ANNOTATION

dissertation work of Ainura Imarzhanovna Yuldasheva
on the theme: "**New possibilities of optimization of elective caesarean section**" submitted for the degree of Doctor of Philosophy (PhD)
on specialty 6D110100 - "Medicine".

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Relevance of the research topic

Maternal and child health protection is one of the topical problems of medical science and practical health care. In our country and international medical community the problem of caesarean section is given special attention.

Childbirth is an important event that ensures the continuation of the human race. Childbirth in women can be divided into physiologic and pathologic, vaginal and abdominal.

Ideally, natural childbirth is the logical conclusion of the physiological process of human reproduction, when both the woman in labor and the fetus participate in the biomechanism of labor. Natural childbirth is accompanied by positive effects: there is psycho-emotional satisfaction in the birthing woman because of participation in labor and the opportunity to contact with the newborn from the first seconds of his life, and the baby, passing through the natural birth canal, experiences "birth" stress, which contributes to its better adaptation in the period of newborn and subsequent life.

The first hours and days of a newborn's life are an important period not only for the child, but also for the mother. In physiological delivery, the first contact between mother and child occurs immediately after the birth of the newborn, which has a favorable effect on the psycho-emotional satisfaction of the birthing woman and early full-fledged lactation (Hung K.J.,2011). After delivery through natural birth, early skin-to-skin contact between the mother and the newborn contributes to the contamination of the newborn with maternal flora, improving the health of the newborn and improving the health of the newborn (Hung K.J.2011). After delivery through natural birth, early contact between the mother and the newborn "skin to skin" contributes to the contamination of the newborn with maternal flora, improves its adaptation, reduces perinatal morbidity.

According to WHO and UNICEF recommendations, breastfeeding should be initiated within the first hour after delivery, exclusive breastfeeding should be practiced for the first 6 months of the child's life, and then, together with appropriate and safe complementary feeding, breastfeeding should be continued until 2 years of age or later. Globally, these recommendations are followed for a smaller proportion of children: only 44% of infants start breastfeeding within the first hour after delivery, mostly after vaginal delivery. Children with late initiation of breastfeeding have a high risk of neonatal morbidity relative to infants attached to the mother's breast immediately after delivery (WHO, 2018).

One of WHO's objectives is to ensure that every mother has the opportunity for a natural and safe birth, with the right to participate fully in the decision on the method

of delivery. It is very important that every woman can discuss her obstetric condition with a doctor, receive comprehensive information about the benefits and risks of a particular method of delivery and participate in the planning of the upcoming birth (Entre N., 2015).

If there are contraindications to natural childbirth, abdominal delivery is indicated. Cesarean section is an operation of induced delivery where the fetus and afterbirth are removed through an incision in the anterior abdominal wall and uterus. Caesarean section is performed when the fetus is alive and the woman has contraindications for natural childbirth and/or to save the mother's life in case of nonviable fetus and obstetric hemorrhage (WHO, 2021; Curran E.A.,2016).

While initially cesarean section was a forced surgical solution to complex obstetric problems, nowadays more and more women give birth by cesarean section. The popularity of abdominal deliveries has provoked an increase in the frequency of caesarean sections worldwide, which is one of the pressing problems in modern obstetrics (WHO, 2021).

According to the WHO report, if the current trend continues, this indicator will increase to 30% by 2030 (Curran E.A.,2016; Betrán A.P.,2014).

In the Republic of Kazakhstan, the cesarean section rate increased from 6.7% in 2000 to 21.8% in 2023 (Ministry of Health of the Republic of Kazakhstan. Statistical compilations on public health, 2000-2023).

The development strategy of the Republic of Kazakhstan (RK) until 2050 envisages the entry of Kazakhstan into the thirty developed countries of the world, which means further improvement of health care, the presence of a strong demographic policy with the achievement of the UN Millennium Development Goals - reducing maternal and child morbidity/mortality (UN, 2015). Within the framework of implementation of the State Health Development Programs “Densaulyk” (2016-2019 and 2020-2025), highly effective perinatal technologies are being introduced in the Republic.

The relevance of the problem is due to the widespread and high frequency of caesarean section as a delivery operation.

Abdominal delivery, both emergency and elective, should be as safe as possible for the mother and the newborn. Improvement and development of rational tactics of labor management, improvement of caesarean section technique contribute to the reduction of perinatal and maternal morbidity and mortality.

