

**UNIVERSITY OF MEDICINE AND PHARMACY
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*ENDOMETRIOSIS IN THE CONTEXT OF FERTILITY
PRESERVATION*
SUMMARY OF THE DOCTORAL THESIS

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1. Introduction

Motivation for Choosing the Research Topic

I chose the topic of endometriosis due to my experience as a gynecologist specialized in assisted human reproduction. I would like to investigate the connection between surgical interventions for endometriosis and their impact on fertility. Endometriosis is an increasingly common condition, with diverse symptoms and often diagnosed late. The available treatments do not guarantee a permanent cure or a consistent improvement in fertility rates. Thus, I wish to explore how surgical procedures can be integrated into a personalized treatment plan to maximize effectiveness and fertility-related outcomes.

2. General part - current state of knowledge

2.1 Epidemiology

The study falls within the international, national, and regional concerns for improving the diagnosis and treatment of endometriosis. Research in this field is making remarkable progress and paving the way for more effective and less invasive therapies. The hypothesis of the study refers to the optimal use of surgery in the treatment of endometriosis.

Endometriosis, an increasingly common condition with diverse symptoms, is often diagnosed late, and the available treatments do not guarantee complete healing or consistent improvement in fertility. Recent studies indicate that optimizing surgical indications can significantly improve clinical outcomes in terms of pain reduction and quality of life enhancement. (1,2) Additionally, it seems that adjuvant medication treatment after surgery and the need for postoperative medication can prevent recurrences and improve long-term prognosis. The research hypotheses include examining the volume of endometriotic implants over time and the resistance to stimulation treatments, as well as the low success rates in patients with endometriosis. The research objectives include determining the effectiveness of different types of surgery for endometriosis and conducting a comparative analysis of the long-term outcomes of patients who underwent surgery versus those who received other treatments. The research has an interdisciplinary character, addressing various fields such as gynecology, endocrinology, and reproductive biology.

Endometriosis, a chronic gynecological disorder present in 10-15% of women of reproductive age, significantly affects health, impacting professional activity and quality of life due to associated chronic pain and infertility. The disease is more common in women between the

ages of 25 and 45, and 7% of women have a genetic predisposition. The risk is highest among Asian women and lowest among women of color. Surgical treatments and adjuvant medication can prevent recurrences and improve long-term prognosis. The condition can present various localizations, ranging from the pelvic area to regions such as the lungs or brain. Controlling diet, especially the consumption of green vegetables and fresh fruits, can prevent the development of endometriosis. The disease, characterized by a combination of genetic, immunological, and environmental factors, is more frequently diagnosed in infertile women who are active smokers and have a normal or low body mass index. Future research aims to determine the effectiveness of different types of surgery for endometriosis and to analyze the long-term outcomes of patients who have undergone surgical interventions compared to those who have received other treatments. Endometriosis, a chronic gynecological disorder, affects 10-15% of women of reproductive age, having a major impact on health, professional life, and quality of life due to associated chronic pain and infertility.

2.2 Diagnostic

This affects women more frequently between the ages of 25 and 45, with a higher risk in Asian women and a lower risk in women of color. The diagnosis of endometriosis is a complex issue, presenting challenges in the absence of a non-invasive diagnostic technique, which results in significant diagnostic biases due to access to definitive surgical or imaging diagnosis. Ovarian endometrioma or deep endometriosis can be identified through imaging, while superficial peritoneal disease can be diagnosed through surgical evaluation if the symptoms are severe enough. Diagnosis can be complicated by limited access to specialists, geographical and economic barriers, as well as variations in symptoms among populations. Among the symptoms of endometriosis are persistent pelvic pain, painful menstruation, painful intercourse, and discomfort during urination and bowel movements. There is a variety of clinical aspects of the disease, which can range from occasional discomfort to chronic pain that can be debilitating, differing among women. Future studies aim to establish the effectiveness of different types of surgery for endometriosis and to analyze the long-term outcomes for patients who have undergone surgery compared to those who have pursued other forms of treatment. The connection between surgeries for endometriosis and their effect on fertility is being examined. Endometriosis is a chronic gynecological condition that affects 10-15% of women of reproductive age, with significant impacts on health, professional life, and quality of life. The diagnosis of this disease represents a complex issue, with significant implications in the absence of a non-invasive diagnostic method. The symptoms of

endometriosis vary, including chronic pelvic pain, discomfort during urination and bowel movements, and range from occasional discomfort to debilitating pain.(3,4)

