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EFFECT OF PREGNANCY ON ENDOMETRIOSIS SYMPTOMS

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ABSTRACT

Endometriosis is a disorder in which tissue that normally lines the uterus, called the endometrium, grows outside the uterine cavity. It can adhere to the outside of the uterus, the ovaries, and the fallopian tubes. The ovaries are responsible for releasing an egg each month, and the fallopian tubes carry the egg from the ovaries to the uterus. When any of these organs are damaged, blocked, or irritated by endometrium, it can become more difficult to get and stay pregnant. Your age, health, and the severity of the condition will also affect your chances of carrying a baby to term. pain symptoms at two years after delivery are improved when compared to the prepregnancy situation. The pregnancy-related hormonal milieu and the psychological benefits of parenthood may both contribute. However, as for hormonal medical therapy, symptoms relapse in the vast majority of cases. These considerations are particularly important given that endometriosis patients are often strongly advised by doctors to conceive as soon as possible to avoid future problems, which has been reported as a significant source of distress, especially for women who are not currently willing to have a child. Overall, pregnancy is associated with a substantial improvement of pain symptoms but cannot be viewed as a definitive cure of the disease.

KEYWORDS: pregnancy, endometriosis.

INTRODUCTION

Pregnancy is commonly believed to confer a symptomatic benefit to women with endometriosis.[1] Dysmenorrhea, a typical symptom of the disease, cannot occur and the steadily elevated peripheral progesterone levels induce decidualization of the endometriotic lesions[2].

The psychological benefits of childbearing may also contribute to the general improvement experienced by affected women especially if one considers that the threat of infertility represents a major source of distress for women with endometriosis.[3]

Some hemorrhagic and life-threatening endometriosisrelated complications of pregnancy, such as spontaneous haemoperitoneum, have recently received attention. However, these events are extremely rare and the vast majority of women have unremarkable and physiological pregnancies.[4] In fact, the beneficial effects of pregnancy have inspired modern therapy of endometriosis. The idea of curing the disease with progestins, thus mimicking pregnancy, has guided investigators for decades.

At present, the medical treatment of endometriosis is mainly based on long-term regimens of progestins or estroprogestins. The most commonly used agents include noretisterone acetate, medroxyprogesterone acetate, dienogest, levonorgestrel released via a medicated intrauterine device, and oral contraceptives.[5]

A neglected but relevant point here is the different duration of the benefits. While pregnancy is generally claimed to determine long-term benefits that can definitely cure endometriosis or at least determine very long-term protection from recurrences, the benefits of therapeutic progestins are well-known to rapidly vanish once treatment is discontinued. If true, this contrast is somewhat surprising. In fact, the notion of the long-term benefits of pregnancy on endometriosis seems to be based on scanty scientific evidence, despite being popular for decades.

Some observational studies showed short-term beneficial effects on ovarian endometriomas[6] but more comprehensive data focusing in particular on pain symptoms are lacking. On these bases, we deem of interest exploring more in details the potential long-term benefits of pregnancy on endometriosis symptoms.

To this aim, we retrospectively reviewed data from women attending our referral center for the treatment of endometriosis and selected those who had a live birth. The main aim of the study was comparing endometriosis-related pain symptoms before and two years after delivery.

Mental health (anxiety and depression) and quality of life were also assessed to investigate the possible psychological benefits of childbearing. Because research has demonstrated the relationship between pain symptoms, mental health and quality of life[7], we also examined whether pre-/post-pregnancy changes in pain symptoms were associated with changes in psychological status and health-related quality of life (including sexual functioning).

