

## РЕЗУЛЬТАТИ ДИСЕРТАЦІЙНИХ ТА НАУКОВО-ДОСЛІДНИХ РОБІТ / RESULTS THESIS AND SCIENTIFIC-RESEARCH

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RISK FACTORS OF UMBILICAL CORD  
PATHOLOGY AND FACTORS OF NEGATIVE  
PERINATAL CONSEQUENCES AND  
NEWBORN INCIDENCE

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### Summary

According to literature sources, the real frequency of many umbilical cord pathologies differs significantly from the statistical data indicated by researchers in their works (from 15% to 38%). The implementation of a system of diagnostic and treatment and preventive measures, based on mandatory antenatal and postnatal assessment of the features and characteristics of the umbilical cord, allows to improve perinatal outcomes and reduce perinatal morbidity.

**The aim of the work** was to identify the main risk factors of umbilical cord pathology and negative perinatal consequences; to develop elements of standardization of antenatal and postnatal diagnosis of umbilical cord pathology.

**Research materials and methods.** A retrospective assessment of medical documentation data (3,280 individual medical records of pregnant women) made it possible to establish the frequency of umbilical cord pathology in the population. In the future, a more detailed extended antenatal and postnatal examination of the umbilical cord and placenta after delivery was carried out in 637 patients of reproductive age with pregnancy complicated by pathology of the umbilical cord (main group). The control group was formed by 40 patients with an uncomplicated course of pregnancy and live birth of full-term healthy children.

The study was conducted taking into account the main principles of the Helsinki Declaration on Biometric Research and the powers of the GCH ICH, in accordance with biometric norms with compliance with the principles of confidentiality and ethics (excerpt from protocol No. 128/22 of the meeting of the Bioethics Commission dated September 29, 2022, Ivano-Frankivsk National Medical University, Ministry of Health of Ukraine).

Data analysis was performed using the Statistica 7.0 package of statistical programs (StatSoft Inc., USA). The association of independent variables with the condition being studied is presented as odds ratio (OR) and 95% confidence interval (CI).

The materials of the article are the result of the research of the complex research work fragment of the Department of Obstetrics and Gynecology named after I.D. Lanoviyi of the Ivano-Frankivsk National Medical University: "Development of diagnostic tactics and pathogenetic substantiation of effective methods of preserving and restoring reproductive potential and improving parameters of a woman's quality of life in obstetric and gynecological pathology" (state registration number 0121UI09269, implementation dates 2021-2026), the author is a co-executor of the topic.

**Research results and their discussion.** The following data were noted: an excess of the population norm of the length of the umbilical cord, a high proportion of eccentric and marginal insertion of the umbilical cord (22.14%) and umbilical cord coiling (33.28%), a decrease in the proportion of the reference limits of the umbilical cord tortuosity index (15.86%), in 56.7% of observations, the specific gravity of the umbilical cord was lower. Probable risk factors for umbilical cord pathology with a predominance of age over 35 years, nicotine addiction in pregnant women, multiple fertility, use of IVF programs, change in the amniotic fluid index, overweight and obesity, other clinical conditions associated with metabolic disorders (gestational diabetes, insulin resistance) were identified.

**Conclusion.** The share of the umbilical cord pathology both in the isolated type and in the combination of characteristic features of the umbilical cord is 40.98%. The increase in the risk of negative perinatal consequences has a close relationship with the umbilical cord pathology and the combination of different types of pathology, as well as the addition of gestational complications, which allows for the formation of screening programs and optimization of the diagnostic algorithm.

**Key words:** Umbilical Cord Pathology; Placental Dysfunction; Reproductive Disorders; Perinatal Morbidity; Risk Factors; Overweight; Obesity; Gestational Diabetes.

