

Short Communication

Association Between Fallopian Tube Length and Genital Endometriosis in Infertile Patients Retrospective Cohort Study

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Abstract

Background: Information about the prevalence of fallopian tube pathology in the early stages of endometriosis is scarce. The aim of our study was to examine the association between genital endometriosis and the lengths of fallopian tubes in infertile women. Settings and Design: retrospective cohort study. **Methods:** We studied 651 infertile patients in the 20–40 year age group, who visited a Reproductive Clinic for treatment between 2012–2018. After laparoscopy, endometriosis (detected by histomorphology) was indicated in 472 cases and absent in 179 cases. The length of the fallopian tubes was estimated in 193 primary infertile women with endometriosis. We excluded patients from the study who had surgical intervention on their tubes. Appearance of tubes and fimbriae was assessed in 177 patients without endometriosis and in 461 patients with endometriosis. **Results:** The proportion of women with shorter (<8 cm) right and left fallopian tubes was significantly greater in those with endometriosis. Conversely, the proportion of women with longer (>12 cm) left fallopian tubes was significantly higher in the group of patients without endometriosis. Correlation analysis showed significant positive correlations of endometriosis with: a short (<8 cm) right fallopian tube- $r = -0.504^{**}$ ($p < 0.001$); Significant negative correlations of endometriosis were with: a medium (8–12 cm) length right fallopian tube- $r = -0.639^{**}$ ($p < 0.001$); a long (>12 cm) left fallopian tube- $r = -0.596^{**}$ ($p < 0.001$); **Conclusions:** Infertile women with minimal or mild endometriosis have been shown to have anatomical and structural changes in the fallopian tubes and fimbriae compared to those without endometriosis. The presence of genital endometriosis (I;II stage) maybe associated with shorter fallopian tubes.

Keywords: early stage (I,II) endometriosis; infertility; fallopian tube length; fimbria; laparoscopy

1. Introduction

Endometriosis is a condition in which endometrial tissue, which normally lines the uterus, develops outside of the uterine cavity in abnormal locations such as the ovaries, fallopian tubes, and the abdominal cavity [1].

Classical studies suggested that 25% to 50% of infertile women have endometriosis. According to Nicolaus K *et al.* [2], its incidence in infertile women reaches 67% and that 30% to 50% of women with endometriosis are infertile [3].

Peritubal and peri-ovarian adhesions are considered the main mechanisms by which advanced endometriosis causes infertility. The mechanisms by which adhesion formation in advanced endometriosis reduces fecundity rate include a reduced ovum pick-up mechanism, luteinized un-ruptured follicle syndrome, poor follicular growth, and tubal occlusion [4].

Information about the prevalence of fimbrial pathology of fallopian tubes in early stages of endometriosis is scarce. Peritubal and peri ovarian adhesions are considered the main mechanisms of infertility caused by progressive endometriosis [5].

In addition, endometriosis without adhesions may contribute to reduced fertility potential [6]. On the other hand, the mechanisms by which early stages of endometriosis interfere with fertility are not fully understood.

The reference standard for diagnosing endometriosis is laparoscopy, preferably including histological verification by biopsy of any suspected lesion [7].

The aim of our study was to determine the correlation between genital endometriosis and fallopian tube pathologies.

2. Materials and Methods

A retrospective cohort study was conducted. Patients were recruited between June 2012 and December 2018. A total of 651 infertile women underwent laparoscopy in our clinic. All the women met the following criteria: age between 20 and 40 years; infertile for ≥ 24 months; normal ovulatory cycles, defined as regular menstrual cycles (21–35 days); bilateral tubal patency as documented by a hysterosalpingogram (see Fig. 1 below) performed before the laparoscopy or a tubal patency Dye test (see Fig. 2) performed during the laparoscopy; a semen test in the part-



