic methods, providing detailed information about the characteristics of the epithelial-stromal-vascular component (Figure 8). Furthermore, it enables the evaluation of their role in chronic or acute hemodynamic disorders in the fetoplacental circulation. It also allows for the objective analysis of clinically significant information by determining and estimating morphological factors of obstetrical, ultrasound, and neonatal importance.

Analyzing the CAP of placental CAP established the predominance of irregular wavy surface (χ^2_{1df}=54.3727, V Cramer 0.53; p<0.0001), plaque thickness up to 0.5 cm (χ^2_{2df}=10.3836, V Cramer 0.23; p=0.005), and disordered vascularization (χ^2_{4df}=47.3820, V Cramer 0.50; p<0.0001) in the eccentric zones in cases with UC abnormality.

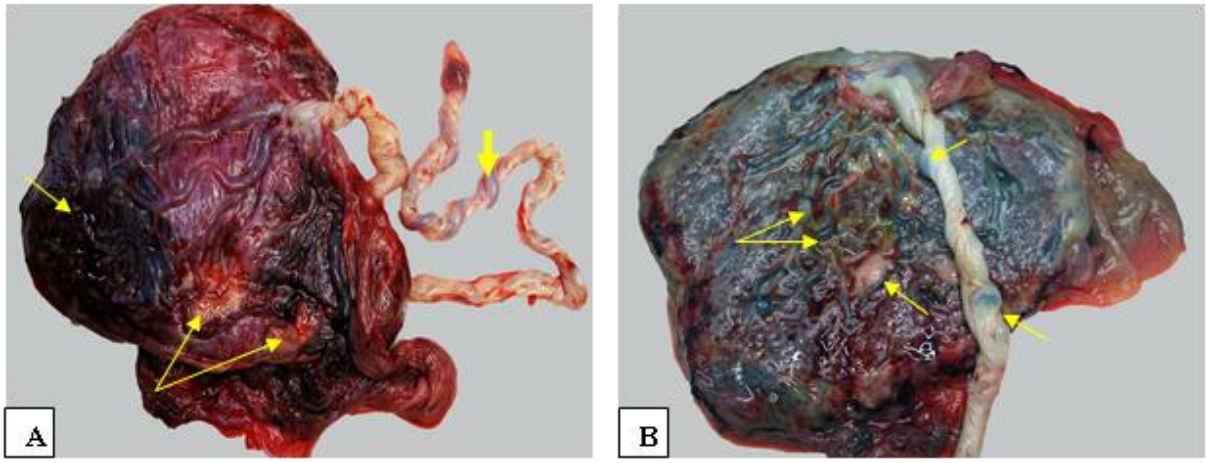

Figure 8. **Overview aspects of the umbilical-chorioamniotic placental component:** A – varicose ectasia of an umbilical vessel, predominantly in the fetal segment, and segmental zonal involvement of the chorionic plate with hemorrhage and ischemic infarcts; B – segmental dilations in a pseudodiverticular loop-like appearance along the UC, segmental varicose ectasia of the vessels in the CAP with a straight and wavy course, and small infarcts.

The morphological and morphometric study of UC found that the compared study groups is different in the following organometric indicators. The proposed method of organometric assessment of the UC has allowed for the determination of risks associated with pathological manifestations in newborns due to placental-umbilical-fetal dysfunctions, as follows:

• *Normal umbilical cord* (D = 0.8-1.2 cm, ULM = 0.5-0.98 g/cm, SMI = 25-49 g) – absence of the risk of pathological clinical manifestations in the newborn.

• *Suspected pathological UC* (D = < 0.8 or > 1.2 cm, ULM = < 0.55 or > 0.98 g/cm, SMI = < 25 or > 49 g) – minor risk of pathological clinical manifestations in the newborn.

• *Suggestively pathological UC* (D = < 0.8 cm or > 1.2 cm OR ULM = < 0.55 or > 0.98 g/cm, SMI = < 25 or > 49 g) – moderate risk of pathological clinical manifestations in the newborn

• *Evidently pathological UC* (D = < 0.8 or > 1.2 cm; ULM = < 0.55 or > 0.98 g/cm, SMI = < 25 or > 49 g, with morphofunctional changes) – high risk of pathological clinical manifestations in the newborn.

The correlational analysis, performed to determine the relationship between the average diameter of UC and the unit of linear mass (ULM), the standard mass indicator of UC (SMI), established a direct Pearson linear correlation in L_1 (rxy=0.512; p=0.0001).

Therefore, we can conclude that the determination of organometric indicators of the UC allows us to diagnose its pathology, including these newborns in the high-risk group for the development of pathological processes and immediate or delayed hypoxic complications. This calls for more careful monitoring of these calculable indicators, performing additional paraclinical investigations, and avoiding premature discharge of the newborns. The proposed examination method represents the standardized clinical and organometric express method of diagnosis to dermine the predictors of newborn morbidity and mortality.

4.3. Microscopic morphofunctional characteristics of the epithelial-stromal-vascular components of the umbilical cord and the chorioamnionic plaque

Within the conducted study, the microanatomical and morphometric characteristics of the epithelial-stromal-vascular structural components of the UC and placental CAP were evaluated and determined in normal and abnormal cases of UC diagnosed by US and confirmed morphologically. The morphological profile of the UC was examined in both groups in three segments: placental, middle (intermediate, central) and fetal, which varied in a diverse ratio both in terms of length and structure of the UC. Analyzing the UC in cross-section, it was observed that in L_1, modified forms predominated in all three segments: curved, coiled, scalloped, triangular, knotted, twisted, flattened, and dissociated forms, which were practically absent in the control group. These findings were statistically significant ($p<0.05$).

The study established the cellular heterogeneity of the UC stroma, which, in correlation with the vascular component, manifested in four cellular-functional zones: peripheral or subepithelial zone (SEZ); intermediate zone (IMZ), divided into subepithelial and perivascular zones; perivascular zone (PVZ); and intervascular zone (IVZ) (Figure 9).