Recently, the attitude towards cesarean section has changed not only among pregnant women, but also among physicians, who perceive abdominal delivery as a routine method of labor. The unjustified expansion of indications for cesarean section is alarming and this leads to a subsequent increase in the proportion of pregnant women with uterine scar requiring repeated abdominal delivery.

Modern medicine is committed to ensuring that cesarean sections are used only in justified cases and in accordance with best clinical practice. Physicians and obstetricians should work together with pregnant women to assess the indications and risks of cesarean section and make informed decisions about delivery based on the individual medical needs and preferences of the mother.

With this in mind, such important issues as the technique of caesarean section,

the technique of its performance, the early provision of skin-to-skin contact between mother and newborn, the initial contamination of the baby with the mother's microflora, and the participation of the woman in labor require optimal solution.

The aim of the dissertation research: to scientifically substantiate and implement a modified “natural” caesarean section as an innovative perinatal technology.

Objectives of the study:

1. To study the medical and social characteristics of pregnant women and the structure of indications for elective cesarean section.
2. To develop and implement the author's method of abdominal delivery - modified “natural” CS.
3. To conduct a comparative analysis of the outcomes of modified “natural” cesarean section, traditional CS, and vaginal delivery.
4. To evaluate the condition of newborns and their hormonal status after modified “natural” CS, traditional CS and VB.

Research methods: we studied the main medical and social characteristics, such as: women's age, social status, level of education, marital status, reproductive history, gynecological and somatic pathology, peculiarities of the course of pregnancy, the structure of indications for elective cesarean section. Perinatal outcomes were analyzed in comparative aspect at different methods of delivery - MNCS, TCS, VB. We studied such parameters as the beginning of the initial immediate skin-to-skin contact between mother and newborn, the average duration of the operation, intraoperative blood loss, Apgar score of the newborn, the beginning of lactation in women in labor, and the level of stress hormone in newborns. The main methods of data collection were anamnestic data, analysis of primary medical documentation, protocols of abdominal delivery, assessment of perinatal period indicators and subsequent data processing using medical statistics methods.

Ultrasound examination (USG) was performed to assess the fetal condition, to determine the amount of amniotic fluid, the position and presentation of the fetus. Ultrasound was performed using modern scanners of expert and premium class: Samsung HS50, GE Voluson E8 Expert, convex sensors (abdominal) with a frequency of 2-5 MHz were used: CA1-7AD (Samsung) and RAB6-D (GE).

Various techniques of abdominal delivery in elective CS: MNCS, TCS were performed.

Stress hormone levels were determined in mixed blood from the umbilical cord of the newborn. Stress hormone level determination was performed in the laboratory corresponding to international standards - Invitro, using semi-automatic analyzer Abbott Architect ci8200, structurally consisting of 2 independent modules - immunochemical and basic biochemical.

Intraoperative blood loss was determined using the R.L. Fisher method of blood loss calculation.

$$Vопв = \frac{ИАЖ \times ВЕС\ НОВОРОЖДЕННОГО \times \pi}{СГ^2}$$

where, AIJ- amniotic fluid index,

π is a mathematical constant,
SG- gestational age.

Statistical processing of data was performed using SPSS v.28.0 software (IBM Corp., Armonk, NY, USA). Quantitative variables were described through the mean (M) and standard error of the mean (±m). Nonparametric and parametric criteria were used to evaluate differences between groups: Mann-Whitney U-test, Student's t-test, ANOVA, Pearson's χ^2-criterion, Fisher's criterion, Spearman and Pearson correlation analysis. Statistical significance was determined by the level of $p<0.05$.

Correlation and regression analyses were also performed between indicators of early skin-to-skin contact and the onset of lactation, as well as between the volume of blood loss and the decrease in hemoglobin levels. In accordance with the Declaration of Helsinki, the approval of the local ethical committee at the Kazakh National Medical University named after S.D. Asfendiyarov was obtained for the scientific study, the number of the minutes of the meeting 11(90) dated 25.12.2019, it is recognized as ethical and complies with all requirements of medical ethics and patient safety.

Object of the study: pregnant women, women in labor at full-term gestation with different methods of delivery, women in labor and their newborn children, N - 230. The examined women, depending on the method of delivery, were divided into 3 groups: with MNCS (main group) - 120 women, with TCS (control group) - 70 women, and the group with VB (comparison) - 40 women.