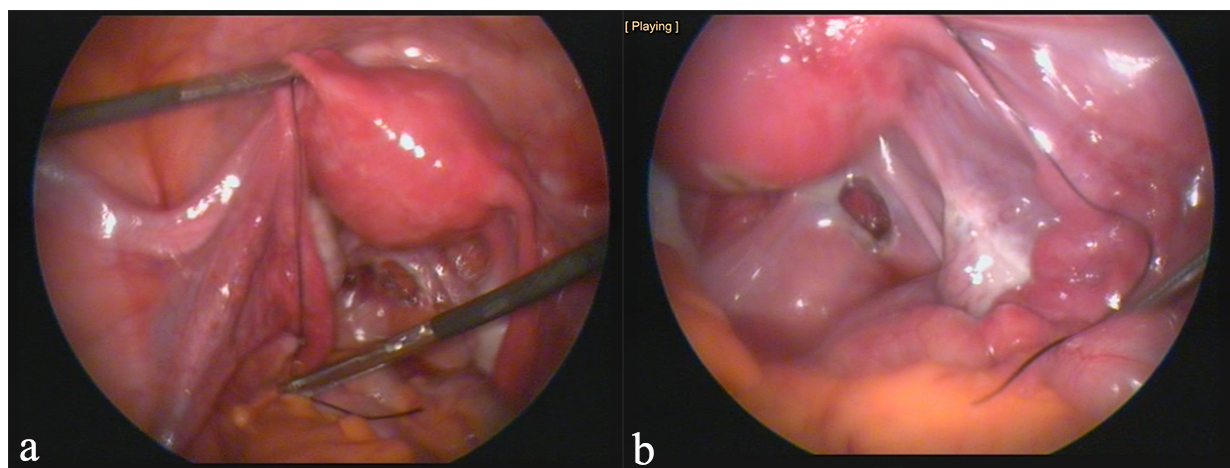


Fig. 1. Measurement of the length of the left and right fallopian tube. (a) Ampullary part. (b) The end of fimbriae.

ner showing at least 15×10^6 motile spermatozoa (WHO 2010) [8]; no previous surgical therapy for endometriosis; no medical treatment of endometriosis in the last 9 months; no ovulatory agents or IUI with the partner's sperm in the last month; no other medical or surgical therapy for infertility; no previous oophorectomy or salpingectomy; no history of pelvic inflammatory disease; and absence of severe pelvic pain precluding expectant management, and no history of genetic pathologies. Other surgical interventions (Appendectomy etc.) were not excluded.

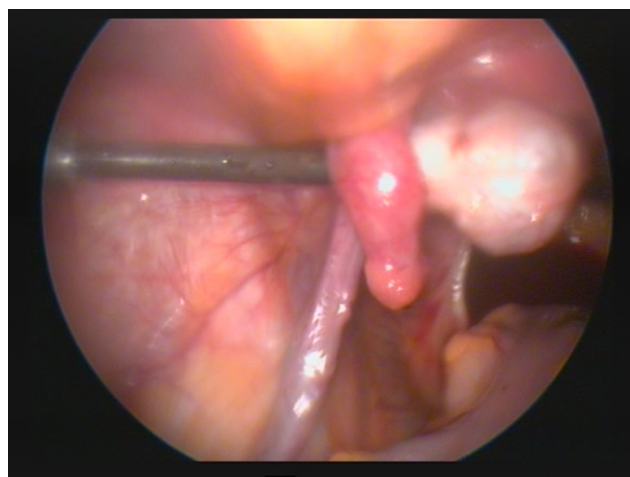


Fig. 2. Fimbriae.

Laparoscopy was performed on any day of the menstrual cycle under general anaesthesia. Endometriosis was diagnosed and staged according to the revised classification of the ASRM. In this classification, endometriosis is divided into four stages according to the number of lesion and depth of infiltration: minimal (Stage I), mild (Stage II), moderate (Stage III) and severe (Stage IV) [9].

After laparoscopy, a total of 461 infertile cases (Group I) were diagnosed with endometriosis by histomorphology.

They were assigned to stage I or II groups according to ASRM classification. Laparoscopic treatment included excision of ovarian endometriosis lesions, lysis of adhesions, endo coagulation of pelvic endometriosis lesions with controlled heating (100 degrees C) and lavaging of the peritoneal cavity. The duration of follow-up after laparoscopic surgery was censored at 36 weeks.

Group 2 consisted of 177 infertile patients who had no endometriosis by laparoscopy and histomorphology.

From our study sample of 651 women, we separately distinguished 193 patients with primary infertility (with or without endometriosis) and evaluated the length of their fallopian tubes. The aim of the study was to compare the length of tubes in patients with or without endometriosis and determine the association between tube length and endometriosis.

Hysterosalpingography was done in the first half of menstrual cycle, on protected sexual intercourse. Under aseptic conditions, a HSG 5-French balloon tipped catheter was inserted through the cervix into the uterine lumen. Sterile contrast material was utilized to distend the uterine lumen and fallopian tubes. Images were obtained after 6 minutes [10–12].

We refined our protocol for hysterosalpingography and for assessing normal and abnormal fallopian tube patency [10].

We measured the fallopian tubes during laparoscopy using a device we developed. A sterile flexible plastic thread (polyethylene) or suture thread was introduced from the 5 mm trocar into the abdominal cavity. One end of the thread was positioned to the cornua of the tube, care was taken that the thread was lying all along the tube until reaching the end of the fimbria. The thread was then cut at this point, removed from the abdominal cavity and measured in centimeter. The length of fallopian tubes is the maximum and minimum lengths we have obtained by laparoscopic measurements.