The structure of the umbilical vessels was identified as elastico-muscular, with the importance of the elastic component in the correct and orderly development of vessels, mechanical resistance, maintenance of blood flow, prevention of collapse, circulatory disorders, and thrombosis formation. Thus, the decrease in the vascular elastic component leads to the development of structural-functional abnormalities with disturbances in placental circulation (Figure 10).

Vascular abnormalities of the UC are directly related to vascular abnormalities of the CAP and the intermediate and trunk villous chorion, which largely contribute to various disorders in the villous vascular network and blood flow in the subchorion area. All above-mentioned are associated with rheological disorders, appearance of pseudoinfarcts, intervilous thrombosis (Figure 11), which subsequently have a negative impact on the fetus.

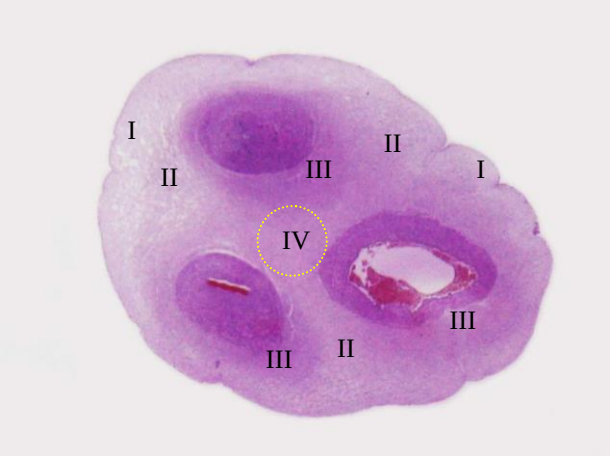

Figure 9. **Topographic histological section of the stromal cellular zones:** I - Subepithelial Zone (SEZ); II - Intermediate Zone (IMZ), divided into subepithelial and perivascular subzones; III - Perivascular Zone (PVZ); IV - Intervascular Zone (IVZ) *x 6. H&E staining*

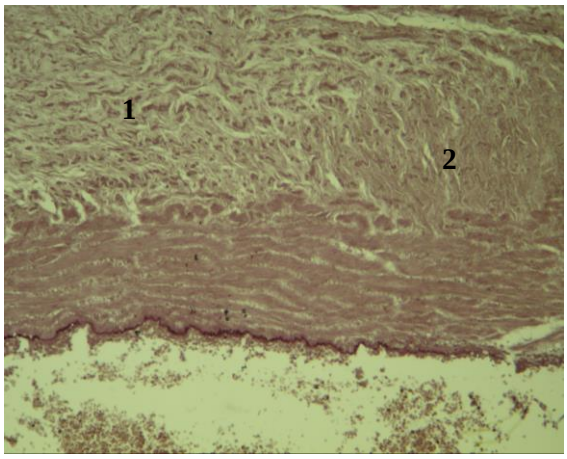

Figure 10. **Umbilical vein:** absence of elastic component in the muscle layer, atrophy of the outer muscle layer with accentuation of the connective tissue component (1) and focal sclerogenic changes (2) *x250. Orcein staining*

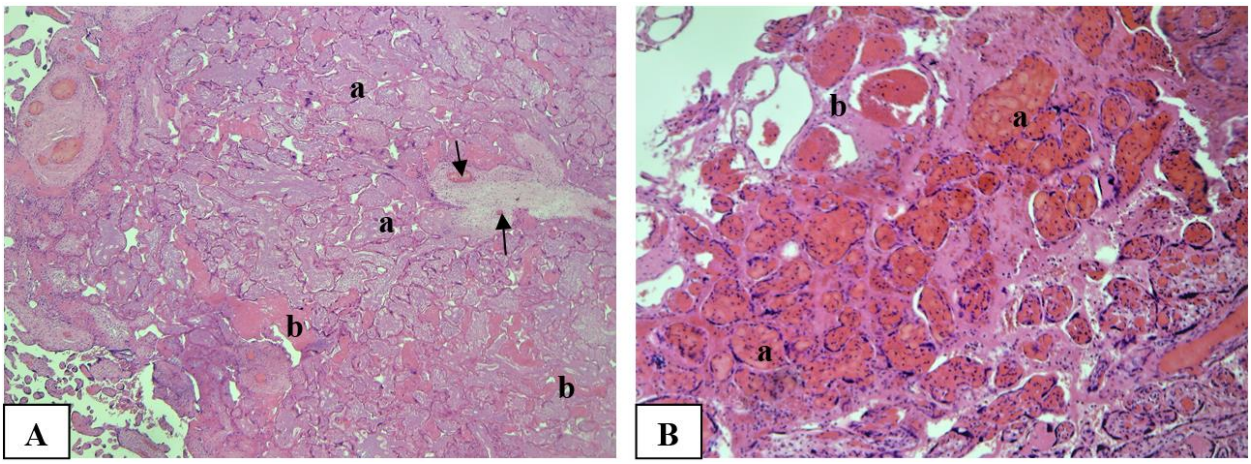

Figure 11. **Aspects of focal acute circulatory disorders in placental parenchyma: A** - acute thrombosis of intermediate villous vessels (arrow) with ischemic necrosis of distal-terminal villi with empty vessels (a), deposition of intervillous fibrin (b) at the periphery of the villous tree; **B -** thrombotic congestive stasis with hemorrhage in villous stroma (a), intermediate-type villous with varicose dilation of vessels (b) *x50. H&E staining*

Thus, during the study, a connection was established between the microscopic epithelial-stromal-vascular changes detected in pathological UC (irregular cord forms in cross-section, flattened unistratified amniotic epithelium with squamous metaplasia, loose cellular stroma, Wharton's jelly edema, focal intraparietal vascular and perivascular hemorrhage) and the pathological discirculatory status of the placental chorionic villous zone and subchorionic intervilous spaces. This was manifested by increased perinatal morbidity in the research group ($p<0.05$).