Inclusion criteria in the main and control groups: age older than 18 and younger than 45 years, pregnant women with gestational age not earlier than 39 weeks, singleton pregnancy, head presentation, absence of severe somatic pathology and malignant neoplasms, provision of informed written consent.

Exclusion criteria for the main and control groups on the part of the mother: Lack of informed consent, the need for general anesthesia (anesthesia), urgent conditions of the pregnant woman / woman in labor requiring emergency cesarean section, pelvic organ tumors, uterine malformations, severe somatic pathology (CCC, respiratory, renal, retinal detachment mental), infectious disease (HIV, hepatitis B, C, recurrent HPV, Covid-19), extragenital cancer and cervical cancer.

Fetal exclusion criteria for the main and control groups: antenatal fetal death, fetal malformations, fetal CHD, chronic fetal hypoxia according to CTG, chorionamnionitis, fetal emergencies requiring ECS, multiple pregnancies, fetal malposition, placenta previa, PONRP, fetal anomalies, umbilical cord antegrowth and prolapse.

Inclusion criteria for the comparison group: pregnant women with premature term, singleton pregnancy, fetal head presentation without severe gynecologic and somatic pathologies, with no urgent conditions of the pregnant woman/ woman/ fetus requiring emergency cesarean section.

Subject of the study: peculiarities of the course and results of different modes of delivery (MNCS, TCS, VB), including assessment of surgical stages, blood loss volume, neonatal condition, initiation of breastfeeding, level of neonatal stress hormones, as well as medical and social characteristics.

The main provisions put forward for defense:

1. The choice of the method of abdominal delivery depends on a number of medical and social factors: among pregnant women who have chosen MNCS predominate repeatedly giving birth, legally married women with higher education, active life position, uterine scar in combination with obstetric and somatic pathology, who are interested in favorable perinatal outcomes.

2. MNCS is as close as possible to natural childbirth, provides optimal comfort and safety for mother and child, eliminates their intraoperative separation due to the author's modification of the abdominal delivery technique with the use of specially designed surgical underwear, which allows the mother to be an active participant in labor, to visualize the moment of birth of the baby, to provide initial early contact with the newborn “skin to skin”, to carry out intraoperative debut of breastfeeding, which contributes to the strengthening of breastfeeding.

3 The author's modification of “natural” cesarean section has significant clinical advantages compared to TCS: it reduces the duration of surgery, the amount of intraoperative blood loss, provides a more physiologic birth of the child, reduces the risks of PPH and postpartum diseases of the mother, improves the formation of lactation, contributes to a faster recovery of women in labor.

4. The developed author's modification of “natural” cesarean section improves the indicators of newborns' condition relative to newborns after traditional cesarean section, which is manifested by a high Apgar score, better adaptation of the newborn in the early neonatal period, which is more comparable with physiological birth than with TCS, as evidenced by the indicators of stress hormone in newborns.

Description of the main results of the study:

The comparative analysis between the MNCS, TCS and BP groups demonstrated a number of statistically significant differences reflecting the advantage of the MNKS technique from both surgical and neonatal positions.

The age composition of the women in the study was comparable; however, women with higher education (51.7%) and employees (51.7%) predominated among the patients with MNCS. In the structure of obstetric indications for previous cesarean sections, the highest proportion was due to combined pathology (30.0%) and fetal distress (25.79%).

Among the surgical parameters, the total duration of surgery and its key stages were significantly different. The mean duration of surgery was 38.1±0.68 minutes for MNKS, whereas for TCS it was 43.5±1.2 minutes ($p<0.001$). The neonatal torso delivery stage was significantly longer at 110.1±20.9 sec with MNCS than with TCS at 16.6±5.9 sec ($p<0.001$). The uterine suturing time was 684.1±191.8 sec with MNCS versus 1173±356.1 sec with TCS ($p<0.001$).

The mean volume of blood loss in labor was the least in the VB group (213.0±7.72 ml), compared to MNCS (250.3±9.06 ml) and especially TCS (525.3±7.95 ml) ($p<0.001$). Meanwhile, the hemoglobin level after delivery in the VB group was similar to the MNCS group (111.6±1.68 g/L and 111.8±0.89 g/L, respectively), significantly higher than that in the TCS group (105.1±0.93 g/L, $p<0.01$).