### Topicality

According to literature sources, the real frequency of many umbilical cord pathologies differs significantly from the statistical data indicated by researchers in their works (from 15%

to 38%) [1-4]. As demonstrated by the studied literary sources, on the modern scientific discussion panel the question of the relationship between the pathology of the umbilical cord and its insertion, as well as reproductive losses in such pregnancy, are

usually presented in foreign studies; unfortunately, domestic scientific search contents are sporadic and unsystematized [1-4]. The thanatogenic value of umbilical cord abnormalities is often exaggerated, or retains aspects of underestimation and controversy [2, 3, 5]. However, they can also significantly worsen the perinatal outcome when combined with pathology or against the background of gestational complications, which requires systematization of diagnostic approaches and standardization of treatment and preventive measures when they are detected [5]. The combination of umbilical cord pathology with placental dysfunction, preeclampsia, arterial hypertension, gestational diabetes can serve as markers of potential fetal distress [1-4]. Therefore, the introduction of a system of diagnostic and treatment and preventive measures, based on mandatory antenatal and postnatal assessment of the characteristics of the umbilical cord, allows to improve perinatal outcomes and reduce perinatal morbidity.

**The aim of the work** was to identify the main risk factors of umbilical cord pathology and negative perinatal consequences and to develop elements of standardization of antenatal and postnatal diagnosis of umbilical cord pathology.

#### Research materials and methods

At the first stage, a retrospective evaluation of medical documentation data was carried out – 3,280 individual medical records of pregnant women who were observed in the family planning center at the Municipal Non-Commercial Enterprise “Ivano-Frankivsk Regional Perinatal Center of the Ivano-Frankivsk Regional Council”. According to the developed maps, 82 parameters were evaluated, including anthropometric parameters, body mass index (BMI), indications of social and professional status, frequency of harmful habits (smoking), parity of pregnancy, its course and birth outcomes. Subsequently, a more detailed analytical processing of the data of an extended antenatal and postnatal examination of the umbilical cord and placenta after childbirth in 637 patients of reproductive age with pregnancy complicated by the pathology of the umbilical cord (main group) was carried out. The control group was formed by 40 patients with an uncomplicated course of pregnancy, childbirth and live birth of full-term healthy children. Exclusion criteria were: malformations of the fetus, fetopathy associated with other conditions, severe somatic diseases, refusal of the patient to participate in the study. An extended antenatal examination of the umbilical cord included: determination of the number of vessels of the umbilical cord, measurement of their average diameter, evaluation of the umbilical cord tortuosity index, determination of the place of insertion to the placenta, wrapping of the umbilical cord around the neck (nuchal cord) and other parts of the body. An extended macroscopic examination of the placenta consisted in determining the dimensions of the placenta (average diameter, thickness) weight, length and weight of the umbilical cord with the determination of its specific gravity (g/cm), vector of the umbilical cord twist and umbilical cord tortuosity index, the type of insertion to the placenta (central,

eccentric, marginal, velamentous, insertio furcata) and diagnosis of true and false umbilical cord knots.

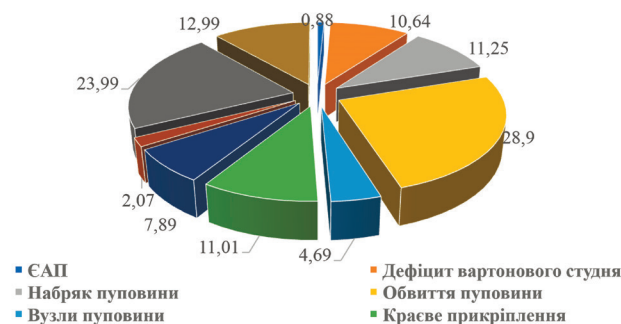
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#### Research results and their discussion

The terms of diagnosis of umbilical cord pathology ranged from 11 to 40 weeks of pregnancy; in every third case, umbilical cord insertion anomalies or its pathology were diagnosed after delivery. Characterizing the frequency of umbilical cord pathology (Figure 1) at the stage of a retrospective study, the following should be noted: the syndrome of a single umbilical vessel (SUV) is the rarest type of its pathology and was observed in 29 cases (0.88%).