4.4. Morphopathological structural and functional features in different pathologies of the umbilical cord

This subchapter describes the anatomical, structural and functional profile of pathological UC and its influence on the placenta's chorionic plate and subchorionic intervillous spaces, aiming to determine the morbid-lesional and discirculatory status. The impact on the perinatal period and the well-being of the fetus and newborn was also assessed.

Umbilical cord abnormalities were classified into three main groups: 1) macro/microanatomical developmental abnormalities; 2) morphofunctional abnormalities acquired during pregnancy and childbirth; 3) incidental abnormalities, which included many subgroups with descriptions of macro- and microscopic features for each.

Thus, the examination of micro/macroanatomical structural and functional features of fetal annexes found a wide range of UC abnormalities with various repercussions on the placental chorionamnion plaque and subchorial intervillous spaces, manifested by the disruption of placental function and intrauterine hypoxia with fetal growth disturbances, which dictate the need to identify these UC pathologies during pregnancy, with appropriate obstetric clinical management adjustments.

CONCLUSIONS

1. The results of the study demonstrate the importance of researching the determinants of UC pathology, which negatively influence the fetal state. The development of Cord pathology was frequently observed in pregnant women with harmful workplace factors (psychological and emotional stress, p=0.01), harmful habits (smoking, p=0.04), primiparas (p=0.005) with complicated gynecological (infertility, p=0.02) and somatic (urinary tract diseases, p=0.02) histories, as well as those with a history of UC pathology in previous pregnancies (p<0.0001).
2. The evolution of pregnancy and labor in patients with cord pathology highlighted a high rate of complications compared to control group, including preterm labor at 27-28 weeks (p=0.01), polyhydramnios ten times more frequent (p=0.002), and fetal growth restriction (p=0.02). In the study group, labor dystocia was determined (p=0.02), with a high level for dynamic dystocia [OR=4.26; CI 95% 1.14-15.9; p<0.05], prolonged second stage (p=0.01), amniotic fluid stained with meconium (p=0.03), and acute fetal hypoxia, which required urgent termination of the pregnancy (p=0.01) through vacuum extraction (p=0.0009) or C-section (p=0.04).
3. The study showed that UC pathology had a negative impact on the fetus and newborn, which developed an increased incidence of perinatal mortality and morbidity (p<0.0001). Newborns from the study group were more frequently appreciated with different level of asphyxia, being assessed with a significantly lower Apgar score, requiring a pathological adaptation period (p=0.0001), compared to newborns in the control group (p<0.0001).
4. The morbidity level among newborns was higher in the study group and frequently developed as FGR, intrauterine infection, birth trauma, respiratory, neurological, metabolic, and circulatory disorders, requiring additional postnatal care (p<0.05). Therefore, the immediate identification of cord pathology after birth requires including these newborns in the high-risk group for possible neonatal complications.
5. The study established a correlation between the UC abnormalities and various pathological changes in the chorioamnionic plaque and intervillous space, presented by irregular surface (p<0.0001), thickening of the chorion (p=0.005), and disordered vascularization in peripheral

zones ($p<0.0001$). These morphopathological placental changes were associated with ultrasonographically established placental circulatory insufficiency during pregnancy ($p=0.001$) in cases of UC pathology, leading to the development of intrauterine hypoxia. This highlights the importance of early identification of umbilical pathologies during pregnancy and appropriate adjustment of obstetric clinical management.

PRACTICAL RECOMMENDATIONS

For the effective and rational management of patients with UC pathology and improvement of perinatal outcomes, the following recommendations are suggested:

1. To perform an US examination with Doppler velocimetry, which will include a detailed study of the UC structure on longitudinal and transverse sections (number of umbilical vessels, Wharton's jelly, UC diameter, coiling index, insertion site of the umbilical cord in the placenta, its position in relation to the fetus, and diagnosis of different anomalies) and fetal-placental circulation (type of blood flow of the umbilical cord vessels). This examination should be performed between 10-14 weeks of gestation (I screening), then repeated in the second and third trimesters of pregnancy, only this approach will help to determine UC anomalies in early pregnancy, in order to decide about a proper management.
2. To use the Standardized clinical protocols *Umbilical Cord Procidence and Prolapse* and *Management of Pregnancy and Delivery in Patients with Umbilical Cord Pathology* (Annex 5) to optimize obstetric management.
3. To use the CTG to monitoring the fetal state and appreciate the fetal distress in early time, in order to decide the best management.
4. To assess mandatory the UC characteristics, morphological and morphometric indicators in postpartum, according to the *Protocol for examining the structural-functional characteristics of the umbilical cord and chorionamnion plaque* (Annex 2) and *Morphopathological classification* (in the thesis – subchapter 4.4).
5. To use the assessment of UC organometric indicators (MDUC, UVM, ULM, SMI), as predictive markers of fetal development disorders, in order to determine the neonatal morbidity and mortality risks and prevent immediate or late hypoxic complications (in the thesis – subchapter 4.2).
6. To include the study results, related to the morphological and functional structure, and the classification of UC, also CAP abnormalities and their influnce on neonatal complications, in *Nicolae Testemitanu* State University of Medicine and Pharmacy educational programms, in order to informe medical staff.

