“CAROL DAVILA” UNIVERSITY OF MEDICINE AND PHARMACY

BUCHAREST

DOCTORAL SCHOOL

MEDICINE

ULTRASOUND AND BIOLOGICAL PARAMETERS IN MONITORING HIGH-RISK PREGNANCY

SUMMARY OF THE DOCTORAL THESIS

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FUNDAMENTAL PROBLEM

The scientific motivation of the present research regarding the ultrasound and biological parameters in monitoring pregnancies with obstetrical risk is closely linked to the significant impact of pregnancy-associated pathologies on maternal and fetal morbidity and mortality.

The topic addressed is highly relevant, both nationally and internationally, given, among other things, the increasing number of births by cesarean section and the alarming number of patients who do not benefit from prenatal care.

Pregnancy is a complex stage in a woman's life, considering the physical, psychological, and social changes that occur during it [1]. Inefficient adjustment to these changes can lead to the appearance of pathologies in pregnancy, transforming it into a pregnancy with increased obstetrical risk, with a significant psychological impact[1,2]. Any medical or obstetrical pathology that appears during pregnancy, with the possibility of increasing maternal or fetal morbidity, leads to its classification in the category of pregnancies with obstetrical risk [1,3]. Since there are no clear criteria for assessing risk in pregnancy, this being the result of a subjective assessment by the patient or doctor[1], we can state that the number of high-risk pregnancies is increasing, directly proportional to the increase in the use of screening and diagnostic methods, and implicitly early treatment[2].

The purpose of prenatal visits is to promote maternal and fetal health by carefully monitoring risk factors and treating complications that occur, from their onset[4,5]. Clinical and psychological outcomes during pregnancy and the postpartum period are improved by proper pregnancy monitoring, thus decreasing maternal and fetal morbidity and mortality[4,6]. It has been demonstrated that the phenomenon of lack of pregnancy monitoring is mainly the result of the negative impact of several factors – socioeconomic, through reduced income and lack of education, difficult access to health services, the quality of medical services, as well as the lack of social support[7–9].

Although patients' access to health services during pregnancy has been facilitated, the number of pregnant women who choose not to have prenatal visits is still high, with the associated implications for reproductive health[7–9]. On the other side of the spectrum, there are patients who follow medical recommendations, thus observing in parallel an increase in the number of pregnancies that are classified as being high-risk – the reason being multiple investigations performed early, with early diagnosis and treatment instituted in time to avoid complications[8].

This paper mainly focuses on patients who do not access health services until obstetric complications arise. These cases are frequently represented by patients with unmonitored pregnancies, who present to the doctor when the pathology has advanced, at which point therapeutic resources are limited and more financial resources are used to treat complications. A representative example for our population is the patient with undiagnosed and untreated preeclampsia, who presents to the doctor with various complications, such as intrauterine growth restriction, premature detachment of normally inserted placenta, severe preeclampsia, or even eclamptic crisis. Frequently, these patients who access medical services in the event of complications end up giving birth by cesarean section. Given the ever-increasing number of births by cesarean section in this case[10,11], it is of real interest to find the surgical technique that is associated with the lowest rate of development of isthmocele, which in turn has implications and repercussions on women's health [11–13].

PERSONAL CONTRIBUTIONS

WORKING HYPOTHESIS AND STRUCTURE

This paper aims to identify certain medical peculiarities associated with this trio of phenomena that frequently occur in cascade – unmonitored patients who present with an obstetrical complication and give birth by cesarean section.

The paper is structured in two main parts, which harmoniously combine theoretical aspects with original personal research.

The general part of the thesis aims to prepare and frame the studies carried out in the context of the data existing in the specialized literature. It is configured in two chapters, so that the first chapter is entitled "High-risk pregnancy - hypertensive pathology and its impact", and the second is entitled "Prenatal care and the implications of the lack of medical assistance".