Neonatal Apgar score showed higher scores in infants born via MNCS and VB compared to TCS. At the 1st minute of life, the mean score was 8.64±0.06 for MNCS

and 8.65±0.09 for VB, compared to 7.43±0.06 for TCS ($p<0.001$). At the 5th minute: 9.66±0.05 and 9.65±0.09 for MNCS and VB, respectively vs. 8.43±0.06 for TCS ($p<0.001$).

Neonates in the VB group had the highest cortisol levels (188.5±9.2 nmol/L) compared to TCS (78.0±1.3 nmol/L) and MNCS (134.3±2.2 nmol/L) ($p<0.001$).

Initial skin-to-skin contact between the newborn and the mother occurred on average after 1.9±0.8 min in MNCS and 1.4±5.2 min in VB, versus 77.7±9.7 min in TCS. The duration of skin-to-skin contact reached 114.6±10.3 min with MNCS and 107.9±12.4 min with VB, compared with 63.8±11.3 min with TCS.

The onset of lactation was 2.2±0.3 days in women with MNCS, 2.1±0.04 days in VB, and 2.9±0.3 days in TCS ($p<0.001$).

Correlation analysis confirmed a strong association between the time of first apposition and lactation establishment ($r=0.61$; $p<0.001$), as well as between the duration of skin-to-skin contact and the success of breastfeeding initiation ($r=-0.54$; $p<0.001$).

Scientific novelty:

1. For the first time the integration of elements of natural labor into abdominal delivery was carried out. Modification of the “natural” caesarean section includes visualization of the labor process by the woman in labor, her active participation in the birth of the child - imitation of pushing, contributing to the slow birth of the newborn, which improves its natural adaptation to the external environment, strengthens the emotional bond between them, which contributes to successful breastfeeding and has long-term positive consequences for their health (patent for invention №35677, RK).
2. For the first time scientifically substantiated and implemented author's technique - modified “natural” caesarean section with the use of specially designed operating underwear, which allows to provide visualization of child birth, early contact of mother and child “skin to skin”, bypassing the contact with indirect persons, as well as the initial contamination of the newborn with microflora of the maternity woman. (patent for utility model No. 7441, RK).
3. With the introduction of MNCS, for the first time, the intraoperative stay of mother and child together from the first minute of life is ensured, which allows to concentrate the focus on the psychological well-being of mother and child.
4. The relationship between the level of hormonal responses in newborns and the method of delivery (MNCS, TCS, VB) was revealed for the first time.
5. It was proved for the first time that MNCS takes into account individual preferences of a woman in labor more widely and provides her with more pronounced psychological comfort in relation to TCS, which makes MNCS more patient-oriented and inclusive.

Practical significance of the results obtained:

1. The introduction of modified “natural” cesarean section as an innovative perinatal technology into obstetric practice allows to reduce stress for mother and child due to the elimination of their forced intraoperative separation, reduce the likelihood of respiratory problems in newborns, and also contributes to a faster recovery of the laboring woman.

2. Introduction of specially designed surgical undergarments for performing a modified “natural” cesarean section. Visualization of the birthing process, immediate skin-to-skin contact between mother and baby, and the possibility of early initiation of breastfeeding strengthen the bond between mother and baby, which promotes early establishment and maintenance of lactation.

3. Reduced incidence of PPH during elective abdominal delivery due to the advantages of the implemented innovative technology. Rapid recovery after delivery and reduction of complications lead to shorter length of stay in the clinic and less need for additional medical interventions.

4. Better adaptation of the newborn after modified “natural” cesarean section in the early neonatal period, reduction of perinatal morbidity.

5. Creating conditions during MNCS for early initial contact between mother and newborn “skin to skin” and its contamination by the mother's microflora.

6. As of introduction of the modified “natural” caesarean section into the practical health care of the Republic of Kazakhstan were obtained.

7. Introduction of modified “natural” cesarean section in the educational process of students of KazNMU.

8. Development of a training manual “Modified ‘natural’ caesarean section” for obstetricians, gynecologists, neonatologists, anesthesiologists, residents.

Personal contribution of the doctoral student: the author personally formed the direction and program of the study, conducted an analytical review of domestic and foreign literature on the problem under study, made a program of collection and processing of material, all operations with modified “natural” cesarean section were performed by the author personally (surgeon and assistant), conducted statistical processing of data, interpretation and discussion of the results, formulation of the provisions to be defended, conclusions and practical recommendations.