REFERENCES

1. Alsatou A. Morbiditatea și mortalitatea nou-născuților în diferite patologii ale cordonului ombilical. In: *Buletin de perinatologie*. 2018; 2(78): 118-124. ISSN 1810-5289.
2. Bursacovschi N. Rolul patologiei placentei și anexelor în decesul intrauterin al fătului. In: *Buletin de perinatologie*. 2019; 4(85): 45-51. ISSN 1810-5289.
3. Cotorcea V, Fuior-Bulhac L. *Ecografia în obstetrică: noțiuni generale*. Asociația de Medicină Perinatală din Republica Moldova. Ch.: ”Foxtrot” SRL, 2010. 38 p. ISBN 978-9975-4138-8-6.
4. Gladun E, Ștemberg M, Stratulat P, Friptu V, Petrov V, Corolcova N. *Complexul fetoplacentar (aspecte perinatale)*. Chișinău, 2000. 190 p.
5. Paladi Gh, Tabuica U, Stavinskaia L. Aspecte contemporane de conduită şi rezultatele perinatale ale naşterii premature. *Buletin de perinatologie*. 2014; 2(62): 5-8.
6. Paladi Gh, Tabuica U. Fiziologia și patologia cordonului ombilical. *Buletinul Academiei de Științe a Moldovei. Științe medicale*. 2007; (2):102-110.
7. Rădulescu C, Pătraşcu G, Mateescu R, Matei A, Antoine E. Mortalitatea perinatală. Studiu clinic. *Practica medicală*, București. 2014; 9(2/34): 95-100.
8. Serbencu A, Fuior I, Moșin V, Darii A. *Dezvoltarea, structura și funcțiile placentei umane: material didactic*. Chișinău, 1999. 48 p.
9. Stratulat P, Curteanu A. Proiectul „Modernizarea sistemului perinatal din Republica Moldova”. Realizări principale şi perspective (2006-2011). *Buletin de perinatologie*. 2010; 4(48): 3-12.
10. Tăutu R, Bogdan A. Influența patologiei anexelor fetale asupra morbidității și mortalității perinatale. In: *Materialele Conferinței de medicină perinatală cu participare internațională. Buletin de perinatologie*. 2011; 3-4: 82-85.
11. Baergen RN. *Manual of pathology of the human placenta.* New York: Springer; 2011. 540 p. ISBN 978-0387220895.
12. Baron J, Weintraub AY, Sciaky Y, Mastrolia SA, Speigel E, Hershkovitz R. Umbilical artery blood flows among pregnancies with single umbilical artery: a prospective case-control study. *J. Matern Fetal Neonatal Med*. 2015; 28(15):1803-1805.
13. Bhadrashetty N, Gomathy E. Association of umbilical cord abnormalities and nonreassuring fetal heart rate and its perinatal outcome. *Int. J. Clin. Obstet. Gynaecol*. 2021; 5(2): 28-32. doi: 10.33545/gynae.2021.v5.i2a.862
14. Dogan S, Özyüncü Ö, Atak Z, Turgal M. Perinatal outcome in cases of isolated single umbilical artery and its effects on neonatal cord blood gas indices. *J. Obstet. Gynaecol*. 2014; 34: 576-579.
15. Ghezzi F, Raio L, Gunter Duwe D, Cromi A, Karousou E, Dürig P. Sonographic umbilical vessel morphometry and perinatal outcome of fetuses with a lean umbilical cord. *J. Clin. Ultrasound*. 2005; 33(1): 18-23.
16. Grottling E, Gisselsson D. Changes in the Prevalence of Embryologic. Remnants in Umbilical Cord with Gestational Age. *Pediatric and Developmental Pathology*. 2018: 1-4.
17. Güven D, Altunkaynak BZ, Altun G, Alkan I, Kocak I. Histomorphometric changes in the placenta and umbilical cord during complications of pregnancy. *Biotech. Histochem*. 2018; 93(3): 198-210. doi: 10.1080/10520295.2017.1410993.

18. Jessop FA, Lees CC, Pathak S, Hook CE, Sebire NJ. Umbilical cord coiling: clinical outcomes in an unselected population and systematic review. *Virchows Arch*. 2014; 464(1):105-112. ISSN 0945-6317.

19. Jo YS, Jang DK, Lee G. The sonographic umbilical cord coiling in late second trimester of gestation and perinatal outcomes. *Int J Med Sci.* 2011; 8: 594-598.

20. Kellow ZS, Feldstein VA. Ultrasound of the placenta and umbilical cord: a review. *Ultrasound Q*. 2011; 27(3): 187-197.

21. Olaya-C M, Gil F, Salcedo JD, Salazar AJ, Silva JL, Bernal JE. Anatomical pathology of the umbilical cord and its maternal and fetal clinical associations in 434 newborns. *Pediatr Dev Pathol*. 2018; 21(5): 467-474. doi: 10.1177/1093526618758204.

22. Pergialiotis V, Kotrogianni P, Koutaki D, Christopoulos-Timogiannakis E, Papantoniou N, Daskalakis G. Umbilical cord coiling index for the prediction of adverse pregnancy outcomes: a meta-analysis and sequential analysis. *J. Matern Fetal Neonatal Med*. 2020; 33(23): 4022-4029. doi: 10.1080/14767058.2019.1594187.

23. Rebecca NB. Umbilical cord pathology. *Surgical Pathol Clin*. 2013; 6(1): 61-85.

24. Sabnis AS. Umbilical cord morphology and its clinical significance. *Med Case Rep.* 2012; 3(1): 30-33. ISSN 2638-4558.

25. Silini AR, Di Pietro R, Lang-Olip I, Alviano F, Banerjee A, Basile M, et al. Perinatal Derivatives: Where Do We Stand? A Roadmap of the Human Placenta and Consensus for Tissue and Cell Nomenclature. *Frontiers Bioengineering and Biotehnology*. 2020; 8:1-33, art. 610544.

26. Tulek F, Kahraman A, Taskin S, Özkavukçu E, Söylemez F. Determination of risk factors and perinatal outcomes of singleton pregnancies complicated by isolated single umbilical artery in Turkish population. *J Turkish German Gynecol Assoc*. 2015; 16(1):21-24. ISSN 0301-2115.

27. World Health Organization. *Born too soon: the global action report on preterm birth.* Geneva: WHO; 2012. 126 p.

28. Абдулаева ЖО, Омаров С. Перинатальные исходы при патологии пуповины плода. *Вестник новых медицинских технологий*. 2008; 15(2): 52-53.

29. Абдулаева ЖО, Омаров С-МА. *Патология пуповины плода*: *Монография.* Махачкала: РАМН; 2009. 121 с. ISBN 978-5-94434-143-3.