It is well known that endometriosis is a chronic inflammatory disease characterized by the presence of endometrial-like tissue outside the uterine cavity; the disease may be asymptomatic or it may cause pelvic pain and/or infertility. Endometriosis has been the objective of extensive research in the last 40 years; although several characteristics of this disease remain unclear, its diagnosis and management have significantly changed in the last 10 years. If fact, the attention of the physicians has progressively moved from the disease to the symptoms, the desires and the expectations of the patients.[8]

The main limit to the successful treatment of endometriosis is the diagnosis of the disease. Although the only laparoscopy provides a confirmed diagnosis of endometriosis[9], nowadays, one of the key topics in endometriosis management is the non-invasive diagnosis of deep infiltrating endometriosis (DIE) (lesions penetrating more than 5 mm under the peritoneal surface) which is the most severe form of the disease.[10]

A study included in the Special Issue presents a model predicting the presence of DIE in patients with ovarian endometriomas. Over the last few years, one of the major advances in endometriosis research has been the validation of transvaginal ultrasonography as the first-line investigation to diagnose DIE[11] and this Special Issue will include an update on the role of ultrasound in the diagnosis of DIE.

BACKGROUND

Pain is the most debilitating complain of patients with endometriosis. Two reviews included in the Special issue describe the mechanisms underlying endometriosis-associated pain including the alterations in the peripheral and central nervous system of women with endometriosis-associated pain and the direct innervation of endometriotic lesions. Hormonal therapy is the first-line treatment of endometriosis associated pain.[12]

Its primary aims to suppress ovarian function thus decreasing the effects of estrogen on ectopic endometrial implants. The studies included in this Special Issue demonstrate that a

better understanding of the molecular pathways involved in the pathogenesis of endometriosis allows prescribing drugs which are not only efficacious in improving pain by decreasing estrogen levels but also by affecting cell proliferation, apoptosis, cell adhesion, inflammation and neuroangiogenesis.

These drugs also have a role in improving symptoms and preventing disease recurrences after surgery. Since patients with endometriosis require a multidisciplinary long-term treatment, a deep knowledge of their symptoms and comorbidities allows improving their quality of life. An original study included in this review showed that DIE is associated with impaired sleep quality while a review described the comorbidities of women with endometriosis, that may affect not only the quality of life but also the adherence of the patients to long-term hormonal therapies. Despite the efficacy of hormonal therapies for the treatment of endometriosis-associated pain, a review included in the Special Issue highlights the role of surgery in patients with symptomatic bowel stenosis, ureteral stenosis with secondary hydronephrosis, and when hormonal treatments fail.[13]

Ovarian endometriomas affect a large portion of women with endometriosis and they can be reliably diagnosed by transvaginal ultrasonography.[14] Endometriomas may have a detrimental impact on the intrafollicular environment; however, they do not affect spontaneous ovulation and patients with endometriomas have good spontaneous pregnancy rates.[5]

While it is accepted that the laparoscopic excision of endometriomas improves pain; the role of surgery in infertile patients is more debatable. A review included in this Special Issue addresses the treatment of endometrioma for improving fertility. When patients with endometriomas conceive, the endometriomas may undergo doubtful ultrasonographic changes that are described in a case series included in this Special Issue. Symptoms caused by rectosigmoid endometriosis may be improved both by hormonal and surgical treatment. A review and a prospective longitudinal cohort study included in this Special issue describe the fertility outcomes of patients surgically treated for colorectal endometriosis. Obviously, surgery is required when bowel stenosis is present and/or the patients suffer severe pain not responsive to hormonal treatment. Unfortunately, up to now no study investigated the rate of spontaneous conception in patients with a colorectal endometriotic nodule that does not cause clinically relevant bowel stenosis.[16]

This issue of the EJOGRB aims to provide an overview of the modern management of endometriosis. Because of the complexity of this disease, it is almost impossible to cover all the aspects of the ongoing research on endometriosis in one special issue.

