

IMPACT OF ENDOMETRIOTIC CYST POSITION ON INFERTILITY

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Abstract

Endometriosis is one of the most common benign gynecologic disorders affecting reproductive health. There are many theories regarding how endometriosis affects fertility, but the exact mechanisms are still uncertain.

We evaluated 100 patients with unilateral ovarian endometriosis and infertility who underwent ovarian cystectomy. The women had at least one patent tube after surgery and were observed for spontaneous pregnancy for up to one year. Patients were divided into two groups according to the endometrioma position. The first group included 67 women with an endometriotic cyst in the left ovary, and the second group included 33 with an endometrioma in the right ovary. Groups were similar according to age, type of infertility, BMI, and size of the endometrioma.

The number of patients was significantly higher in the first group. Spontaneous pregnancy after cystectomy occurred in 28.4% of the patients with an endometrioma in left ovary, and in 9.1% with a right endometriotic cyst.

The better results regarding spontaneous conception with a left-sided endometrioma in our study are most likely related to the permeability of the fallopian tubes and adhesions in the Douglas pouch as a result of endometriosis. Further investigations are necessary to assess the influence of the laterality of endometriosis on infertility.

Key words: endometriosis surgery, endometriotic cyst, infertility

Introduction. Endometriosis is one of the most common gynecologic disorders in reproductive age [1]. Frequency is 12–35% in women aged 25–35 years [2]. The most common locations of endometriotic implants are ovaries and pouch of Douglas [3]. There are few publications that report an increased frequency of endometrioma in the left ovary compared to the right ovary [4, 5]. This could be related to differences in the pelvic anatomy on the left and right sides and supports Sampson’s retrograde menstruation theory. MATAILLIOTAKIS et al. [6] suggest that female varicocele could play an important role in endometriosis development. Endometriosis can be related to infertility. Different pathologic mechanisms might be involved, such as distorted pelvic anatomy [7], abnormal uterotubal transport [8], altered peritoneal function [9], endocrine and ovulatory abnormalities [10], impaired implantation [11], decreased oocyte and embryo quality [12], and altered hormonal and cell-mediated function [13].

The possible impact of the distribution of endometriosis on the left and right sides of the pelvis on fertility is still not well investigated. Publication by FUJISHITA et al. [14] shows no relationship between the side of endometrioma and chance for spontaneous pregnancy. YU et al. [15] investigates the pregnancy rate after laparoscopic removal of an endometriotic cyst and IVF or IUI and relationship with the side of the endometrioma. The authors described results with no relationship between the endometrioma side and success of the ART procedures. Despite these results we believe that there is little data on this topic, particularly regarding convincing data for the differential distribution of the disease in the pelvis [4–6], and it remained unexplained until now. Therefore, we conducted a study comparing women with a laparoscopically removed unilateral endometriotic cyst from the left or right ovary by different indicators. The aim of this study is to confirm present data on this matter.

Materials and methods. We conducted a qualitative study among women with ovarian endometriosis who failed to conceive for more than one year. The aim was to determine how endometrioma removal affects infertility and if there were specific characteristics of the disease that affect pregnancy rate after surgery. Size and side of the cyst were assessed.

In total, 100 patients with ovarian endometriosis and infertility who underwent ovarian cystectomy by laparoscopy or laparotomy were investigated. Over the period January 2014 – April 2016, 64 patients were included retrospectively; for the period May 2016 – January 2018, another 36 patients were examined prospectively. Data were collected after signed written informed consent was obtained. All surgeries were performed by trained reproductive surgeon in “Dr. Shterev” Hospital, Sofia. The surgical procedures included exploring the abdominal cavity for endometriotic lesions and other concomitant pathologies, adhesiolysis if necessary, ovarian cystectomy by the stripping technique and blue dye test for tubal patency. Hemostasis of the ovary was performed by bipolar energy and suturing with 3/0 stitches if necessary. All specimens were examined by a pathologist

who confirmed endometriosis. The extent of disease was scored by revised American Society for Reproductive Medicine (rASRM) classification. Before surgery, all patients underwent an ultrasound examination. The size of the endometrioma was measured by the largest diameter and the position in the ovary was recorded. All patients met the inclusion criteria for the study: primary or secondary infertility, one unilateral endometriotic cyst confirmed histologically, age < 41 years, informed consent, at least one patent tube after surgery. Exclusion criteria were: non endometriotic ovarian cysts, bilateral endometrioma, blocked uterine tubes, concomitant infertility factors.

General data such as age, duration and type of infertility, Body Mass Index (BMI), size of endometrioma and stage of endometriosis were obtained. Patients were divided in two groups according to the position of the endometriotic cyst. The first group included 67 women with an endometriotic cysts in the left ovary. The second group included 33 women with a cyst in the right ovary. The main measured outcome was achievement of spontaneous pregnancy up to 1 year after surgery. We considered an ultrasound diagnosed gestational sac as positive confirmation of pregnancy.

The results are reported as means \pm SD or as percentages where appropriate. Statistical significance of differences was assessed by Fisher's exact test. Differences were considered statistically significant at $p \leq 0.05$.

Results. The indications for surgery in both groups of our study were infertility and the presence of a chocolate cyst in one of the ovaries diagnosed by ultrasound. All patients in both groups were diagnosed with stage III endometriosis according to rASRM (Table 1).

The frequency of intraperitoneal adhesions was similar – 62.7% of patients with a left endometrioma and 42.4% of patients with a right cyst (Table 2). The patent tube test showed similar numbers of patients with uni- and bilateral tubal patency after surgery (Table 2).