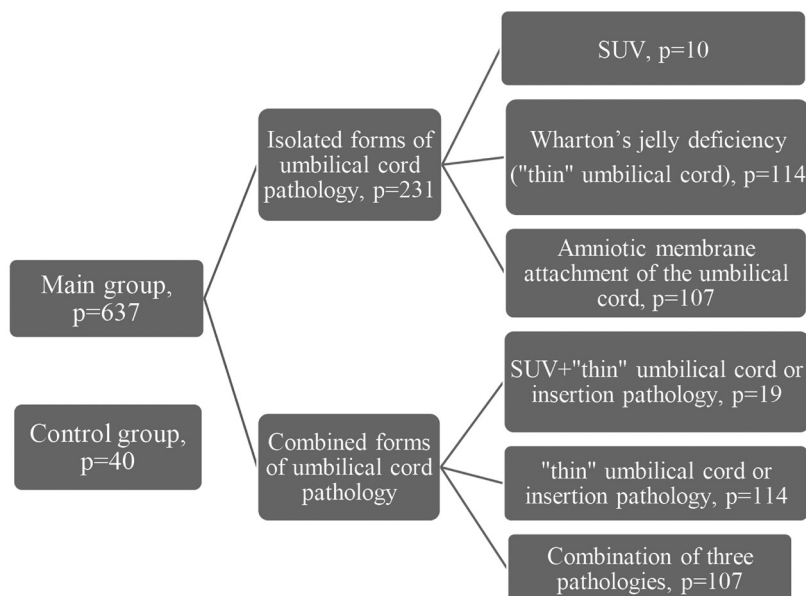


**Figure 1. Structure of umbilical cord pathology, n=3280, %**

The so-called “thin” umbilical cord (<0.5 g/cm) (Wharton’s jelly deficiency) – in 349 observations (10.64%), “thick” umbilical cord (1.1 g/cm) – in 369 cases (11.25%), umbilical cord wrapping around the neck and parts of the body – in 948 patients (28.90%), true umbilical cord knots – in 154 (4.69%). Other conditions, such as anomalies of the umbilical cord insertion, were noted in 688 cases (20.98%), while a marginal one – in 361 (11.01%), velamentous – in 259 women (7.89%), insertio furcata – in 68 cases (2.07%). Prolapse of the umbilical cord was found in 19 patients (0.58%), absolutely short umbilical cord

– in 83 (2.53%), long (>70 cm) – in 1384 observations (42.19%), hypocoiling – in 787 (23,99%), hypocoiling – in 426 cases (12.99%), a combination of different characteristics of the umbilical cord was noted in 987 cases (30.09%). Thus, a significant share of the pathology of the umbilical cord was established in 1344 cases (40.98%) both in an isolated type and in a combination of characteristic features of the umbilical cord.

The next stage of the study was the assessment of the age factor, features of gynecological and somatic morbidity and reproductive potential in two studied groups – the main group (637 patients), 29 of them had SUV, 349 patients had Wharton's jelly deficiency, 259 women with a velamentous insertion of the umbilical cord. The control group consisted of conditionally healthy pregnant women (40 patients) (Figure 2).



**Figure 2. Study groups of patients with pregnancy complicated by umbilical cord pathology, p=637.**

It should be noted that at this stage of the scientific search, the formed groups demonstrated isolated types of the umbilical cord pathology in 231 cases (36.26%), while a combination of characteristic features of the umbilical cord (in particular, with Wharton's jelly deficiency, or with a velamentous insertion of the umbilical cord or a combination of a "thin" umbilical cord, SUV and umbilical cord insertion pathology) were noted in 406 observations (63.74%).

The studied groups differed in the average age of  $37.3 \pm 3.1$  years – in the basic main group versus  $28.2 \pm 1.3$  years – in the control; pregnant women over the age of 30 made up 121 patients (18.99%), and at the age over 35 years old – 246 persons (38.62%). In the main group, the high parity of pregnancies and the share of primiparous women were comparable, while in the control group the parity of pregnancies was lower (32.5%). The use of IVF programs was noted in 146 cases (22.92%), the frequency of multiple pregnancy both with isolated and combined pathology of the umbilical cord was in 30.76% (196), the share of microparesis and polyparesis was 17.89% (114) and 13.65% (87) respectively, which is significantly higher than the population norm. The distribution of newborns by gender showed a higher proportion of male fetuses (363 – 56.98%).