30. Коган ЯЭ. Патология пуповины и ее роль в перинатальных осложнениях. *Практическая медицина*. 2016; 93(1): 22-25. ISSN 2072-1757.

31. Кондакова ЛИ. Органометрические показатели пуповины в норме и при патологии беременности. *Успехи современного естествознания*. 2009; (6):34-38. ISSN 1681-7494.

32. Медведев МВ. *Трехмерная эхография в акушерстве* (т. 7). М.: Реал Тайм; 2007. 168 с. ISBN 9785903025091.

33. Фадеева ТЮ. *Клинико-функциональные особенности развития плода и новорожденного с задержкой внутриутробного развития*: автореф. дис... канд. мед. наук. Владивосток; 2012. 23 с.

34. Флейшер А. Эхографическое обследование пуповины и плодных оболочек. *Эхография в акушерстве и гинекологии*: *теория и практика*. 6-е изд. В 2 ч. Ч. 1. Пер. с англ. М.И. Агеевой. М.: Видар-М. 2005; 247-268.

LIST OF PUBLICATIONS

- **Articles in scientific journals abroad**
  - ✓ **articles in peer-reviewed foreign journals:**

1. **Alsatou AS**, Voloceai VF, Corolcova NM. Intrauterine fetal death after multiple umbilical cord abnormalities. Clinical case. [Антенатальная гибель доношенного плода при сочетанной патологии пуповины. Клинический случай]. In: *MEDICUS. International Medical Scientific Journal.* Volgograd, 2018; 5(23): 8-11. ISSN 2409-563X.
2. **Alsatou AS**, Burac MM, Corolcova NM, Petrovici VG. Clinical and histological aspects of the umbilical cord abnormalities as a risk factor for perinatal mortality. *MEDICUS. International Medical Scientific Journal*. Volgograd, 2020; 1(31): 8-14. ISSN 2409-563X.

- **Articles in accredited national scientific journals**
  - ✓**B + category:**

3. **Alsatou A.** Umbilical cord coiling abnormality as a predictor of maternal and fetal outcomes. In: *Moldovan Medical Journal.* 2020; 63(1): 29-32. ISSN 2537-6373. DOI:10.5281/zenodo.3685677.
4. **Alsatou A**, Petrovici V, Corolcova N. Clinico-morphological aspects and outcomes of the lean umbilical cord. *Moldovan Medical Journal.* 2020; 63(2): 25-30. ISSN 2537-6373. DOI:10.5281/zenodo.3865990.

  - ✓**B category:**

5. **Alsatou A**. Morbiditatea și mortalitatea nou-născuților în diferite patologii ale cordonului ombilical. *Buletin de perinatologie.* 2018; 2(78): 118-124. ISSN 1810-5289.

  - ✓**C category:**

6. **Alsatou A**. Particularitățile materno-fetale în diferite anomalii ale cordonului ombilical. *Buletinul Academiei de Ştiinţe a Moldovei. Ştiinţe Medicale.* 2018; (2-3/59-60): 144-148. ISSN 1857-0011.

- **Articles in the proceedings of scientific conferences**
  - ✓**internaţional events held abroad:**

7. **Алсатоу А**, Дондюк Ю. Особенности аномального прикрепления пуповины: современный взгляд. В: *Материалы XXXIV Международной научно-практической интернет-конференции «Тенденции и перспективы развития науки и образования в условиях глобализации»: Сб. науч. трудов.* 30 марта 2018 года, Украина, Переяслав-Хмельницкий; 2018. с. 561-563.

- **Abstracts in the proceedings of national and international scientific conferences:**

8. **Alsatou A**. Analysis of the risk factors for development of umbilical cord entanglement. In: *The 15th International Congress for Medical Students and Young Doctors. May 3-6, 2018, România, Iași;* 2018, p. 89. ISSN 2501-4641.
9. **Alsatou A**. Maternal risk factors in umbilical cord entanglement. In: *The 7th International Medical Congress for Students and Young Doctors. MedEspera, May 3-5, 2018*. Chisinau, 2018; pp. 80-81. ISBN 978-9975-47-174-9.
10. **Алсатоу АС.** Истинный узел пуповины: клинический случай. In: *VI Bukovinian International Medical Congress, BIMCO JOURNAL, Abstracts book. 2-5 April 2019. Chernivtsi*. 2019; p. 9. ISSN 2616-5392.

11. **Alsatou A**. Structural lesions of the umbilical cord and their outcomes. In: *The 8th International Medical Congress for Students and Young Doctors. MedEspera, September 24-26, 2020*. Chișinău. 2020; 177-178. ID 194. ISBN 978-9975-151-11-5.
12. **Алсатоу АС.** Исходы родов в зависимости от структурных особенностей пуповины. В: *XXI Всероссийский Научно-образовательный форум „Мать и Дитя“, 28-30 сентября 2020, Красногорск*. 2020; с. 3. ISBN 978–5–906484–57–4.
13. **Alsatou A**, Iliadi-Tulbure C. ID: 79 Adverse outcomes in abnormal cord insertion. In: *BIRTH Congress. 6th edition Clinical Challenges in Labor and Delivery. A virtual experience (online), October 1-3, 2020*; p. 43. Disponibil: https://www.mcascientificevents.eu/birth/
14. **Alsatou A**, Iliadi-Tulbure C, Corolcova N, Dondiuc Iu. Structural and functional particularities of the umbilical cord in perinatal outcomes. [Particularitățile structural-funcționale ale cordonului ombilical în rezultatele perinatale]. In: *Congresul consacrat aniversării a 75-a de la fondarea Universităţii de Stat de Medicină şi Farmacie „Nicolae Testemiţanu” din Republica Moldova. 21-23 octombrie 2020,* Chișinău. 2020; p. 591. Disponibil: https://conferinta.usmf.md/congres-2020/
15. Iliadi-Tulbure C, **Alsatou A.** Lean umbilical cord and perinatal outcomes. *ECPM 2021: XXVII European Congress of Perinatal Medicine, LIVE ONLINE CONGRESS, 14-17 July 2021. Lisbon; 2021*. Disponibil: https://www.mcascientificevents.eu/ecpm/