2.3 Treatment

Treatments include medication, hormonal, and non-hormonal variables. Progestins and GnRH inhibitors are effective in pain management, but the latter can have severe side effects, such as menopause. GnRH agonists are effective, but their use is limited to a maximum of 6 months. Non-hormonal treatments include NSAIDs and various classes of innovative medications, including selective estrogen and progesterone modulators (SERMs and SPRMs), aromatase inhibitors (AIs), anti-angiogenic agents, immunomodulators, statins, cannabinoids, and dopaminergic agonists. All these treatments must be personalized for each patient based on symptoms, desire for fertility, and treatment tolerance. In this context, the author emphasizes the need for further research to improve treatments and develop a more effective and universal classification system for endometriosis. The discussion also includes surgical options, especially for ovarian endometriomas, cysts found in approximately 44% of patients with endometriosis. Endometrial polyps can have a negative impact on fertility, which is why selecting the correct method of intervention and post-operative care is important(5,6). Laparoscopic surgery is the current standard, but it is crucial to keep in mind that the procedure can affect ovarian tissue. Dienogest, a medical treatment for endometriomas, proves to be safe, effective, and well-tolerated.

3. The special part. Personal contributions to endometriosis regarding reproductive effects

The need for gentler approaches for patients who wish to preserve their fertility after surgery is emphasized. In this regard, various methods are discussed, some more promising than others, such as laser-based hemostasis techniques. These showed promising results in reducing the recurrence rate of endometrial fibrosis and significantly lowering AMH levels after the intervention.

A personalized approach to the treatment of endometriosis is necessary, with a focus on therapies that preserve fertility. Innovative methods such as CO₂ laser vaporization and the use of the PlasmaJet device are discussed, which allow for the detachment of the superficial layer of the cyst without affecting the fibrotic cortex. Combined techniques, which merge the advantages of excision and ablation, offer lower recurrence rates and preserve more ovarian

tissue (7–9). Coagulation treats the last 10-20% of the surface attached to the ovarian hilum, after 80-90% of it has been removed. It is also emphasized the need for preoperative diagnosis, which includes clinical examination, transvaginal ultrasound, and may include magnetic resonance imaging. A careful surgical strategy is necessary to treat deep infiltrating endometriosis, addressing the dense adhesions between the rectum and other structures. Studies indicate that plasma energy can control heat penetration and dissipation, promoting charge rate and reducing the risk of recurrence. Various innovative techniques are being discussed, such as laser vaporization or PlasmaJet, which facilitate the removal of the cystic layer while minimizing damage to the fibrotic cortex. Studies indicate the benefits of the combination of excision and ablation, which ensures lower recurrence rates and the preservation of a larger proportion of ovarian tissue.(10,11) The surgical intervention for deep endometriosis involves actions such as separating the rectal wall from the nodule, dissection, and, if necessary, repairing any muscular defects encountered. In the case of the presence of endometriosis in the intestines, various procedures can be approached, such as dissection, according to certain methods described in the specialized literature, or segmental resection of the sigmoid colon. Another procedure suggests the removal of the lower part of the rectum, which could reduce the risk of resection and denervation. The main objective is to improve the quality of life and fertility rates of patients with endometriosis.

The main goal of the work is to improve treatment approaches and, implicitly, the chances of conception for women affected by endometriosis. There is also a significant contribution aimed at the medical field, particularly in gynecology and reproductive medicine, through results that could facilitate the creation of new clinical guidelines and the optimization of surgical treatments. The author mentions the need for a better understanding of this complex condition and the development of effective and personalized treatments. The main objectives of the research include investigating the pathophysiological mechanisms of endometriosis, evaluating the effectiveness of surgery, identifying prognostic factors, studying the impact on quality of life, and collecting and analyzing retrospective data and case studies. The secondary objectives include investigating biological markers, the impact of endometriosis on ovarian reserve, comparing minimally invasive surgical interventions with conventional ones, evaluating the impact of surgery on pregnancy rates, and investigating the role of complementary medical therapy.