As a result of the study, it was established that in the cohort of patients with a combination of selected features of the umbilical cord and types of its insertion, patients over the age of 35 years (246 – 38.6%) are significantly more common compared to 17.5% in the control group ( $p < 0, 05$ ). The umbilical cord pathology was noted mostly in patients who

suffer from cardiovascular diseases (226 – 35.48%), acute respiratory infection, influenza and in those who underwent COVID-19 in the first trimester of pregnancy (152 – 23.87%), chronic nicotine addiction (211 – 33.12%), arterial hypertension (149 – 23.39%), endocrine pathology (thyroid diseases, carbohydrate metabolism disorders, insulin resistance, etc.) (147 – 23.08%), varicose veins of the lower extremities (203 – 31.87%), chronic foci of infection (pyelonephritis, asymptomatic bacteriuria, etc.) (236 – 37.05%). A high body mass index in the main group (248 patients, 38.93%) should be emphasized; excess weight and body mass index above  $30 \text{ kg/m}^2$  were significantly more often observed in women with pregnancy complicated by umbilical cord pathology, against the data in the control group – in 7.5% ( $p < 0.05$ ).

Peculiarities of the course of pregnancy are characterized by an increase in the share of preeclampsia (226 – 35.48% against 17.50% in the control,  $p < 0.05$ ), premature births (115 – 18.05%) and the birth of low-birth-weight children (12.56% in the absence of control,  $p < 0.05$ ), every third pregnant woman (198 – 31.08%) with a threat of spontaneous abortion was hospitalized (Figure 3). It should be noted that with isolated types of the umbilical cord pathology, premature termination of pregnancy was revealed in (26) 11.68% of cases, while with the combined type almost twice (1.9 times) more often – in (89) 21.92% ( $p < 0.05$ ). The birth weight of children was  $2384.0 \pm 29.6 \text{ g}$ , and in the control group –  $3468.0 \pm 31.8 \text{ g}$  ( $p < 0.02$ ). It was established that the weight of fetuses, even with isolated types,

is significantly lower than the population norm, and the birth of full-term low-weight newborns was 12.56% (29).

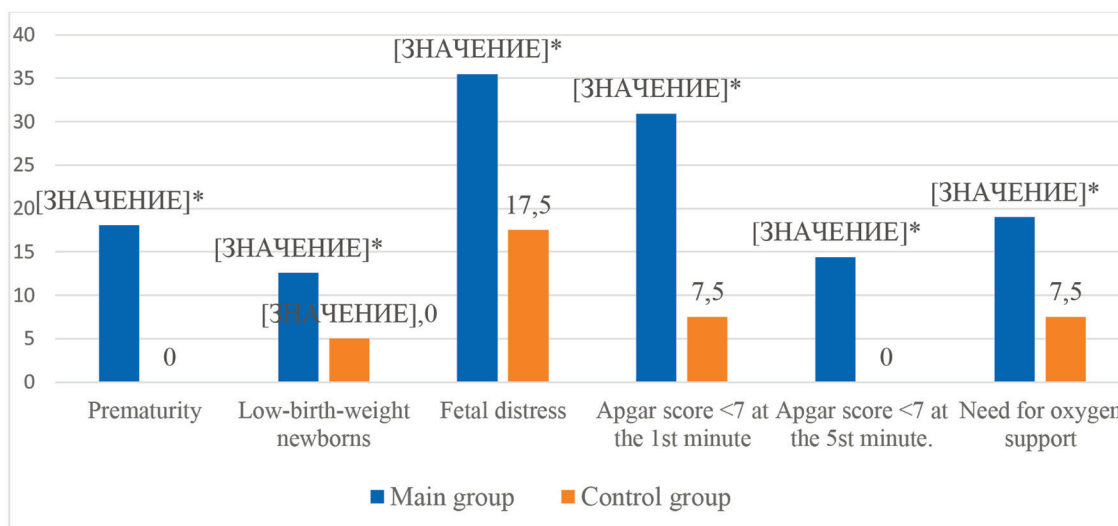
Caesarean section was performed for almost every fifth patient – 126 (19.78%), vacuum extraction and obstetric forceps were used in 52 cases (8.16%). The score on the Apgar scale was significantly lower than in the general population, and at the first minute it was 7 points and below in every third patient (30.93%), at the fifth minute –

in 92 observations (14.44%), first of all, in the case of the addition of gestational complications

(placental dysfunction and preeclampsia).