The original part of the thesis is configured in three parts. The working hypothesis revolves around the predisposition of unmonitored pregnant women to develop obstetrical complications, the directions of study being the study of Doppler changes in term pregnancy at the level of the uterine arteries, the identification of the surgical technique with minimization of long-term complications, and the impact of lack of prenatal care on patients.

Thus, three emerging themes have been divided, with the aim of integrating the information obtained into the arsenal of data with importance in obstetrical practice.

The first study, entitled "Contributions regarding the study of pulsatility and resistivity indices of uterine arteries in term pregnancies," aims to identify possible correlations of pulsatility and resistivity indices of uterine arteries, evaluated during the ultrasound examination of pregnant women at term.

The second study, entitled "Prenatal care – discrepancies between recommendations and reality," aims to shed light on the complications associated with the lack of prenatal care.

The third study, entitled "Isthmocele – an iatrogenic pathology" aims to identify the patient and technical variables within the cesarean section operation that lead to the formation of isthmoceles.

The three listed directions and related results constitute a concrete and personal contribution, with subjects that blend harmoniously to outline a type of patient frequently encountered in medical practice.

Chapter 4 – Contributions regarding the study of pulsatility and resistivity indices of uterine arteries in term pregnancies

Normal blood flow in the feto-placental circulation is important for creating a healthy intrauterine environment, which ensures harmonious fetal growth. The relationship between abnormal Doppler indices at the level of the uterine arteries and the appearance of various obstetrical complications has been extensively studied. Although trophoblastic invasion cannot be directly assessed, Doppler studies allow non-invasive evaluation of uteroplacental circulation by comparing systolic and diastolic waves.

With the aim of confirming the hypothesis that the pulsatility and resistivity indices of the uterine arteries correlate with certain aspects that can be highlighted in pregnancies with increased obstetrical risk, the following objectives were stated: (i) identifying the anamnestic characteristics of the patients, (ii) quantifying the relevant variables, respectively the pulsatility and resistivity index of the uterine arteries and the umbilical artery, objective evaluation of the amount of amniotic fluid, the position and grade of the placenta, as well as the fetal weight estimated by ultrasound with the related percentile and the percentile of the abdominal circumference, (iii) identifying patients with associated pathologies, as well as (iv) evaluating how the pulsatility and resistivity indices of the uterine arteries correlate with various variables and (v) evaluating the correlation between the pulsatility and resistivity indices of the uterine arteries and the associated pathologies.

The present paper brings together the results of prospective analysis of medical data from 60 pregnant patients with single live fetus pregnancies, at term (with gestational ages >37 weeks and <41 weeks), admitted to the Obstetrics-Gynecology department of the Emergency Clinical Hospital "Sf. Pantelimon", between 01.05.2024 – 31.08.2024. The research plan was implemented in compliance with the norms of scientific, professional and academic ethics, in accordance with the provisions of the code of ethics and deontology of the institutions involved. The scientific research activity was previously approved by the Ethics Committee of the Emergency Clinical Hospital "Sf. Pantelimon", by decision no. 47/20.11.2023.

The results of the study demonstrated that there is a statistically significant correlation between systolic blood pressure and the average RI value of the uterine arteries, as well as between diastolic blood pressure and the average PI and RI values of the uterine arteries. There is evidence to support that trophoblast invasion is maximal in the first trimester, which

is why Doppler evaluation of the uterine arteries is recommended as early as the first trimester of pregnancy. Continuous monitoring of patients through Doppler studies and measurement of indices throughout pregnancy has proven useful, as patients with persistently elevated PI have been shown to be at higher risk of developing preeclampsia. This is due to an association between continuous impairment of blood flow through the uterine arteries and gestational hypertension, independent of RI measured in the second trimester of pregnancy.

Secondly, there is a moderate and significant negative correlation between the amount of amniotic fluid and the average RI value. The association between oligohydramnios and elevated RI reflects the complex interaction between amniotic fluid levels, placental health, and fetal well-being. Oligohydramnios may indicate compromised placental function, which can lead to inadequate blood supply to the fetus. This can cause constriction of blood vessels, increasing RI as the body tries to maintain adequate perfusion under stress. Part of the pathophysiological mechanism is also explained by the fact that the average value of PI differs significantly between grades 2 and 3 Grannum of placental maturation, with higher values observed in the more advanced grade.