Conclusions:

1. Medical and social factors such as marital status, education level, reproductive and somatic history influenced pregnant women's informed choice of more physiologic and adaptive abdominal delivery - MNCS. Among the women who opted for MNCS, repeat births (44.2%), active reproductive age (45.0%), registered marriage (96.7%), higher education (51.7%), uterine scar combined with obstetric and somatic pathology (48.3% and 39.2%, respectively) were significantly predominant.

2. The developed modification of NCS, as close as possible to natural childbirth, allowed the mother to be an active participant of labor and visualize the moment of childbirth, excluded intraoperative separation of mother and newborn, contributed to a significant decrease in the volume of intraoperative blood loss by 2.1 times. Despite the lengthening of the third stage of the operation, the total duration of the operation did not increase, but even decreased. The absence of postpartum purulent-septic infections led to a decrease in the duration of postpartum bed-day by 0.7 days relative to TCS, which makes this method an economically more advantageous method of abdominal delivery by optimizing the expenditure of health care resources.

3. MNCS provided conditions for a significantly early debut of breastfeeding and prolonged skin-to-skin contact between mother and newborn: as

early as 3.51 minutes after birth and for 107.9 minutes, while with TCS - only after 77.7 minutes and for 63.8 minutes ($p<0.001$). The duration of the primary skin-to-skin bodily contact between mother and child in MNCS is comparable to that in VB (114.6 minutes).

4. The author's modification of "natural" cesarean section as a method of abdominal delivery with a high degree of "physiological" contributed to a more active activation of stress-adaptation mechanisms and a favorable level of hormonal response in newborns, which was manifested by a significant increase in the level of cortisol in newborns by 1.7 times, approaching the similar index after VB and improvement of Apgar scale scores of newborns both at the 1st and 5th minutes of life (higher by 1.21 and 1.23 points, respectively) relative to newborns after TCS.

5. Delayed umbilical cord crossing was performed after 69.2 seconds in MNCS, which is 2.8 times later than in TCS ($p<0.001$), approaching the same indicator in VB - 96.3 seconds ($p=0.006$), which demonstrates the implementation of physiologically oriented abdominal delivery, providing the newborn with a more complete CABG and mild adaptation in the early neonatal period.

6. The onset of lactation in post-MNCS women was identical to the onset of lactation after VB and had no significant differences (2.2 and 2.17 days) and occurred 0.7 days earlier than in TCS ($p<0.001$), which is due to a complex of factors, such as minimal surgical blood loss, immediate application of the newborn to the mother's breast and prolonged skin-to-skin contact immediately after birth.

Approbation of the results of the dissertation:

The main provisions and results of the work were repeatedly reported at the International and Republican Scientific and Practical Conferences:

1. "Innovative elective caesarean section: myths and reality" (IV International Scientific and Educational Forum "Ana Men Bala", May 20-21, 2021),
2. "Abdominal delivery in modern obstetrics" (IV International Scientific-Educational Forum "Ana Men Bala", May 20-21, 2021) - awarded 2 prizes in the section of young scientists,
3. "Personalization of delivery management in high-risk pregnancy" (Scientific - practical conference with international participation "Innovative technologies in the service of perinatology and pediatric cardiac surgery", November 19, 2021),
4. "Influence of the method of delivery on the level of stress hormone in newborns" (V International Scientific-Educational Forum "Ana Men Bala", May 19-20, 2022),
5. "Cortisol in the blood of newborns as a marker of "Healthy stress" in childbirth" (Scientific and practical conference "I International Congress of Obstetricians and Gynecologists of Kazakhstan "Family Health - Future of Kazakhstan", Almaty, March 30-31, 2023), awarded 1 prize-winning place in the section of young scientists,
6. "Abdominal delivery: NEW HORIZONTES" (VI International Scientific-Educational Forum "Ana Men Bala", May 19-20, 2023).

Information about implementation:

The main results of the conducted research are used in the work of maternity hospitals of the city of Almaty № 5 and № 1, the results of the work are implemented in the practice of doctors of perinatal centers of the "Karasay Central District Hospital", Kaskelen, "Regional Perinatal Center" State Institution "HD of Zhetysu region", Taldykorgan, "Maternity Center", Taldykorgan. Kaskelen, "Regional Perinatal Center" State Institution "HD of Zhetysu region", Taldykorgan, "Mother and Child Center", HD of East Kazakhstan regional akimat, Ust-Kamenogorsk, "Regional Perinatal Center №3" HD of Turkestan region, Turkestan city.