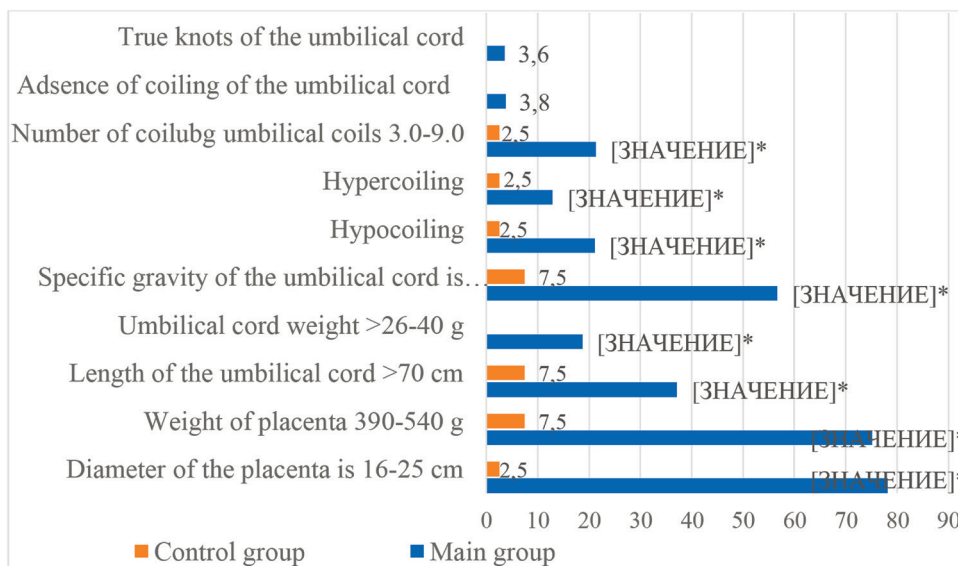
Neonatal morbidity in the indicated category of patients was increased, even with full-term pregnancy; 121 newborns (18.99%) required oxygen support, 19 (2.98%) required mechanical support (ventilation), the discharge was delayed for more than 8 days in 249 patients (39.09%), and the share of those transferred to the second stage of the nursery was 7.06% (45).

The results of the postnatal examination of the placenta and the umbilical cord are presented in Figure 4.



**Figure 3. Perinatal consequences of pregnancy complicated by the umbilical cord pathology, p=637, %.**

*Note.* \* - the difference is significant relative to the data of the control group, p<0.05.



**Figure 4. Peculiarities of postnatal examination of the placenta and umbilical cord, p=637, %.**

*Note.* \* - the difference is significant against the data of the control group, p<0.05.

Extended antenatal and postnatal examination of the umbilical cord showed the following: the length of the umbilical cord significantly exceeded the population norm (69.8±8.9 vs. 56.2±4.4 cm in the control, p<0.05), and the share of long umbilical cords (70 cm and more) was in 236 samples (37.05%), absolutely short umbilical cord was in 23 patients (3.61%), the frequency of eccentric and marginal insertion of the umbilical cord was revealed in 141 observations (22.14%), the umbilical cord wrapping

around the neck and around other parts – in 212 cases (33.28%). The specific gravity of the fetal fragment of the umbilical cord was significantly higher than that of the placental fragment (0.9 g/cm vs. 0.6 g/cm), in the dynamics of ultrasound monitoring, the diameter of the umbilical cord decreased from the fetus to the placenta from 17.6 mm to 15.4 mm, the diameter of the vein and the average diameter of the umbilical artery increased slightly (from 7.6 mm to 8.2 mm – for the vein and from 3.6 mm to 4.0



mm – for the artery), while a uniform linear increase in the diameter of the vessels of the umbilical cord was noted up to 28-30 weeks of pregnancy, after which the growth of blood vessels in this cohort of patients was practically not noted, including due to the regression of Wharton's jelly.

We noted a rather wide range of indicators of the umbilical cord weight from 20 g to 140 g; almost half of the samples were in the range from 30 g to 60 g. The range from 0.5 g/cm to 1.1 g/cm should be considered the population norm of the specific gravity of the umbilical cord in a full-term uncomplicated pregnancy. In 56.7% of observations, the specific gravity of the umbilical cord was lower and ranged from 0.3 g/cm to 0.6 g/cm. According to the results of the postnatal measurement of the umbilical cord tortuosity index, the parameters according to generally accepted criteria (0.3/cm) were noted only in 15.86% of cases.