3.1 Study 1. The Impact of Surgical Technique on Endometriosis

Recurrence

The main goal of the study is to improve treatment approaches and chances of conception. The research extends to the analysis of the economic costs and benefits of various treatments, evaluating the cost-effectiveness ratio for different types of treatment. The study also includes an examination of the risk factors for endometriosis recurrence and ways to prevent the disease from returning. The author evaluates the effectiveness of psychological counseling for patients and investigates the specific psychological needs of these patients. Another component of the research is the comparison of international practices in the treatment of endometriosis. Additionally, the author conducted a prospective study at Colțea Clinical Hospital in Bucharest between 2018 and 2022, investigating the impact of surgical techniques on the recurrence of endometriosis, as well as evaluating the ovarian function of patients through certain biochemical and imaging tests. The research aims to make a significant contribution to the medical field, particularly in gynecology and reproductive medicine.

I conducted a comprehensive study on endometriosis and its impact on women's reproductive health and quality of life. A significant part of this study focuses on laparoscopic cystectomy as a primary surgical option for ovarian cysts, due to its numerous benefits: reduced pain and the need for postoperative analgesics, shorter hospital stays, fewer postoperative complications, rapid recovery, and cost savings. However, the long-term impact of this intervention on ovarian reserve is still unclear. To clarify this aspect, the author conducted a study between 2018 and 2022, aimed at examining the possible risks of disease recurrence and the impact of surgical technique on ovarian function. The results are eagerly awaited as they could influence the way endometriosis is treated, thereby contributing to the improvement of the prognosis and quality of life for these patients.

The inclusion criteria for the study involve screening tests for infertility or benign gynecological indications such as benign pelvic masses, abnormal uterine bleeding, and the absence of signs of malignancy or pre-malignant changes. Participants over 40 years old required a normal mammogram within one year of enrollment.

Among the exclusion criteria were severe hypersensitivity to any medication, a history of drug or alcohol abuse, pregnancy or breastfeeding, as well as significant abnormalities in clinical chemistry, blood count, or urinalysis. The subjects should not have suffered from any

recently diagnosed or unstable significant condition, should not have a history of metabolic diseases or severe depression, and should not have undergone any surgery that affects gastrointestinal motility, pH, or absorption.

Before inclusion in the study, the treatment was personalized according to the stage of endometriosis, adhering to the guidelines of international recommendations. This included the use of Dienogest 2 mg/day, combined oral contraceptives with microdoses of levonorgestrel and 30 micrograms of ethinylestradiol, as well as the GnRH agonist, triptorelin, administered in depot form every 84 days. The cases were carefully selected based on the stage of endometriosis, the appearance of the myometrium, and the presence of endometriomas, with those over 5 cm indicating surgical intervention prior to infertility treatment.

The patients in the study were analyzed by a multidisciplinary team that made the therapeutic decision, consisting of a surgeon, radiologist, endocrinologist, gynecologist specialized in infertility, and pathologist. After the applied therapies, the staging of endometriosis was reevaluated from a clinical and ultrasound perspective. The participants in the study were divided into two groups: one consisting of 49 women diagnosed with ovarian endometriosis (ages 28-42) and the second consisting of 16 women with deep endometriosis (ages 29-42). For each batch, specific clinical and imaging criteria were used for diagnosis. The objective was to highlight the differences in the recurrence of endometriosis and the prognosis on short- and medium-term infertility. The surgical techniques used in the treatment of endometriomas included complete ovarian cystectomy (stripping), the use of bipolar energy electrocoagulation for hemostasis, and suturing to prevent thermal damage. These procedures were performed by experienced surgeons from the Colțea Surgery Clinic, having access to high-performance technology.

A multidisciplinary team analyzed and made therapeutic decisions for the studied patients. These were divided into two groups: one of 49 women with ovarian endometriosis and the second of 16 women with deep endometriosis.

The 65 patients represent 5.2% of the total number of patients with endometriosis who presented during this period at the Colțea Surgery Clinic. The average age of the patients in the study was 35 years. The data distribution suggests a variable prevalence of the two forms of endometriosis, with a relatively higher frequency of ovarian endometriosis among younger women.