- **Invention patents, registration certificates, materials for invention salons:**

16. **Alsatou A**, Petrovici V, Dondiuc I, Siniția L. *Metodă morfometrică de evaluare a cordonului ombilical prin determinarea indicatorilor organometrici predictivi.* Certificat de inovator nr. 454, 26.12.2019.
17. **Alsatou A**, Petrovici V, Dondiuc I, Siniția L. *Metodă morfometrică de evaluare a cordonului ombilical prin determinarea indicatorilor organometrici predictivi.* Certificat de inovator nr. 5731, 26.12.2019.
18. **Alsatou A**, Petrovici V, Iliadi-Tulbure C, David V. *Aplicarea protocolului examinării particularităților structural-funcționale ale cordonului ombilical și ale plăcii corioamnionale.* Certificat de inovator nr. 455, 07.02.2020.
19. **Alsatou A**, Petrovici V, Iliadi-Tulbure C, David V. *Aplicarea protocolului examinării particularităților structural-funcționale ale cordonului ombilical și ale plăcii corioamnionale.* Certificat de inovator nr. 5734, 07.02.2020.
20. **Alsatou A,** Petrovici V, Dondiuc I, Rotari M. *Diagnosticul prenatal şi macroscopic al cordonului ombilical în stabilirea indicilor morfometrici şi morfologici cu impact în disfuncţia placentară şi în rezultatele perinatale.* Certificat de înregistrare a obiectelor dreptului de autor și drepturilor conexe seria O nr. 7299, 28.07.2022. Disponibil: http://www.db.agepi.md/opere/Details.aspx?id=316666444768388115642 38&nr=316766444728 38811569239
21. **Alsatou A**, Dondiuc I, Iliadi-Tulbure C. *Particularităţile clinico-anamnestice şi de evoluţie ale perioadei perinatale în patologia cordonului ombilical.* Certificat de înregistrare a obiectelor dreptului de autor și drepturilor conexe seria O nr. 7300, 28.07.2022. Disponibil: http://www.db.agepi.md/opere/Details.aspx?id=316666444768388115642 39&nr =3167664447383881156023 0
22. **Alsatou A**, Petrovici V. *Profilul morfopatologic structural-funcţional al cordonului ombilical şi al plăcii corioamnionale cu standardizarea şi clasificarea clinico-morfologică*

aplicativă. Certificat de înregistrare a obiectelor dreptului de autor și drepturilor conexe seria O nr. 7303, 28.07.2022. Disponibil: http://www.db.agepi.md/opere/Details.aspx?id=316666444768388115652 32&nr=31676644473838811560233

- **Participation with communications at scientific forums**

✓**internaţional:**

23. **Alsatou A**. *Maternal risk factors in umbilical cord entanglement.* The 7th International Medical Congress for Students and Young Doctors. MedEspera. Chișinău, 3-5 mai 2018.
24. **Alsatou A.** *Analysis of the risk factors for development of umbilical cord entanglement*. The 15th International Congress for Medical Students and Young Doctors. România, Iași, 3-6 mai 2018.
25. Дондюк Ю, **Алсатоу А.** *Роль клинико-морфологических особенностей пуповины в перинатальных осложнениях.* IV Международный междисциплинарный саммит "Женское здоровье". Москва, 25-27 мая, 2020. Disponibil: https://xn--80aqlawk.xn----dtbfcadbly3amea1ah0q.xn--h1akdx.xn--80aswg/
26. **Алсатоу АС.** *Исходы родов в зависимости от структурных особенностей пуповины.* XXI Всероссийский научно-образовательный форум „Мать и дитя“. Красногорск, 28-30 сентября, 2020. Disponibil: https://mother-child.ru/moscow/
27. Дондюк ЮВ, **Алсатоу АС.** *Наслідки пологів в залежності від структурних особливостей пуповини* [Структурно-функциональные особенности пуповины и их роль в перинатальных исходах]. Міждисциплінарна науково-практична конференція з міжнароднім участем «Сучасні напрямки перинатальної та репродуктивної медицини: від теорії інноваційного пошуку до практики», присвяченої пам’яті вчителя, професора Олександра Олексійовича Зелінського. Одеса, 16-17 квітня, 2021 р. Disponibil: https://conf.od.ua/

✓**naţional:**

28. **Uşanlî Alina**. *Rolul patologiei cordonului ombilical în rezultatele perinatale.* Conferința Științifică Anuală consacrată aniversării a 90 de ani de la nașterea ilustrului medic și savant Nicolae Testemițanu. Chișinău, 16-20 octombrie 2017.
29. **Alsatou Alina.** *Circulare de cordon ombilical: factori de risc prenatali.* Conferința Zilele Universității de Stat de Medicină și Farmacie „Nicolae Testemițanu“. Chișinău, 15-19 octombrie, 2018.

- **Participation with posters at scientific forums**

✓**internaţional:**

30. **Alsatou A**. Structural lesions of the umbilical cord and their outcomes. In: *The 8th International Medical Congress for Students and Young Doctors. MedEspera, September 24-26, 2020*. Program-book p. 32. Chișinău; 2020. Disponibil: https://medespera.asr.md/
31. **Alsatou A**, Iliadi-Tulbure C. *E-Poster ID: 79 Adverse outcomes in abnormal cord insertion. BIRTH Congress*. 6th edition Clinical Challenges in Labor and Delivery. A virtual experience, October 1-3, 2020. Disponibil: https://www.mcascientificevents.eu/birth/
32. Iliadi-Tulbure C, **Alsatou A.** *E-Poster: Lean umbilical cord and perinatal outcomes.* ECPM 2021: XXVII European Congress of Perinatal Medicine, Live online congress, 14-17 July 2021. Lisbon, 2021. Disponibil: https://www.mcascientificevents.eu/ecpm/

✓**național:**

33. **Alsatou A,** Iliadi-Tulbure C, Corolcova N, Dondiuc Iu. Structural and functional particularities of the umbilical cord in perinatal outcomes. *Congresul consacrat aniversării a 75-a de la fondarea Universității de Stat de Medicină şi Farmacie „Nicolae Testemiţanu”*. Chișinău, 21-23 octombrie 2020. Culegere de postere, p. 360. Disponibil: https://conferinta.usmf.md/congres-2020/

- **Methodological-didactic documents**

✓***Clinical protocols*:**

34. Cernețchi O, Dondiuc Iu, **Alsatou A**. *Procidența și prolabarea cordonului ombilical*. Protocol clinic standardizat pentru medicii obstetricieni-ginecologi. Ordinul MSMPS nr. 751 din 26.06.2019. Chișinău; 2019. 5 p.