Discussion issues of this problem are multifaceted. According to Hayes DJL, et al., anomalies of the development of the umbilical cord are usually described in the literature as clinical conditions of disruption (reduction or critical suspension) of fetal blood flow due to a changed structure of the umbilical cord or functional failure [6-8]. The umbilical cord is a continuation of the fetal cardiovascular system, an anatomical bridge between the placenta and the fetus [9]. This structure is critical to human development, it ensures fetal mobility within the gestational sac and is protected by unique, reliable anatomical features including the length of the umbilical cord, Wharton's jelly, two umbilical arteries, coagulation, and suspension in amniotic fluid [9]. All of these functions contribute to the protection and buffering of this important structure from potentially harmful forces of coiling, shifting and compression during pregnancy, especially during labour [10-13]. In scientific sources, there are informative reports indicating a strong association between the diameter of the umbilical cord and the weight of the placenta and the weight of the newborn [14-16]; the connection with oligohydroamnion, fetal distress, delayed fetal development, perinatal mortality and morbidity has also been proven [1, 4, 17-19].

Another prospective study by Lee SM, Kim DY et al. demonstrated that thin umbilical cord diameter was associated with low Apgar score, intensive care unit stay, and need for oxygen support. The authors concluded that the assessment of the diameter and condition of the umbilical cord in newborns is an important tool for the prevention of negative perinatal consequences [20].

With hypercoiling of the umbilical cord vessels, premature birth, delayed fetal development (up to 32%), an increase in the resistance index, systolic-diastolic ratio in the umbilical cord arteries and aorta of the fetus, as well as an increase in prenatal morbidity and mortality [21, 22] are observed more often. If we focus is on the single umbilical artery (SUA) syndrome, it should be noted that it is the most frequent anomaly associated with perinatal morbidity and mortality, although the information about this syndrome is contradictory and debatable,

as are the data on the frequency range from 0.13% to 3.9 % [23]. In the literature, there are reports that children with SUA are less often born in Japan and among representatives of the Negroid population; they are more often female fetuses, and the presence of isolated SUA is associated with low-birth weight and is an indirect indicator of chromosomal abnormalities, congenital malformations and premature birth [23, 24]. When carefully evaluating the history, a number of scientific reports put forward the position that the cause of non-dividing of one artery into two arteries is the influence of a damaging factor at the 6-7th weeks of pregnancy, and, as confirmation, the authors demonstrate frequent acute respiratory viral infections in the 1st trimester, a high proportion of smoking, diabetes mellitus and hyperglycemia [23, 24].

According to the results of our research, possible risk factors for umbilical cord pathology were identified, dominated by age over 35 years (OR=2,68; 95% CI:2,08–3,46,  $p<0,05$ ), nicotine addiction (OR=2,33; 95% CI:1,02–5,37,  $p<0,05$ ), multiple pregnancy (OR=5,48; 95% CI:1,67–17,99,  $p<0,05$ ), IVF programs (OR=11,59; 95% CI:1,58–85,13,  $p<0,05$ ), change in amniotic fluid index (OR=4,15; 95% CI:1,46–11,81,  $p<0,05$ ), overweight and obesity (OR=7,87; 95% CI:2,39–25,78,  $p<0,05$ ), other metabolic disorders (gestational diabetes, insulin resistance) (OR=3,7; 95% CI:1,12–12,17,  $p<0,05$ ). An increase in the risk of negative perinatal outcomes has a close relationship with the pathology of the umbilical cord (in particular, amniotic membrane attachment of the umbilical cord) (OR=2,5; 95% CI:1,51–4,13,  $p<0,05$ ), a combination of types of umbilical cord pathologies (OR=1,85; 95% CI:1,28–2,67,  $p<0,05$ ), the addition of gestational complications, such as prematurity (OR=2,06; 95% CI:1,23–3,45,  $p<0,05$ ), preeclampsia (OR=3,06; 95% CI:1,01–4,66,  $p<0,05$ ), fetal growth retardation syndrome (OR=3,96; 95% CI:2,6–6,04,  $p<0,05$ ), gestational diabetes (OR=1,89; 95% CI:1,21–2,95,  $p<0,05$ ).

## Conclusion

The share of the umbilical cord pathology both in the isolated type and in combination is 40.98%. Development of screening programs based on identified risk factors and optimization of the diagnostic algorithm with detailed antenatal and postnatal assessment of the structural components of the umbilical cord and the placenta will create prerequisites for the development of preventive measures and improvement of perinatal indicators in this category of patients.