The modified method of abdominal delivery and specially designed surgical underwear developed in the course of the work were approved and implemented in the practical health care of the Republic of Kazakhstan, which is confirmed by the relevant acts of implementation at the bases of obstetric and gynecological institutions.

Publications:

12 printed works have been published on the materials of the dissertation, of which:

- - Two publications in journals included in the international database Scopus:

1. Ainura Yuldasheva, Gulzhakhan Omarova, Zhanara Begniyazova, Shynar Saduakassova, Elmira Makhmutova, Aliya Meirmanova. Comparison of different cesarean delivery techniques: A systematic review and meta-analysis. 2023, 20(6), em539, e-ISSN: 2516-3507 Electronic Journal of General Medicine. https://doi.org/10.29333/ejgm/13590 - 77% percentile (Q1).
2. Gulzhakhan Omarova, Zhanat Sultanova, Aliya Aimbetova, Shynar Saduakassova, Ainura Yuldasheva (author correspondent). Cesarean Section: Medical, Social and Moral and Ethical Factors. 2024; 4:1337 Salud, Ciencia y Tecnología. https://doi.org/10.56294/saludcyt20241337 - 75% percentile (Q1).

- - Two articles in journals included in the List of publications recommended by the Committee for Quality Assurance in Science and Higher Education of the Ministry of Education and Science of the Republic of Kazakhstan:

1. A.I. Yuldasheva, G.K. Omarova, A.T. Mustafazade, Z.M. Nashekenova, A.O. Meirmanova "A new look at an old problem: 'natural' cesarean section (literature review)", "Obstetrics, Gynecology and Perinatology",1-2-2019;
2. A.I. Yuldasheva, G.K. Omarova, R. Tameliene, Zh.S. Begniyazova, A.T. Mustafazade "Old and new opportunities in optimization of the elective caesarean section", "Bulletin of KazNMU", No. 2 2019;

- - Two articles published on the results of scientific works in the proceedings of international conferences:

1. A. I. Yuldasheva, G. K. Omarova, R. Tameliene "Medical - social aspects of pregnant women with elective caesarean section", The fifth international scientific-practical conference "Global science and innovations: Central Asia", Nur-Sultan, Kazakhstan, March 2019;
2. A.I. Yuldasheva, G.K. Omarova, E.A. Makhmutova "Comparative characteristics of stress hormone in newborns depending on the method of delivery", Journal - collection "Obstetrics, Gynecology and Perinatology", Almaty 2022, №1(87). - c.80;

- - Four protected documents were obtained, including two patents and two certificates of authorship:

1. A.I. Yuldasheva, G.K.Omarova, patent for invention “Method of elective abdominal delivery”, №35677 from 31.03.20212.
2. A.I. Yuldasheva, G.K.Omarova, patent for useful model “Operating underwear for modified caesarean section”, № 7441 from 02.05.2022;
3. A.I. Yuldasheva, G.K.Omarova, copyright certificate “New possibilities of optimization of elective caesarean section in RK”, №3361 from 16.05.2012;
4. A.I. Yuldasheva, G.K. Omarova, J.A. Mukhamedjanova, copyright certificate “Innovative elective caesarean section in the Republic of Kazakhstan”, №16435 from 08.04.2021.

Implementation in the educational process:

1. A.I. Yuldasheva, G.K. Omarova, B.N. Bishekova “Practical training by teamwork on the example of operation ”Modified “slow/gentle” caesarean section", Protocol № 7, from 11.04.2023.
2. G.K. Omarova, A.I. Yuldasheva, Textbook “Modified ‘natural’ caesarean section”, recommended for use in the educational program of higher medical education. Extract from the Protocol of the meeting of the Academic Council № 13 from 30.05.2024, Approved and allowed to publish by printing method RSE “Republican Center for Health Development” (minutes of the meeting of the Department of Medical Science and Education Development RSE RCHD“ № 2 from ”02" 2025).

Scope and structure, and volume of the dissertation:

The dissertation is outlined on 113 pages of typewritten text, consists of an introduction, literature review, material and methods of research, chapter of the results of own research, conclusion, conclusions, appendices. The dissertation is illustrated with 26 tables, 17 figures, 6 appendices. The bibliographic index includes 191 sources, including 106 foreign ones.