Fimbrial pathology was identified in all involved patients, especially fimbrial adhesives and fimbrial phimosis. Fimbrial phimosis describes an actual narrowing of the fimbriated end. If fimbrial pathology was found, it was classified as unilateral or bilateral.

We have calculated the rate of big (Morgani cyst) and small (appendix vesiculosa) paratubal cysts in both groups of patients. See Table 1.

We have no data about the ectopic pregnancy rate after laparoscopy in the study. We think it is an interesting issue to consider in the future. Informed consent was obtained in advance from all patients participating in the study. The study was approved by the Ethics Committee of the clinic.

2.1 Inclusion Criteria

Patients with infertility duration of more than 2 years with or without endometriosis symptoms.

2.2 Exclusion Criteria

Genetic anomalies of the woman or her partner, male factor infertility, a history of pelvic or abdominal surgery for tubal ligation, chlamydia or gonorrhea infection; pelvic inflammatory disease (PID).

2.3 Examination Methods

Medical history, clinical-biochemical laboratory, morphological laboratory, ultrasound examinations, hysterosalpingography.

Statistical analysis was performed using SPSS for Windows, version 23 (SPSS Inc, Chicago, IL, USA). Correlation analysis between categorical variables was performed by Spearman correlation analysis, p value < 0.05 was considered as statistically significant. Continuous variables are expressed as mean \pm SD, and categorical variables as frequencies and percentages. Continuous variables were compared with the use of the independent Student's t -test and categorical variables with the use of the Fisher's Exact test and Pearson's χ^2 test.

3. Results

Among laparoscopically examined patients, endometriosis was detected by histomorphology in 472 cases and was absent in 179 cases.

Tubal patency prior to laparoscopy is shown in Fig. 3.

The rate of non-patent tubes in the group of patients with endometriosis was 7.2% and in the group without endometriosis 4.4%. Weakly (partial) patent tubes was 25.9% in the group with endometriosis and 16% without it. $\chi^2 = 7.03$, $p = 0.003$.

After laparoscopy it was found that in 96.8% of patients with endometriosis have completely patent tubes

The length of the fallopian tubes was estimated in 193 cases. Table 2 shows the length of fallopian tubes measured during laparoscopy.

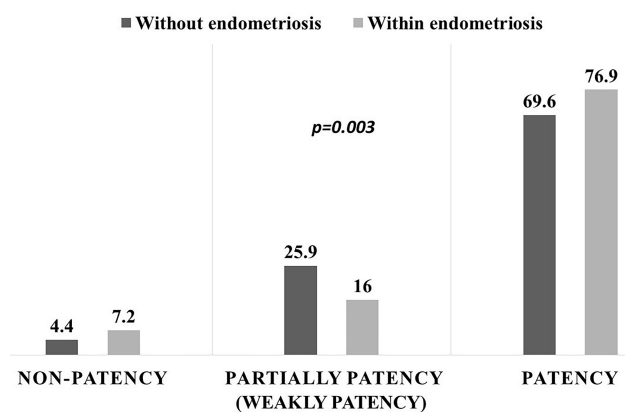


Fig. 3. Tubal patency prior to laparoscopy defined by hysterosalpingography.

The proportion of short (< 8 cm) right and left fallopian tubes was significantly higher among women with endometriosis. Also, the proportion of long (> 12 cm) right and left fallopian tubes was significantly higher in the group of patients without endometriosis.

Laparoscopy also showed significant differences between the groups in the appearance of fallopian tubes and fimbriae of fallopian tubes, assessed during the laparoscopy (Table 1). We excluded patients from the study who had surgical intervention on their tubes.

Appearance of tubes and fimbriae was assessed in 177 patients without endometriosis and in 461 patients with endometriosis.

The proportion of women with normal appearance of fallopian tubes and fimbriae was significantly lower in women with endometriosis. The proportion of women with adhesions and Morgani cysts was higher in the group of patients with endometriosis. The occurrence of small paratubal cysts (appendix vesiculosa) was greater in the group of patients without endometriosis.

Correlation analysis showed significant positive correlations of endometriosis with: a short (< 8 cm) right fallopian tube- $r = 0.504^{**}$ ($p < 0.001$); Significant negative correlations of endometriosis were with: a medium (8–12 cm) length right fallopian tube- $r = -0.639^{**}$ ($p < 0.001$); a long (> 12 cm) left fallopian tube- $r = -0.596^{**}$ ($p < 0.001$);

4. Discussion

Endometriosis is a common, oestrogen driven chronic gynaecological condition, where endometrium-like epithelial and stromal cells exist in ectopic sites beyond their native location; the internal lining of the uterine cavity. Approximately 10% of reproductive age women are affected by endometriosis, which equates to around 190 million women worldwide [13,14]. It is most commonly associated with chronic pelvic pain (CPP) and accounts for up to 70% of such diagnoses [14,15]. Other associated symptoms include pain during menstrual periods (dysmen-

Table 1. Distribution of variations in appearance of fallopian tubes and fimbriae in the groups of patients with and without endometriosis.