Regarding the location of the placenta, the insertion of the placenta on the anterior or posterior uterine wall does not have a significant impact on the PI and RI values of the uterine arteries, while the average values of PI and RI of the uterine arteries are significantly higher on the contralateral side of the placental insertion. This suggests that the insertion of the placenta may influence uterine hemodynamics, having a significant impact on vascular resistance and blood flow.

It is also important to mention that Doppler evaluation of the uterine arteries not only helps to identify the risks of complications, but can also guide the clinical management of pregnancy. Careful monitoring of PI and RI can allow early interventions if significant changes are observed, thus contributing to the improvement of materno-fetal outcomes.

Given the results of the statistical analysis, these suggest that PI and RI values are higher in the group of patients with gestational diabetes, pregnancy-induced hypertension, oligoamnios, intrauterine growth restriction, and drug users. Other pathologies such as pregnancy cholestasis, chronic hypertension, SGA fetuses, polyhydramnios or maternal obesity do not influence the PI and RI index values at the level of the uterine arteries.

In conclusion, although there is variability in PI and RI values depending on different conditions and factors, it is essential to continue research to better understand these relationships and to develop evidence-based screening and management protocols. This will

allow a more personalized and effective approach in the care of pregnant women, especially in cases with an increased risk of complications.

Summarizing, these conclusions highlight the importance of careful monitoring of the pulsatility and resistivity indices of the uterine arteries by Doppler velocimetry, as they provide essential information about the health of the placenta and the fetus. Further studies are needed to better understand the relationships between these indicators and variable factors, as well as to update evidence-based diagnostic and management protocols. This will allow a personalized and effective approach in providing prenatal care, especially in high-risk pregnancies.

Chapter 5 – Prenatal care – discrepancies between recommandations and reality

The fundamental objective of prenatal care is to optimize the health of the pregnant woman and the fetus by carefully monitoring risk factors and early therapeutic intervention in case of complications. Adequate monitoring of pregnancy significantly improves clinical and psychological outcomes both during gestation and in the postpartum period.

In order to confirm the hypothesis that antenatal care decreases maternal and fetal morbidity, a series of objectives were stated: (i) characterizing patients from a demographic, social, and medical point of view, (ii) quantifying relevant variables, namely age, parity, presence of prenatal care, mode of delivery, presence of antepartum and/or postpartum anemia, administration of iron supplements, values of various hematological parameters, presence of vaginal infections, establishing the severity of anemia and transfusion requirements, as well as quantifying the length of hospitalization of newborns and the need for antibiotic therapy in newborns, (iii) identifying patients with antepartum and postpartum anemia, (iv) identifying correlations between the lack of antepartum care and the presence of anemia, (v) evaluating how the lack of pregnancy monitoring influences the length of hospitalization of newborns.

In this study, the medical data of 125 patients who gave birth between 01.08.2024 – 28.02.2025, in the Obstetrics and Gynecology department of the Emergency Clinical Hospital "Sf. Pantelimon" were retrospectively analyzed. The research plan was implemented in accordance with the norms of scientific, professional, and academic ethics, respecting the provisions of the code of ethics and deontology of the institutions involved. The scientific research activity was previously approved by the Ethics Committee of the Emergency Clinical Hospital "Sf. Pantelimon", according to decision no. 98/20.11.2024.