## Prospects for further research

The research of the criteria for standardization of antenatal and postnatal assessment of the structural components of the umbilical cord and the placenta with the aim of developing a diagnostic algorithm for possible perinatal complications, obstetric tactics and delivery is promising.

**Conflict of interest** – the authors have declared no conflict of interest.

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## ФАКТОРИ РИЗИКУ ПАТОЛОГІЇ ПУПОВИНИ І ЧИННИКИ НЕГАТИВНИХ ПЕРИНАТАЛЬНИХ НАСЛІДКІВ ТА ЗАХВОРЮВАНOSTІ НОВОНАРОДЖЕНИХ

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### Резюме

**Вступ.** За даними літературних джерел, реальна частота багатьох патологічних станів пуповини значно відрізняється від статистичних показників, зазначених дослідниками у своїх роботах (від 15 % до 38 %). Впровадження системи діагностичних і лікувально-профілактичних заходів, заснованих на обов'язковій антенатальній і постнатальній оцінці особливостей і характеристик пуповинного канатика, дозволяє поліпшити перинатальні результати та знизити перинатальну захворюваність.

**Метою роботи** стало виділити основні фактори ризику патології пуповини та негативних перинатальних наслідків та розробити елементи стандартизації антенатальної та постнатальної діагностики патології пуповини.

**Матеріали та методи дослідження.** Проведена ретроспективна оцінка даних медичної документації – 3280 індивідуальних карт вагітних дозволила встановити частоту патології пуповини у популяції. У подальшому проведено більш детальне розширене антенатальне і постнатальне дослідження пуповини та плаценти після розродження у 637 пацієнток репродуктивного віку з вагітністю, ускладненою патологією пуповинного канатика (основна група). Контрольну групу сформували 40 пацієнток з неускладненим перебігом вагітності та живонародженням доношених здорових дітей.

Дослідження проведено з урахуванням основних принципів Гельсінської декларації з біометричних досліджень та повноважень GCH ICH (1996 р.), згідно з біометричними нормами із дотриманням принципів конфіденційності та етики (витяг з протоколу № 128/22 засідання комісії з питань біоетики від 29.09.2022 р. Івано-Франківського національного медичного університету МОЗ України).

Аналіз даних виконано з використанням пакету статистичних програм Statistica 7.0 (StatSoftInc., США). Зв'язок незалежних перемінних зі станом, який вивчали, представлено за відношення шансів (OR) та 95 % довірчим інтервалом (CI).

**Матеріали статті** є результатом досліджень фрагменту комплексної науково-дослідної роботи кафедри акушерства та гінекології ім. І.Д.Ланового Івано-Франківського національного медичного університету: «Розробка діагностичної тактики та патогенетичне обґрунтування ефективних методів збереження та відновлення репродуктивного потенціалу та покращення параметрів якості життя жінки при акушерській та гінекологічній патології» (№ державної реєстрації 0121U109269, терміни виконання 2021- 2026 роки), автор є співавтором теми.

**Результати дослідження та їх обговорення.** Було продемонстровано перевищення популяційної норми довжини пуповини, високу частку ексцентричного та красивого прикріплення пуповини (22,14 %) та її обвиття (33,28%), зниження частки референтних меж індексу звивистості пуповини (15,86 %), у 56,7 % спостережень питома вага пуповини була меншою. Виділено імовірні чинники ризику патології пуповини, де домінує вік старше 35 років, нікотинова залежність у вагітних, багатопліддя, використання програм IVF, зміна індексу навколплідних вод, надмірна вага та ожиріння, інші клінічні стани, пов'язані із метаболічними порушеннями (гестаційний діабет, інсулінорезистентність).

**Висновок.** Частка патології пуповинного канатика як у ізольованому варіанті, так і у поєднанні характеристичних особливостей пуповини становить 40,98 %. Зростання ризику негативних перинатальних наслідків має тісний взаємозв'язок з патологією пуповинного канатика та поєднанням різних варіантів патології, а також приєднанням гестаційних ускладнень, що дозволяє формувати скрін-програми та оптимізувати діагностичний алгоритм.

**Ключові слова:** патологія пуповини; плацентарна дисфункція; репродуктивні порушення; перинатальна захворюваність; фактори ризику; надмірна вага; ожиріння; гестаційний діабет.

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