The multidisciplinary team analyzed and made therapeutic decisions for 65 patients, specifically 49 with ovarian endometriosis and 16 with deep endometriosis. The study

highlighted differences in the recurrence of endometriosis and the prognosis for infertility between the two groups. Among women aged 35-40, the trend has reversed, with deep endometriosis being predominant. After 40 years, the number of endometriosis cases has decreased for both forms, possibly due to the onset of menopause. Cases of ovarian endometriosis are predominant (75.4%), with a tendency to affect the left ovary. In addition, 73% of ovarian endometriosis cases are associated with deep endometriosis. The body mass index was 21.2 kg/m² for patients with ovarian endometriosis and 20.92 kg/m² for those with deep endometriosis. The majority of women (82.8%) reported at least one main symptom of endometriosis, and a significant proportion indicated that endometriosis had a negative impact on their emotional well-being. Additionally, the average number of pregnancies achieved before diagnosis is lower in the case of deep endometriosis (1 pregnancy per patient), compared to those with ovarian endometriosis (3 pregnancies per patient), thus indicating the impact of endometriosis on ovulation, fertilization, and the uterine environment.

Women with ovarian endometriosis have reported 17 miscarriages, indicating possible influences of the condition on the ability to maintain a pregnancy. In the case of deep endometriosis, 20 pregnancies have been lost, suggesting a more severe impact on pelvic structures, potentially increasing the risk of complications during pregnancy. The intervals between pregnancies vary, averaging 1.76 years for ovarian endometriosis and 2.25 years for deep endometriosis. These data could reflect the recovery of fertility, the urgency to conceive again, and the potential complications associated with endometriosis.

The majority of the patients included in the study are under 40 years old, without any associated comorbidities except for autoimmune thyroiditis, which accounts for 23.07%.

There is a direct correlation between the volume of endometriomas and the level of TSH, an extremely important aspect for the development of immunomodulatory therapies. Another aspect taken into consideration was the effect of a higher BMI on the prevention of an endometriosis diagnosis.

The study also showed a direct correlation between the volume of endometriomas and TSH levels, and considered the effect of a higher BMI on the prevention of an endometriosis diagnosis. The majority of the studied patients were under 40 years old, with the exception of a proportion of 23.07% for autoimmune thyroiditis.

A new element introduced in the study is the connection between height and the risk of endometriosis. The average height for women with ovarian and deep endometriosis is above the national average, suggesting that taller women may be more susceptible to these forms of

endometriosis. Nevertheless, this correlation was not observed in the case of bilateral endometriosis.

The multidisciplinary study on the impact of endometriosis on ovarian reserve highlighted more severe symptoms in women with deep endometriosis, such as chronic pelvic pain and infertility. A decrease in serum AMH levels and the number of pregnancies achieved in these cases has been observed.

The group with bilateral endometriosis shows an average CA 125 level of 136.80 ui/mL, indicating a more extensive or severe disease. The group with unilateral endometriosis has an average CA 125 level of 135.20 ui/mL, suggesting that tissue damage is independent of the severity or extent of endometriosis. The group with deep endometriosis has an average level of 116.96 ui/mL, indicating a different involvement of tissues, less associated with acute inflammation.

Elevated levels of CA 125 in individuals with bilateral and unilateral endometriosis indicate the need for ongoing evaluation for optimal disease management. In the case of deep endometriosis, a lower level of CA 125 requires a more detailed understanding of the pathological mechanisms and the specific inflammatory response.

The analysis of the average level of anti-Müllerian hormone (AMH) in cases of endometriosis highlighted different values for each group, reflecting the diverse impact of the disease on ovarian reserve. Patients with bilateral endometriosis may require more aggressive interventions for fertility management, while those with unilateral involvement have better prospects in terms of ovarian reserve and fertility.