The results of the study reinforce the evidence already existing in the literature regarding the fact that young age and multiparity are risk factors for deficient prenatal care. Complete and correct monitoring of pregnancy is more frequent among older people, which may reflect, among other things, an increased need among these patients. Young patients, especially adolescents, may experience socioeconomic difficulties, such as limited financial resources or a disharmonious family environment, which can make access to prenatal care difficult. Young patients may present fear or shame regarding pregnancy, leading to a delay or

even lack of access to medical services during pregnancy. Regarding multiparity as a risk factor, it is possible that patients with previous uncomplicated pregnancies underestimate the importance of prenatal care, believing that subsequent pregnancies will also be risk-free. Also, patients with large families may have multiple responsibilities in caring for children, which leads to the impossibility of making medical visits, due to lack of necessary time.

A significant number of patients in the monitored group give birth by cesarean section. There are a multitude of factors that have led to this increased number, tocophobia being an important factor. Tocophobia, or fear of uterine contractions, is of two types – primary or secondary. This phobia significantly impacts the quality of life, reaching the extreme where patients avoid the occurrence of pregnancies.

Anemia in pregnancy affects a significant proportion of pregnant patients, underlining the need for monitoring and management of this condition in prenatal care. Among the causes of gestational anemia are the increase in blood volume, the increase in the need for iron and the lack of iron supplementation as well as deficiencies of other nutrients, such as folic acid and vitamin B12. Prenatal care is associated with a lower prevalence of gestational anemia, which underlines the importance of repeated testing in pregnancy and early treatment. Medical personnel frequently recommend iron supplementation during pregnancy, especially in the case of patients with anemia or at increased risk of developing anemia. Also, prenatal care includes educating patients regarding proper nutrition, with foods rich in iron, such as red meat, vegetables, and cereals. Through early testing, nutritional counseling and management of possible comorbidities, prenatal care significantly reduces the risk of occurrence and prevalence of anemia during pregnancy. Without these interventions, anemia can worsen, leading to the appearance of more cases of severe anemia, with associated complications.

Prenatal care helps to identify and manage risk factors for premature birth, such as high blood pressure, gestational diabetes, and infections. Thus, pregnancy monitoring decreases the risk of premature birth, which is frequently associated with a longer length of hospitalization of newborns. Regarding infections, there is a significant association between the lack of prenatal care and the need for antibiotic treatment in newborns. This is caused by the fact that during pregnancy the diagnosed infections are treated, decreasing the risk of transmission to the newborn and implicitly the need for treatment. Antibiotic therapy at birth prolongs the length of hospitalization and increases the need for invasive investigations for diagnosis and monitoring of treatment.

Chapter 6 – Isthmocele – an iatrogenic pathology

Recently, the diagnosis of isthmocele has become easier, being a pathology with which we have begun to familiarize ourselves and which we actively seek. The uterine niche, or isthmocele, is thus defined by the ultrasound image that reveals an indentation in the myometrium, at least 2 mm deep. Among the long-term complications that occur are menometrorrhagia, dysmenorrhea, and chronic pelvic pain. Additionally, women may experience subfertility or infertility. If a subsequent pregnancy is achieved, the presence of isthmocele can have obstetrical consequences, such as abnormal placental insertion – spectrum accreta, implantation of the pregnancy at the level of the uterine scar, or uterine rupture.

Given the consequences of the presence of isthmocele and the ever-increasing number of births that end in cesarean section, the number of women facing long-term effects has also increased, thus justifying the interest in analyzing the type of hysterorrhaphy used and its impact on the formation of the uterine scar, in order to adopt a preventive strategy by identifying risk factors.

The hypothesis of this study is based on the suspicion that certain types of uterine sutures during cesarean section are more frequently associated with the appearance of isthmocele. To confirm the working hypothesis, the following objectives were stated: (i) evaluation of the presence of the niche and associated ultrasound characteristics (depth, total myometrium thickness, residual myometrium thickness, shape and depth/total myometrium thickness ratio), (ii) selection of patients with severe niche and (iii) evaluation of the method of hysterorrhaphy according to the number of layers, the type of suture used – continuous locking suture, continuous non-locking suture or interrupted suture, the thickness of the thread used and the presence or absence of peritonization.