35. Cernețchi O, Dondiuc Iu, Corolcova N, **Alsatou A**. *Conduita sarcinii și a nașterii la pacientele cu patologie a cordonului ombilical*. Protocol clinic standardizat pentru medicii obstetricieni-ginecologi. Ordinul MSMPS nr. 750 din 26.06.2019. Chișinău; 2019. 8 p.

ABSTRACTS

ADNOTARE

Alsatou Alina. ***Rolul patologiei cordonului ombilical în mortalitatea și morbiditatea perinatală,*** teză de doctor în științe medicale, Chișinău, 2023

Teza este expusă pe 224 de pagini și include: introducere, 4 capitole, sinteza rezultatelor obținute, concluzii generale și recomandări practice, bibliografie din 270 de surse, 10 anexe, 81 de figuri și 20 de tabele. Rezultatele obținute sunt publicate în 35 de lucrări științifice, inclusiv 3 articole fără coautori.

Cuvinte-cheie: cordon ombilical, placă corioamnională, patologie, anomalie, morbiditate, mortalitate, perioadă perinatală

Domeniul de studiu: medicină, obstetrică și ginecologie

Scopul studiului. Studierea rolului patologiei cordonului ombilical în manifestarea rezultatelor perinatale (morbiditatea și mortalitatea perinatală), pentru optimizarea conduitei obstetricale, îmbunătățirea prognosticului materno-fetal și a indicatorilor statistici.

Obiectivele studiului. 1. Determinarea particularităților clinico-evolutive ale sarcinilor și nașterilor la pacientele cu patologie a cordonului ombilical (CO). 2. Identificarea factorilor determinanți ai patologiei cordonului ombilical și a criteriilor de prognostic al rezultatelor perinatale. 3. Caracteristica morbidității și a mortalității nou-născuților cu patologie a cordonului ombilical. 4. Evaluarea particularităților structural-funcționale ale cordonului ombilical și ale plăcii corioamnionale (PCA) placentare în diferite patologii ombilicale și a efectului acestora asupra rezultatelor perinatale. 5. Elaborarea criteriilor de diagnostic al patologiei CO pentru optimizarea conduitei clinice și îmbunătățirea rezultatelor perinatale.

Noutatea și originalitatea științifică a lucrării. Pentru prima dată în Republica Moldova, studiul efectuat a elucidat particularitățile evoluției sarcinii, a nașterii și a perioadei postnatale la pacientele cu patologii ale CO. Au fost stabiliți factorii determinanți în dezvoltarea acestor stări patologice. În cadrul studiului realizat au fost cercetate tipurile CO anormal și rolul acestora în morbiditatea și mortalitatea perinatală. La pacientele cu patologie a CO au fost estimate: funcția complexului fetoplacentar, evoluția stării intrauterine a fătului pe parcursul sarcinii și rezultatele neonatale timpurii. Au fost cercetate modificările morfologice și histologice structural-funcționale ale CO și PCA în cazurile cu CO patologic. Au fost elaborate criteriile de diagnostic al patologiei cordonului ombilical în scopul optimizării conduitei clinice și îmbunătățirii rezultatelor perinatale.

Semnificația teoretică. Prezenta lucrarea științifică a contribuit la determinarea și evaluarea noilor aspecte în dezvoltarea patologiei CO, bazate pe studiile clinice, paraclinice, organometrice, morfologice, histochimice și statistice cu relevanță practică și teoretico-științifică.

Valoarea aplicativă a lucrării. Cercetările efectuate evidențiază noi particularități evolutive ale sarcinii pe fundalul CO patologic, fapt ce facilitează înțelegerea mecanismelor fiziologice și patologice desfășurate în complexul fetoplacentar în cazurile de anormalități ombilicale, factor important pentru elaborarea conduitei clinice optime a gravidelor cu patologie a CO. S-a stabilit importanța factorilor determinanți implicați în dezvoltarea patologiei cordonului ombilical.

Implementarea rezultatelor științifice. În baza studiului efectuat au fost elaborate două protocoale clinice standardizate, implementate în activitatea practică obstetricală și morfopatologică a IMSP Spitalul Clinic Municipal *Gheorghe Paladi* și a IMSP Institutul Mamei și Copilului, ceea ce va contribui la optimizarea conduitei sarcinii și a nașterii complicate cu patologiile CO și va îmbunătăți indicatorii perinatali (Anexa 5). Principalele rezultate ale studiului sunt aplicate în activitatea științifico-didactică a disciplinei *Obstetrică și ginecologie* în cadrul IP USMF *Nicolae Testemițanu* din Republica Moldova și în activitatea Serviciului de morfopatologie și citopatologie al IMSP Centrul Mamei și Copilului (Anexele 7, 8).

АННОТАЦИЯ

Алсатоу Алина. ***Влияние патологии пуповины на перинатальную заболеваемость и смертность***; на соискание ученой степени кандидата медицинских наук, Кишинэу, 2023.

Диссертация изложена на 224 страницах, состоит из введения, 4 глав, синтеза полученных результатов, выводов, практических рекомендаций, 81 рисунок и 20 таблиц. Библиография включает 270 источников. По теме диссертации опубликованы 35 научных работ.