The study on the impact of endometriosis on ovarian reserve showed severe symptoms in women with deep endometriosis, a reduction in AMH levels and resulting pregnancies, as well as a possible correlation between height, BMI, and the risk of endometriosis. Before the surgical intervention, patients received adjuvant treatment, which included both hormonal and symptomatic therapies. Hormonal therapy involved the administration of Diphereline and Visanne to reduce the volume of endometriosis, while symptomatic treatment included the use of Naproxen for pain control. In the case of deep endometriosis, the surgical procedures performed included ovarian cystectomy and adhesiolysis. The study recorded a recurrence rate in a number of 16 patients with ovarian endometriosis and 2 patients with deep endometriosis. Different correlations have been found between AMH, AFC, and FSH markers for ovarian endometriosis and deep endometriosis. This information is essential for the proper counseling of patients regarding family planning and fertility management, as well as for establishing monitoring and treatment strategies based on the type and severity of

endometriosis.

The study on the impact of endometriosis on ovarian function highlighted severe symptoms and reductions in AMH levels in women with deep endometriosis, affecting pregnancies and suggesting a possible association between height, BMI, and the risk of endometriosis. The pre-surgical treatment included hormone therapies and symptom management. A number of 18 patients experienced recurrences, with aggressive dynamics observed in the progression of tumors in those with recurrent ovarian endometriosis.

The information extracted from the correlation table between AMH, FSH, and AFC markers for ovarian and deep endometriosis shows different correlations, indicating the impact of these conditions on ovarian reserve and function. In ovarian endometriosis, there is a strong and direct relationship between AMH and AFC, as well as an inverse, but not very strong, relationship between AMH and FSH. In deep endometriosis, the connections are weaker, but still consistent.

The comparative study between patients with and without endometriosis recurrence included the analysis of AMH levels, age, and BMI. The acquired data, including an average AMH of 1.20 ng/mL, an average BMI of 21.21 kg/m², an average age of 35.91 years, and the distribution of endometriosis cases (bilateral or unilateral), provide a more detailed perspective on the prevalence and recurrence of endometriosis. These data are useful for advising patients and tailored treatment strategies.

The study regarding the impact of endometriosis on ovarian function highlights severe symptoms and a decrease in AMH levels in women with deep endometriosis, potentially associating height, BMI, and the risk of endometriosis. Before surgery, the patients received hormone therapy and treatment for symptom management. Out of 18 patients, recurrences were present, with aggressive tumor growth observed in those with the recurrence of ovarian endometriosis.

Most patients with recurrences had unilateral endometriosis, suggesting that it is more prone to reappearance than the bilateral form. Only 2 patients experienced a recurrence of deep endometriosis, which could indicate a better efficacy of therapies or insufficient detection and diagnosis of recurrences in the case of deep endometriosis.

Ovarian endometriosis is more common in women under 35, suggesting early detection, while deep endometriosis is slightly more frequent between the ages of 35 and 40, reflecting possibly the longer duration of the condition or complications in the effective treatment of more severe forms. Recidivism is more common in younger age groups, although it is observed in all age groups. This data is essential for informing patients and adapting

treatment strategies.

The study on the impact of endometriosis on ovarian function shows severe symptoms and a decrease in AMH levels in women with deep endometriosis. Most patients have a BMI within the normal or slightly elevated range, indicating a wide variety of BMI values between approximately 18 and 26. The age of the patients mostly falls between 30 and 40 years, suggesting that the recurrence of endometrioma is more common in late reproductive patients. In the pre-surgical phase, women received hormone therapy and treatment for symptom management. Recurrences were present in the examined cases, with an aggressive increase in tumors observed in those with a recurrence of ovarian endometriosis.

Markeri	Ovarian endometriosis	Deep Endometriosis
AMH și AFC	0.781	0.661
AMH și FSH	-0.285	-0.170
FSH și AFC	-0.382	-0.311

Table 3.1 Corelation between ovarian parameters and Endometriosis

The correlation table between AMH, FSH, and AFC markers shows discrepancies, highlighting the different impact of endometriosis on ovarian reserve and function. The representative graph shows a complex relationship between age, BMI, and characteristics of endometriosis in the context of postoperative recurrence, suggesting that the recurrence of endometriosis is influenced by multiple factors and requires an individualized management approach.

The decrease in the number of recidivism cases among women over 40 could be influenced by a decline in hormonal activity or by definitive surgical interventions. Most patients with recurrences had unilateral endometriosis. The study sample included patients with and without the recurrence of endometriosis, focusing on AMH levels, age, and BMI. In this regard, the AMH values for ovarian and deep endometriosis varied, suggesting a reduced ovarian reserve, a common phenomenon in cases of endometriosis.