The present study represents a prospective analysis of 52 patients at the end of the puerperium, who gave birth by cesarean section at the Emergency Clinical Hospital "Sf. Pantelimon", Obstetrics-Gynecology department, between 01.04.2022 – 01.04.2023. The research plan was implemented in compliance with the norms of scientific, university and professional ethics, in accordance with the provisions of the code of ethics and deontology of the institutions involved. The conduct of the research activity was previously approved by the

Ethics Committee of the Emergency Clinical Hospital "Sf. Pantelimon", by decision no. 21/30.03.2022.

Given the results presented following the descriptive and statistical analysis, a series of discussions can be approached and deepened.

Depending on the position of the uterus, 67.3% of patients presented anteverted uterus, the rest having retroverted or intermediate position uterus. Although the retroverted uterus position has been studied and established as a risk factor for the appearance of isthmocele, the statistical analysis failed to prove a statistically significant association. However, analyzing the database, the most severe niches were observed in patients with retroverted or intermediate position uterus (depth/total thickness ratio 66% and 63%, respectively). An explanation for the fact that the retroverted uterus can associate a severe isthmocele is that the surgical technique involves a different angle of the hysterotomy, but this factor is not the only one that contributes to the development of the defect. Starting from this result, it can be concluded that additional studies on larger groups are needed.

The ultrasound appearance of the niche was observed in 22 patients out of the 52 included in the study, its prevalence being 42.3%, in accordance with international studies that show a prevalence of up to 70%. The increased prevalence of isthmocele underlines the importance of prevention measures. Among these patients, I remind you that 31.8% have ultrasound severity criteria.

Although in the past the association between the number of layers and the formation of isthmocele has been both confirmed and disproved, the study did not show significant differences in the formation of isthmocele depending on the number of layers used in the hysterorrhaphy. These results are consistent with the latest findings, so single-layer suture is not a risk factor for the appearance of isthmocele. Even in the case of patients with isthmocele classified as severe, no significant association with the number of layers in the hysterorrhaphy was observed.

However, a significant association was found between the suture of the first layer with continuous locking surjet and the development of isthmocele, probably due to the ischemia associated with this type of suture. Further analyzing and referring strictly to patients with severe isthmocele, in this group of patients it was demonstrated that suture with continuous locking thread predisposes to the appearance of severe defects. These findings suggest that hysterorrhaphy with continuous locking suture is a risk factor for the appearance of isthmocele, particularly severe isthmocele.

In light of this information, the idea emerges that additional extensive research is needed, given the increased prevalence of this pathology.

Conclusions and personal contributions

The three subsidiary directions listed and the related results constitute a concrete and personal contribution to obstetrical practice, with subjects that blend harmoniously to outline a type of patient frequently encountered in our medical practice – a patient without prenatal care, with therapeutically neglected hypertensive pathology, who gives birth by cesarean section due to complications that have occurred.

The first study analyzes the correlations between various factors and the pulsatility and resistivity indices of the uterine arteries. These correlate positively with systolic and diastolic blood pressure, smoking, the degree of maturation of the placenta and the presence of certain pathologies, such as gestational diabetes, pregnancy-induced hypertension, oligoamnios or intrauterine growth restriction. Other pathologies such as pregnancy cholestasis, chronic hypertension, SGA fetuses, polyhydramnios or maternal obesity do not influence the PI and RI index values at the level of the uterine arteries. Summarizing, these conclusions highlight the importance of careful monitoring of the pulsatility and resistivity indices of the uterine arteries by Doppler velocimetry, as they provide essential information about the health of the placenta and the fetus.

The results from the second study contribute to a better understanding of the adverse effects of deficient prenatal care. Prenatal medical visits have the role of promoting maternal-fetal health through careful monitoring of risk factors and early diagnosis and treatment. The phenomenon of lack of monitoring is very frequent, so half of the patients do not perform the recommended medical visits. Among the risk factors identified for the lack of prenatal care are young age and multiparity. Prenatal monitoring is associated with a decrease in the prevalence of anemia in pregnancy and severe postpartum anemia, with a reduction in the number of blood transfusions required after birth. Newborns of mothers who attended prenatal care have a shorter length of hospitalization, with a decrease in the need for antibiotic treatment.