Ключевые слова: пуповина, хориоамниональная пластинка, патология, аномалия, заболеваемость, смертность, перинатальный период.

Область исследования: медицина, акушерство и гинекология

Цель исследования: изучить влияние патологии пуповины на перинатальные исходы (заболеваемость и смертность детей) для оптимизации акушерской тактики ведения данных пациенток, улучшения прогноза и статистических показателей.

Задачи: 1. Определить особенности клинического течения беременности и родов у пациенток с патологией пуповины. 2. Выявить факторы риска, способствующие развитию патологии пуповины, и прогностические критерии перинатальных исходов. 3. Характеристика заболеваемости и смертности новорожденных детей с патологией пуповины. 4. Изучить морфопатологические особенности пуповины и хориоамниональной пластинки при различных патологиях пуповины и оценить их влияние на перинатальные исходы. 5. Разработать диагностические критерии патологии пуповины для улучшения акушерской тактики ведения и перинатальных исходов.

Научная новизна и оригинальность исследования. Впервые в Республике Молдова проведенное исследование выявило особенности течения беременности, родов и послеродового периода у пациенток с патологиями пуповины. Установлены определяющие факторы риска развития этих патологических состояний. В проведенном исследовании изучались аномальные виды пуповины и их роль в перинатальной заболеваемости и смертности. У пациенток с данной патологией оценивали функцию фетоплацентарного комплекса, течение внутриутробного состояния плода во время беременности и ранние неонатальные исходы. Исследованы структурно-функциональные морфологические и гистологические изменения пуповины и хориоамниональной пластинки при различной ее патологии. Разработаны диагностические критерии патологии пуповины для оптимизации клинического ведения и улучшения перинатальных исходов.

Теоретическая значимость. Данная научная работа способствовала определению и оценке новых аспектов развития патологии пуповины на основе клинических, параклинических, органометрических, морфологических, гистохимических и статистических исследований, имеющих практическое и научно-теоретическое значение.

Практическая значимость. Выявлены особенности течения беременности у пациенток из исследовательской группы, что способствует пониманию физиологических и патологических механизмов, осуществляемых в фетоплацентарном комплексе при пупочной аномалии, и разработке оптимальной тактики ведения беременных. Установлена значимость факторов риска, участвующих в развитии патологии пуповины.

Внедрение результатов исследования. Разработаны два стандартизированных клинических протокола, внедренных в практическую акушерско-морфопатологическую деятельность Института Матери и Ребенка и Городской клинической больницы им. Георге Палади, мун. Кишинэу (Приложение 5). Основные результаты исследования применяются в научно-педагогической деятельности Кафедры акушерства и гинекологии ГУМФ им. Николая Тестемицану и в деятельности Отделения морфопатологии и цитопатологии Центра Матери и Ребёнка (Приложения 7, 8).

ANNOTATION

Alsatou Alina. ***The role of umbilical cord pathology in perinatal morbidity and mortality***, PhD thesis in medical sciences, Chisinau, 2023

The present thesis is written on 224 pages and includes: introduction, 4 chapters, conclusions, practical recommendations, bibliography of 270 sources, 10 annexes, 81 figures and 20 tables. The achieved results are published in 35 scientific journals, including 3 articles without co-authors.

Keywords: umbilical cord, chorioamnionic plaque, pathology, anomaly, morbidity, mortality, perinatal period.

The research area: medicine, obstetrics and gynecology

The aim of the study. To study the role of umbilical cord pathology in the manifestation of perinatal outcomes (perinatal morbidity and mortality), for optimizing obstetric management, improving maternal-fetal prognosis and statistical indicators.

Study objectives. 1. To determinate of the clinical particularities of pregnancies and deliveries in patients with umbilical cord pathology. 2. To identify the risk factors of umbilical cord abnormalities and prognosis criteria for perinatal outcomes. 3. Characterization of morbidity and mortality of newborns with umbilical cord pathology. 4. To evaluate the morphopathological changes in UC and chorionic plaque and to study their effect on perinatal outcomes. 5. To develop of diagnostic criteria for umbilical cord pathology to optimize clinical management and improve perinatal outcomes.

The novelty and the scientific originality. For the first time in the Republic of Moldova, the study carried out elucidated the particularities of the evolution of pregnancy, delivery and the post-partum period in patients with UC pathology. The determining factors in the development of these pathological conditions have been established. In the study carried out, abnormal UC types and their role on perinatal morbidity and mortality were investigated. In patients with UC pathology, the function of the fetoplacental complex, the evolution of the intrauterine state of the fetus during pregnancy and early neonatal outcomes were estimated. The structural-functional morphological and histological changes of UC and the chorioamnionic plaque in different pathologies were appreciated. Diagnostic criteria for umbilical cord pathology were developed to optimize clinical management and improve perinatal outcomes.

The theoretical significance. The present scientific work has contributed to determination and evaluation of the new aspects in the development of UC pathology based on clinical, paraclinical, organometric, morphological, histochemical and statistical studies.

The applicable value of this study. The research carried out in the paper highlights new evolutionary peculiarities of pregnancy against the background of pathological UC, a fact that facilitates the understanding of the physiological and pathological mechanisms, carried out in the fetoplacental complex in cases of umbilical abnormalities, an important factor in the optimal development of clinical conduct in pregnant women with UC pathology. The importance of the risk factors involved in the development of umbilical cord pathology has been established.

Implementation of scientific results. Based on the study carried out, two clinical protocols have been developed, the implementation of which in obstetric practice will contribute to the optimization of the managemt of pregnancy and delivery, complicated with UC pathologies and will improve the perinatal indicators (Annex 5). The study results were implemented in clinical work, teaching and research of the Institute of Mother and Child, *Gheorghe Paladi* Municipal Clinical Hospital (Chisinau) and *Nicolae Testemitanu* State University of Medicine and Pharmacy in the Republic of Moldova (Annexes 7, 8).