AMH levels decrease with age in all forms of endometriosis, reflecting the natural decline in fertility and affecting ovarian reserve. The AMH level drops to 0.94 at ages 35-40 and to 0.42 over 40 in the case of ovarian endometriosis, while in the case of deep endometriosis, the level decreases to 0.90 and 0.51 in these age groups.

There is a negative response to ovarian stimulation in fertility treatments, as well as a

deterioration of ovarian function in cases of deep endometriosis. Thus, they affect the assisted conception rate, which is significantly higher in women with endometriosis (14.1%) compared to those without (4.4%).

Additionally, the results show a lack of correlation between FSH levels and pregnancy losses, as FSH, being an indicator of ovarian reserve, does not seem to directly influence the risk of miscarriage. These results are essential for optimizing treatment strategies and reproductive counseling for women with endometriosis. AMH levels decrease with age and affect ovarian reserve.

Deep endometriosis negatively affects the response to ovarian stimulation in fertility treatments, as well as ovarian function, leading to a higher rate of assisted conception in women with endometriosis (14.1%) compared to those without (4.4%). The results highlight the complexity of fertility management in patients with endometriosis and the need for ongoing research. It has been observed that AMH levels decrease with age, affecting ovarian reserve. Deep endometriosis affects the response to ovarian stimulation in fertility treatments, leading to a higher assisted conception rate in women with endometriosis (14.1%) compared to those without (4.4%).

In addition, patients with endometriosis were classified into two groups: those with primary infertility and those with secondary infertility. A contingency table and a chi-square test were used to determine whether AMH levels and the location of endometriosis affect the fertility of patients.

3.2 Study 2. Optimal stimulation protocols for patients with endometriosis in assisted human reproduction techniques

The study proposes an exploration of the efficacy and safety of various ovarian stimulation protocols for in vitro fertilization (IVF) in patients with endometriosis. The objectives include evaluating the success rate of embryo implantation, comparing ovarian response rates, studying the clinical pregnancy rate, assessing the incidence of side effects, and analyzing the impact of endometriosis on the effectiveness of IVF.

The study included a group of 65 patients aged between 18 and 45, diagnosed with endometriosis, who underwent various ovarian stimulation protocols based on their individual characteristics and medical history. The ovarian response, fertilization rate, embryo quality, and outcomes of embryo transfer were monitored and recorded, as well as any adverse effects associated with the treatments.

The psychological impact of IVF treatment has also been analyzed, measuring the stress and anxiety levels of the patients. The results were monitored and recorded regarding the fertilization rate, embryo quality, and outcomes of the embryo transfer.

The descriptive analysis of the sample showed that 65 patients represent only 5.2% of the total number of patients with endometriosis who presented at the tested clinic during the same period. Among these, the majority of cases involved bilateral ovarian endometriosis. The study found that the average age of patients with endometriosis ranged from 28 to 42 years, indicating a predominantly middle-aged population. This information is relevant because age can influence IVF outcomes.

Informed consents were signed by all the female patients before participating in the study. The study analyzes the impact of endometriosis on fertility and the effectiveness of various ovarian stimulation protocols for IVF in 65 women diagnosed with this condition, with an average age ranging from 28 to 42 years.

The body mass index (BMI) of the patients was generally normal or slightly underweight, which is favorable for assisted reproductive procedures. The variable values of FSH, the FSH/LH ratio, and the number of follicles suggest a diversity in ovarian function, ovarian reserve, and response to stimulation.

13 patients received exclusively FSH, indicating the use of a simplified stimulation approach. 34 patients received hCG for ovulation induction, while 29 received a combination of hCG and a gonadotropin-releasing hormone agonist to reduce the risk of ovarian hyperstimulation. 23 of the women reported previous pregnancies, including 24 pregnancies that were halted in development, suggesting an increased incidence of complications during pregnancy caused by endometriosis, particularly the risk of miscarriage.