Analysis of data regarding age, BMI, size of the endometriotic cyst, type and duration of infertility and spontaneous pregnancy rate is presented in Table 3. The mean age in the first group was 30.7 ± 4.6 years, compared with 31.7 ± 4.6 in

T a b l e 1

Distribution of patients in both groups according to rASRM staging

Endometrioma cyst size (cm)	Group	rASRM score (points)	
		Mean	min-max
1-3	L	21.5	16-32
	R	18.5	16-26
4+	L	27.0	20-40
	R	21.8	16-34

T a b l e 2

Frequency of intraperitoneal adhesions and uni- and bilateral tubal patency among patients in both groups

		Group L	Group R	<i>p</i>
Intraperitoneal adhesions	Positive % (<i>n</i>)	62.7 (42)	42.4 (14)	NS
	Negative % (<i>n</i>)	37.3 (25)	57.6 (19)	NS
Tubal patency	Bilateral % (<i>n</i>)	85.1 (57)	84.8 (28)	NS
	Unilateral % (<i>n</i>)	14.9 (10)	15.2 (5)	NS

T a b l e 3

Main characteristics and outcome of the patients with endometrioma in left ovary (group L) and endometrioma in right ovary (group R)

	Group L	Group R	<i>p</i>
Endometriotic cyst location			
Patients [<i>n</i>]	67	33	< 0.01
Mean age	30.7 ± 4.6	31.7 ± 4.6	NS
Primary infertility [%]	86.6	78.8	NS
Mean duration of infertility [years]	2.4 ± 1.8	2.6 ± 1.7	NS
Mean endometriotic cyst size [cm]	4.0 ± 1.5	4.4 ± 1.5	NS
Endometriotic cyst < 3 cm [%]	40.3	24.2	NS
Endometriotic cyst > 3 cm [%]	59.7	75.8	NS
BMI	20.9 ± 3.2	20.6 ± 2.7	NS
Spontaneous pregnancy [%]	28.4	9.1	0.039

the second group and has no statistical difference ($p = 0.34$). Patients were also comparable in term of size of the cyst, BMI, and type and duration of infertility.

We found that 67% of our operated patients were in the first group, and 33% had an endometrioma in the right ovary ($p < 0.01$). Endometriotic cysts sized 1–3 cm was found in 40.3% (27/67) of patients with a left-sided endometrioma and in 24.2% (8/33) of patients with a right endometriotic cyst, which was not significantly different ($p = 0.17$). There was no difference between the number of patients with endometriotic cysts larger than 4 cm in both groups (59.7% vs. 75.8%, $p = 0.17$). All the histopathological results showed the presence of an endometriotic cyst. Spontaneous pregnancy after cystectomy occurred in 19 of 67 patients (28.4%) with an endometrioma in the left ovary. In the group with right endometriotic cyst, 3 of 33 (9.1%) achieved pregnancy (Table 3). The pregnancy rate difference between groups was statistically significant ($p = 0.039$). Women with a left-sided endometriotic cyst had more pregnancies than women with a right-sided endometrioma (Table 3).

Discussion. Our findings convincingly support previous results that show a predisposition of left endometriosis in a higher proportion of patients. Regarding the explanation for the higher pregnancy rate in spontaneously conceiving women with left-sided endometriosis, different suggestions can be discussed.

There are studies on the influence of anatomical differences on the basis of the laterality of ovarian endometrioma [6]. These studies suggest mechanism of delayed drainage of the left ovarian vein due to its longer length compared to the shorter right vein which empties directly into the much larger inferior cava vein. This difference leads to a predisposition for vein congestion and higher hydrostatic pressure in the left ovary. These anatomical differences lead to higher vein pressure, congestion of venous blood, higher concentration of substances such as sex hormones, chemokines and cytokines and higher oxidative stress at the left adnexa, particularly the left ovary, compared to the right one. These findings, however, suggest rather negative conditions in the area of the left adnexa and worse pregnancy outcomes in left-sided endometriosis. In accordance with this suggestion is a study which reports better pregnancy rate after in vitro fertilization (IVF) procedures in right-sided endometriosis [15].

The better results regarding spontaneous conception with left-sided endometrioma in our study are most likely related to the wealth and permeability of the fallopian tubes and adhesions in the Douglas pouch as a result of endometriosis. Some studies report more obliterations in the pouch of Douglas when a right endometrioma is detected. The study by ULUKUS et al. [16] demonstrates that the obliteration of the Douglas pouch is more extensive and severe in women with right-side endometriosis. This finding suggests that the permeability of the right uterine tube is probably negatively altered at different levels in cases with right endometrioma and could negatively impact their chances for spontaneous conception.

These findings support the previous study that investigated the influence of pelvic endometriosis and ovarian endometrioma on pregnancy outcome in women associated with infertility [14]. They do not confirm the influence of the location of ovarian endometrioma on fertility chances but the reproductive outcome strongly correlates with the pelvic adhesions and condition of fallopian tubes as a result of endometriosis regarding spontaneous conception.

The suggestions that the chance for pregnancy when conceiving spontaneously is related to the condition of the tubes are supported by the findings of Yu et al. [15], who showed no association among the laterality of ovarian endometrioma, ovarian reserve and ovarian response in IVF/ICSI cycles when the permeability of the tubes is not important. The implantation rate was significantly lower in patients with left side endometrioma when pregnancy was achieved by IVF.

Conclusion. The position of endometriotic cysts may affect infertility. There are several possible reasons, including anatomical differences between the left and right side of the pelvis and differences between anatomical distortions caused by

endometriosis from the other side. Further investigations including bigger series are necessary to assess the influence of the laterality of endometriosis on the pregnancy chance when conceiving spontaneously or by IVF procedures.

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