Pregnancy will temporarily halt the painful periods and heavy menstrual bleeding that are often characteristic of endometriosis. It might provide some other relief as well. Some women benefit from increased levels of progesterone during pregnancy. It's thought that this hormone suppresses and perhaps even shrinks endometrial growths. In fact, progestin, a synthetic form of progesterone, is often used to treat women with endometriosis.[17]

Other women, however, will find no improvement. You may even find that your symptoms worsen during pregnancy. That's because as the uterus expands to accommodate the growing fetus, it can pull and stretch misplaced tissue. That can cause discomfort. An increase in estrogen can also feed endometrial growths.[18] Even if symptoms do improve during pregnancy, they will resume after the birth of the baby. Breastfeeding may delay the return of symptoms, but once period returns, symptoms will likely return too.[19]

Risks and complications

Endometriosis may increase your risk of pregnancy and delivery complications. This may be caused by the inflammation, structural damage to the uterus, and hormonal influences endometriosis causes.[20]

Miscarriage

Several studies have documented that miscarriage rates are higher in women with endometriosis than in women without the condition. This holds true even for women with mild endometriosis. One retrospective analysis concluded that women with endometriosis had a 35.8 percent chance of miscarriage versus 22 percent in women without the disorder. There's nothing you or your doctor can do to stop a miscarriage from happening, but it's important to recognize the signs so you can seek the medical and emotional help you might need to properly recover.[21] Symptoms after 12 weeks are mostly the same, but bleeding, cramping, and tissue passage might be more severe.

Preterm birth

According to an analysis of several studies, pregnant women with endometriosis are times more likely than other expectant moms to deliver before 37 weeks of gestation. A baby is

considered preterm if he or she is born before 37 weeks of gestation.[22] Babies born prematurely tend to have a low birth weight and are more likely to experience health and developmental problems. Symptoms of preterm birth or early labor include[23]:

- Regular contractions. Contractions are a tightening around your midsection, which may or may not hurt.
- Change in vaginal discharge. It may become bloody or the consistency of mucus.
- The pressure in your pelvis.

Placenta previa

During pregnancy, the uterus will develop a placenta. The placenta is the structure that supplies oxygen and nourishment to your growing fetus. It normally attaches to the top or side of the uterus. In some women, the placenta attaches to the bottom of the uterus at the opening of the cervix. This is known as placenta previa. Placenta previa increases your risk for a ruptured placenta during labor. A ruptured placenta can cause severe bleeding, and put and baby in danger.[24]

Women with endometriosis may be at increased risk for this life-threatening condition. The main symptom is bright red vaginal bleeding. If the bleeding is minimal, you may be advised to limit your activities, including sex and exercise. If bleeding is heavy, you may need a blood transfusion and an emergency C-section.[25]

Treatment

Surgery and hormonal therapy, the standard treatments for endometriosis, are generally not recommended for pregnant women. Over-the-counter pain relievers may help reduce endometriosis discomfort, but it’s important to ask your doctor which ones can be safely used during pregnancy, and for how long.[26]

Some self-help measures include:

- Taking warm baths
- Eating fiber-rich foods to help reduce your risk for constipation
- Walking gently or doing prenatal yoga to stretch the back and relieve endometriosis-related back pain.[27]

METHODS

Outpatient charts of women in an alkhark hospital in Baghdad. Inclusion criteria were as follows:

1) Age 20-44
2) A history of at least one conservative surgical procedure for endometriosis - histologically confirmed - before the index pregnancy (this criterion was decided to more reliably select women with a definite diagnosis of the disease);
3) At least one pregnancy after surgery;
4) Pregnancy resulting in a live birth - if more than one pregnancy were recorded, only the first one was considered;

A 5) presence of moderate to severe pelvic pain symptoms - at least one among dysmenorrhea, deep dyspareunia, non-menstrual pelvic pain, and dyschezia before the index pregnancy;

6) at least two years of follow-up after delivery.

Women achieving pregnancy with the use of assisted reproductive techniques (ART) were not excluded. Conversely, patients were excluded if:

1) They started medical therapy exclusively for contraception or prevention purposes within two years after delivery;
2) A new pregnancy occurred within less than two years from delivery of the index pregnancy;
3) They underwent less than two visits per year - excluding the duration of pregnancy and breast-feeding;
4) They received a diagnosis of psychiatric disorders or had a history of drug and alcohol abuse.