The study also revealed the significant contribution of male factors to reproductive difficulties, with eight cases of infertility associated with sperm DNA fragmentation and 44 cases of oligoasthenoteratospermia, a condition involving sperm with abnormal characteristics. This information emphasizes the importance of identifying and appropriately treating male infertility factors through multidisciplinary approaches.

I evaluated fertility and the effectiveness of ovarian stimulation in a group of 65 women with endometriosis, with the aim of developing a personalized protocol based on individual characteristics and medical history. This study shows that endometriosis may require multiple cycles of in vitro fertilization (IVF), with a minimum of 1 and a maximum of 7 cycles. An increased prevalence of complications during pregnancy has been found for women with endometriosis, including a total of 24 pregnancies that were halted in their progression. It has

also been shown that age is an influential factor regarding the success of pregnancy, especially after the age of 40.

The study also noted the significant contribution of male factors to reproductive difficulties, with issues ranging from sperm DNA fragmentation to oligoasthenoteratospermia, a condition characterized by sperm with abnormal appearances.

Stimulation cycles have often been canceled for women over 35 or with low ovarian reserve, indicating the need to review and adjust stimulation protocols and explore other options, such as egg donation or the use of frozen eggs. The impact of endometriosis on fertility, the effectiveness of ovarian stimulation, and egg retrieval is being analyzed, suggesting the need for personalized treatment protocols. Endometriosis may require multiple cycles of in vitro fertilization (IVF), with increased risks of complications during pregnancy and egg retrieval. A graph from the study illustrates the distribution of stimulation doses used in IVF cycles, with frequent doses of 200 and 300 international units (IU), indicating typical doses for many patients, reflecting a balance between efficacy and minimizing the risk of ovarian hyperstimulation. Additionally, the 100 IU dose is often used in cases of increased risk of OHSS or in patients with good ovarian reserve. Cycles with very low doses or 0 IU can be associated with minimal or natural stimulation protocols, while doses close to 400 IU may indicate patients with a poor response or low ovarian reserve. The study examines the impact of endometriosis on fertility and the effects of ovarian stimulation, supporting the need for personalized treatment plans. Endometriosis may require multiple cycles of in vitro fertilization (IVF) and can increase the risk of complications during pregnancy and egg retrieval. A graph from the study presents the distribution of stimulation doses used in IVF, with common doses of 200 and 300 IU, and shows that most doses are concentrated around a median value of 255.06 IU, with an average of 235.12 IU. Moreover, most cycles produce between 5 and 10 oocytes, with a decrease in density for a higher number of oocytes, indicating that obtaining a large number of oocytes is rarer.

The research included 64 patients, and variations in stimulation doses were observed, indicating the possibility of dose adjustments to meet the individual needs of the patients. With an average stimulation dose of 235.12 UI and a median of 255.06 UI, with the minimum stimulation dose being 0 UI, the study suggests a balance between efficacy and minimizing the risk of ovarian hyperstimulation. Additionally, there is an observed increase in the average and median stimulation doses as age increases, indicating a decline in ovarian reserves and sensitivity to medications over the years. The average number of harvested oocytes is 5.85, with a maximum value of 20 and a minimum of 1, highlighting the need for

careful monitoring and dose adjustments. Additionally, the average of 1.9 mature oocytes per cycle highlights a variability in response to stimulation, indicating the need to more explicitly analyze the characteristics of the patients in order to optimize the process.

An evident relationship was observed between the age of the patients and the number of oocytes collected. As one ages, fertility declines due to the reduction in the quality and quantity of available eggs. At the same time, a greater dispersion in the number of oocytes collected was observed in patients aged between 34-36 and 40-42 years, suggesting a significant impact of individual factors or differences in stimulation protocols. Additionally, the efficiency of ovarian stimulation in patients with endometriosis is highlighted by a ratio of approximately 0.67 between the total number of antral follicles and the number of oocytes obtained. The study highlights the importance of careful assessment and personalized planning of ovarian stimulation in patients with endometriosis.

Additionally, the average number of embryos on day 2 is 2.67, and the fertilization rate is approximately 44.3%, indicating that nearly half of the mature oocytes were successfully fertilized. It is crucial to ensure that the techniques for handling oocytes and sperm are optimized to maximize the fertilization rate.