The third study states important aspects that contribute to a better understanding of the process of isthmocele development and the associated risk factors. The increased prevalence of isthmocele underlines the importance of prevention measures. Although in the

past the association between the number of layers and the formation of isthmocele has been both confirmed and disproved, the study did not show significant differences in the prevalence of isthmocele depending on the number of layers used in the hysterorrhaphy, so single-layer suture is not a risk factor for the appearance of isthmocele. A significant association was found between the suture of the first layer with continuous locking suture and the development of isthmocele, probably due to the ischemia associated with this type of suture. Hysterorrhaphy with continuous locking suture is a risk factor for the appearance of isthmocele, particularly severe isthmocele.

Personal contributions

The examination of the results obtained following the intense study and statistical analyses has led to the possibility of outlining the following personal contributions:

Chapter 4

- There is no statistically significant correlation between maternal age or weight and the PI and RI index values at the level of the uterine arteries – p=0,604 and p=0,989 (subchapters 4.3.2 and 4.3.3)
- There is a statistically significant correlation between systolic and diastolic blood pressure values and the average PI and RI index values – p=0,014 and p=0,001 (subchapters 4.3.4 and 4.3.5)
- The data suggest a trend that smoking may be associated with higher average PI values, but the differences are not significant (subchapter 4.3.6)
- There is a significant negative correlation between the amount of amniotic fluid and the Doppler index values (p=0,011, Pearson correlation -0,258) and a positive correlation between them and the degree of maturation of the placenta – p=0,041 (subchapters 4.3.8 and 4.3.9)
- Higher PI values at the level of the uterine arteries are associated with increased PI values at the level of the umbilical artery – p=0,049 (subchapter 4.3.10)
- The insertion of the placenta on the anterior or posterior uterine wall does not have a significant impact on the PI and RI values of the uterine arteries, but the averages of the indices are significantly lower in the case of the placenta being located on the contralateral uterine side – p=0,002 (subchapter 4.3.11)

- PI and RI index values are correlated with various pathologies, these values being higher in the group with gestational diabetes, pregnancy-induced hypertension, oligoamnios, or intrauterine growth restriction – p=0,033 (subchapter 4.3.12)
- Pathologies such as pregnancy cholestasis, chronic hypertension, SGA fetuses, polyhydramnios, or maternal obesity do not influence the PI and RI index values of the uterine arteries - p>0,005 (subchapter 4.3.12)

Chapter 5

- The phenomenon of lack of prenatal care is extremely common, affecting half of the patients – precisely 51,2% (subchapter 5.3.1)
- Prenatal care is more common among older and primiparous patients, while young age and multiparity are risk factors for the lack of prenatal care – p=0,02 (subchapters 5.3.2 and 5.3.3)
- Monitored women give birth more often by cesarean section – p=0,06 (subchapter 5.3.4)
- Anemia is a common pathology in pregnancy, affecting 50.4% of patients (subchapter 5.3.5)
- Unmonitored women have a higher proportion of antepartum anemia cases (60.9%) compared to monitored women (39.3%) (subchapter 5.3.5)
- There is a significant correlation between access to medical services and antepartum iron administration – p=0,001 (subchapter 5.3.6)
- Monitored patients have more cases of mild anemia, while unmonitored patients have a more varied distribution, including cases (0,8%) with severe anemia (subchapter 5.3.7)
- Monitored patients have higher values of hemoglobin, hematocrit, MCV, MCH and MCHC and lower values of leukocytes and neutrophils, compared to unmonitored patients (subchapter 5.3.8)
- There is no significant difference between the average postpartum Hb values in patients who gave birth vaginally and those who gave birth by cesarean section – p=0,780 (subchapter 5.3.9)
- There is a significant difference between the average Hb values in monitored and unmonitored patients, with values lower by approximately 0.5 g/dL among patients without prenatal care – p=0,037 (subchapter 5.3.10)