The primary aim of the study was comparing the four main endometriosis-related pain symptoms (dysmenorrhea, deep dyspareunia, non-menstrual pelvic pain, and dyschezia) before and two-years after delivery. women underwent a clinical assessment, transvaginal ultrasonography and were requested to fill standardized questionnaires investigating pain symptoms, quality of life, psychological status and sexual functioning.

The presence and severity of dysmenorrhea, deep dyspareunia, non-menstrual pelvic pain, and dyschezia were assessed using an 11-point numerical rating scale (NRS), with 0 indicating the absence of pain, and 10 indicating pain as bad as it could be. A score of 5-7

was considered as moderate pain, and 8-10 as severe pain. Women were also requested whether they were using pain killers (even if occasionally).

RESULTS

One-hundred women were identified. Pre-pregnancy moderate to severe dysmenorrhea, deep dyspareunia, non-menstrual pelvic pain and dyschezia were reported. pregnancy outcome is shown,

65 women initiated medical therapy during the follow-up period. Specifically, 9 initiated exclusively for pain complaints whereas the remaining 10 reported also concomitant contraception needs. Four women required surgical intervention for endometriosis and pain (of whom two also assumed medical therapy) two of them underwent removal of large endometriomas while the other two underwent extensive lysis of adhesions and excision of peritoneal nodules. Overall, 49 women (47 + 2) had clinically relevant pain requiring treatment, (95%CI: 29-47%).

The rate of recurrence in women who delivered vaginally or by cesarean section was (32 out of 83) and (17 out of 48), respectively (p=0.85). The average time to the recurrence of pain in the two groups was 11 -8 and 12 - 8 months, respectively (p=0.71).

Table 1 Pelvic pain before and after delivery.

	Pre-pregnancy	Post-pregnancy	P value
Dysmenorrhea			0,000
Mild-absent	6	45	
Moderate	34	45	
Severe	54	23	
Deep dyspareunia			0,0000
Mild-absent	34	44	
Moderate	23	43	
Severe	45	13	
Non-menstrual pelvic pain			0,000
Mild-absent	23	32	
Moderate	42	43	
Severe	35	25	
Dyschezia			0,000
Mild-absent	54	56	
Moderate	22	23	
Severe	24	21	

DISCUSSION

Pregnancy is associated with a significant improvement of endometriosis-related pain symptoms. Two years after delivery, almost two-thirds of affected women did not necessitate endometriosis-specific therapies and all endometriosis-related pain symptoms significantly improved. Moreover, we observed a positive effect on mood and quality of life: HADS anxiety and depression scores decreased whereas physical and mental well-being measured with SF-12 scale increased. On the other hand, our study also demonstrates that the magnitude of the beneficial effects of pregnancy is modest and of practical uncertain importance. Pregnancy was actually not a definitive cure for endometriosis in our patients. A consistent proportion of women still experienced clinically relevant endometriosis-related symptoms after pregnancy. No improvement in sexual function was observed and most participants presented sexual dysfunction either before or after pregnancy, which raises issues about the quality of sexuality in women with endometriosis, as highlighted by other studies.[28]

Noteworthy, a subgroup analysis focusing on women who were assuming medical therapy for pain before seeking pregnancy showed that more than half of them had to resume medical therapy after delivery.

Selection bias cannot be ruled out, as women who did not refer after pregnancy were excluded. However, this is not expected to significantly distort the results, considering that women treated for endometriosis in our unit were systematically informed that endometriosis may relapse after pregnancy and that, therefore, regular follow-up visits have to be planned soon after delivery. Moreover, even if we did not actively manage women during pregnancy, a systematic phone follow-up and an invitation to refer after delivery were regularly done. Fourthly, we arbitrarily set the post-pregnancy assessment at two years after delivery. It might be argued that this period could be adapted according to the duration of breast-feeding. Setting the evaluation at two years after the first post-delivery menstrual flow could be a valid alternative. On the other hand, it has to be pointed out that we were mainly interested on the effects of pregnancy rather than on post-delivery amenorrhea and that the date of the first menstrual flow after delivery is less reliably reported.

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