Additionally, the average number of embryos on day 2 is 2.67, and the fertilization rate is approximately 44.3%, indicating that nearly half of the mature oocytes were successfully fertilized. It is crucial to ensure that the techniques for handling oocytes and sperm are optimized to maximize the fertilization rate.

New information indicates an average number of embryos of 1.42 on day 5 and a blastocyst development rate of approximately 20.7% from 343 mature oocytes. In a particular case, a patient started with 20 oocytes and ended up with 9 blastocyst embryos by day 5, suggesting high-quality oocytes and optimal culture conditions. The data shows an average number of embryos of 1.42 on day 5 and a blastocyst development rate of approximately 20.7% from 343 mature oocytes. A rate of 46.71% indicates that almost half of the embryos evaluated on day 2 progressed to the blastocyst stage by day 5.

An initial FSH level of 18.8 IU/L, for example, may indicate low ovarian reserve and can predict a poor response to ovarian stimulation, necessitating a reconsideration of the stimulation protocol and the evaluation of other treatment options.

The study emphasizes the interaction between endometriosis, FSH, LH, and ovarian reserve in the process of fertilization and ovarian stimulation, highlighting the role of LH values in follicular dynamics and oocyte maturation. The minimum LH value (0.6 IU/L), recorded in a long protocol with GnRH agonist, indicates effective hormonal suppression, which allows for

better control over the stimulation cycle. Elevated LH levels (23.7 IU/L) may indicate resistance to the medications used for suppression, potentially leading to premature ovulation or suboptimal follicle development.

Additionally, the analysis of the average number of follicles on the second day of stimulation - 8.1 in this study - provides information about ovarian reserve and response to stimulation. This number is a key factor in choosing the doses of FSH and planning the stimulation protocol. Patients with a small number of follicles may require more aggressive protocols, while those with a large number may be prone to ovarian hyperstimulation syndrome. The average estradiol level of 51.92 pg/mL observed on the second day of the stimulation cycle reflects the initial hormonal response to fertility treatment and indicates an adequate initial ovarian response. The variability of the results, with a maximum of 224 pg/mL and a minimum of 10 pg/mL, suggests significant differences in the response to stimulation, requiring careful monitoring of LH, FSH, and estradiol levels.

The average stimulation days is 10.81, with a range between 7 and 16 days reflecting the individual variation in response to treatment. Adjusting medication doses, optimizing the stimulation protocol, and closely monitoring estradiol levels are crucial for an optimal response. Psychological support and comprehensive endocrinological assessment play important roles in detecting the causes of infertility.

The analysis showed correlations between the stimulation dose and the number of oocytes, the stimulation dose and AMH, and the stimulation dose and age. A moderate positive correlation was found between age and stimulation dose, suggesting that higher stimulation doses are associated with older ages. Of the 12 pregnancies obtained during the study period, most presented ovarian endometriomas and deep endometriosis, and the majority of cases were associated with in vitro fertilization (IVF) cycles using frozen-thawed embryo transfers. Tasks in individuals with endometriosis showed an increased risk of preeclampsia in the final trimester. Recent analyses have highlighted a correlation between endometriosis and various obstetric and neonatal complications, although interpreting the results is challenging due to the lack of consistent diagnostic criteria and classification systems for endometriosis.

4. Conclusions

Ultrasound evaluation is an extremely useful medical measure for identifying and treating patients with a high suspicion of pelvic endometriosis.

The diagnosis of endometriosis through MRI is significantly superior and more accurate than ultrasound diagnosis, especially in digestive locations.

The study reveals that the number of surgical interventions may not be complete or necessary and should be reduced through precise preoperative evaluations conducted on patients with deep endometriosis. (DIE). An individualized and timely treatment for ovarian dysfunction can prevent recurrence or reduce ovarian reserve and improve fertility quality. The study also found that the stimulation dose in assisted human reproduction procedures can vary significantly depending on the patient's age, indicating a lower ovarian reserve and a decrease in ovarian response in older patients. The study also found that endometriosis can affect ovarian quality and fertilization rates, requiring personalized treatment strategies. The study concludes that by addressing these findings and recommendations, clinicians can improve the efficiency of IVF treatments and provide the best possible outcomes for patients with endometriosis.

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