- Monitored patients have a much lower rate of requiring postpartum red blood cell transfusions (subchapter 5.3.11)
- Regarding the result of the bacteriological examination of the vaginal secretion, monitored patients have a higher incidence (87%) of negative cultures and fewer (13,1%) positive cultures for various bacteria, compared to unmonitored patients (48,4% have negative cultures, 14,1% have positive cultures and 37,5% were not tested) (subchapter 5.3.12)
- Newborns from monitored mothers tend to have a shorter hospitalization (approximately 4 days shorter) and a reduced need for antibiotic therapy – p=0,007 and p=0,041 (subchapters 5.3.13 and 5.3.15)
- Antepartum anemia does not significantly influence the length of hospitalization of newborns – p=0,589 (subchapter 5.3.14)
- Newborns who received antibiotics have a significantly longer length of hospitalization (approximately 7 days longer) – p=0,001 (subchapter 5.3.16)

Chapter 6

- The prevalence of isthmocele is increasing (subchapter 6.3.1)
- The most common forms of niche are triangular (45,5%) and semicircular (36,4%) (subchapter 6.3.1)
- There are no differences in the rate of niche appearance depending on the number of layers used in hysterorrhaphy – p=0,173 (subchapter 6.3.2)
- There is a statistically significant association between the suture of the first layer with continuous locking suture and the presence of the niche, especially the severe one – p=0,006 (subchapters 6.3.2 and 6.3.10)
- There are no significant differences between the total thickness of the myometrium and the residual thickness of the myometrium depending on the number of layers used – p=0,753 and p=0,818 (subchapters 6.3.3 and 6.3.4)
- The average thickness of the residual myometrium in patients with isthmocele is 0.2 cm higher in the case of continuous non-locking suture, compared to locking suture or interrupted suture – p=0,607 (subchapter 6.3.5)
- The total thickness of the myometrium in patients with isthmocele does not differ statistically significantly depending on the type of suture used – p=0,607 (subchapter 6.3.6)

- There are no significant associations between the shape of the niche and the number of layers of hysterorrhaphy or the type of suture of the first layer – p=0,284 and p=0,652 (subchapters 6.3.7 and 6.3.8)
- Approximately one third (31,8%) of patients have ultrasound criteria for severe isthmocele, with depth/total myometrial thickness ratio >50% (subchapter 6.3.9)
- There are no associations between the number of layers used in hysterorrhaphy and the severity of the isthmocele – p=0,899 (subchapter 6.3.9)
- The most severe niches were observed in patients with a retroverted or intermediate uterus (subchapter 6.3.13)
- Fibromatous or adenomyotic uterus is not associated with an increased risk of developing isthmocele – p=0,094 (subchapter 6.3.15)
- There are no associations between the lack of peritonization and the appearance of isthmocele – p=0,790 (subchapter 6.3.11)

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1. **Zampieri G**, Matei A, Roșu GA, Marin A, Poenaru MO, Ionescu CA. Contributions Regarding the Study of Pulsatility and Resistivity Indices of Uterine Arteries in Term Pregnancies—A Prospective Study in Bucharest, Romania. Diagnostics. 2024;14:2556
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(chapter 4)

2. **Zampieri G**, Ionescu CA. The impact of inadequate prenatal care on maternal anemia and pregnancy outcomes in Romania. J Med Life. 2025;18:306–14.
doi: 10.25122/jml-2025-0074. PMID: 40405925; PMCID: PMC12094301.
https://medandlife.org/all-issues/2025/issue-4-2025/original-article-issue-4-2025/the-impact-of-inadequate-prenatal-care-on-maternal-anemia-and-pregnancy-outcomes-in-romania/
(chapter 5)

3. **Zampieri G**, Nitescu B, Pacu I, Neacsu A, Ionescu C. Isthmocele - an iatrogenic pathology: A prospective study in a tertiary unit. Biomed Rep. 2024;22:2
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