Factors	Without endometriosis	At endometriosis	Total	
	(n = 177)	(n = 461)	(n = 638)	
Appearance of the right fallopian tube n (%)				
Normal	130 (73.4%)	266 (57.7%)	396 (62.1%)	<0.001
Adhesions	4 (2.3%)	21 (4.6%)	25 (3.9%)	0.181
Small paratubal cyst	37 (20.9%)	64 (13.9%)	101 (15.8%)	0.030
Morgani cyst	6 (3.4%)	48 (10.4%)	54 (8.5%)	0.004
Endometriotic lesions	0 (0.0%)	62 (13.4%)	62 (9.7%)	<0.001
Appearance of the fimbriae of right fallopian tube n (%)				
Normal	164 (92.7%)	397 (86.1%)	561 (87.9%)	0.023
Adhesion	13 (7.3%)	64 (13.9%)	77 (12.1%)	0.023
Appearance of the left fallopian tube n (%)				
Normal	140 (79.1%)	310 (67.2%)	450 (70.5%)	0.003
Adhesions	4 (2.3%)	57 (12.4%)	61 (9.6%)	<0.001
Small paratubal cyst	25 (14.1%)	46 (10.0%)	71(11.1%)	0.136
Morgani cyst	8 (4.5%)	35 (7.6%)	43 (6.7%)	0.166
Endometriotic lesions	0 (0.0%)	14 (3.0%)	14 (2.2%)	0.019
Appearance of fimbriae of the left fallopian tube n (%)				
Normal	173 (97.7%)	418 (90.7%)	591 (92.6%)	0.003
Adhesion	4 (2.3%)	43 (9.3%)	47 (7.4%)	0.003

$p < 0.05$ was considered as statistically significant.

Table 2. Distribution of the length of fallopian tubes by endometriosis status.

Factors	Without endometriosis n (%)	With endometriosis n (%)	Total n (%)	<i>p</i>
	N = 57	N = 136	N = 193	
Length of the right fallopian tube (cm)				
<8	5 (8.8)	87 (64.0)	92 (47.7)	<0.001
8–12	21 (36.8)	46 (33.8)	67 (34.7)	0.183
>12	31 (54.4)	3 (2.2)	34 (17.6)	<0.001
Length of the left fallopian tube (cm)				
<8	7 (12.3)	70 (51.5)	77 (39.9)	<0.001
8–12	16 (28.1)	57 (41.9)	73 (37.8)	0.540
>12	34 (59.6)	9 (6.6)	43 (22.3)	<0.001
Total	57 (29.1)	136 (70.9)	193 (100.0)	<0.001

$p < 0.05$ was considered as statistically significant.

orrhoea) and/or sexual intercourse (dyspareunia), intermenstrual bleeding and infertility [15]. The most common sites for endometriotic lesions to establish are the ovaries and pelvic peritoneum, yet endometriotic lesions are also found in other sites such as the abdominal wall, fallopian tubes (FT), bowels, bladder, cervix and vagina [14]. Several studies confirmed that infertile women are 6 to 8 times more likely to have endometriosis than fertile women [7].

Fallopian tubes (FT) are implicated in all endometriosis-associated symptomatology and clinical consequences. They may contribute to the origin of endometrial tissue, determine the sites of formation of ectopic lesions and serve as conduits for the spread of proinflammatory media [16,17].

The epithelial cells of the fallopian tube exist as a continuum of the endometrium, the mucosa lining the uterine

cavity and both tissues share the same embryological origin [17].

The shared embryological origin and some similar phenotypical and functional features between the FT and endometriosis compelled us to examine FT involvement in the genesis, pathophysiology and clinical consequences of endometriosis. There are many interesting findings suggesting that both endometrium and tubal mucosa may contribute to the origin of the disease and that presence of endometrial lesions may cause tubal dysfunction [16].

The tortuous course of the intramural portion of the uterine tubes constitutes a normal anatomical finding. It controls the retrograde flow of blood during menstruation and reduces the possibility of developing endometriosis. Straight or curved intramural portions represent an anatomical abnormality that may predispose women to endometrio-

sis [18,19]. Endometriosis was more frequent in women with straight courses and was infrequent in women with tortuous ones [17].

The presence of adhesive disease that may entrap the fimbria in infertile patients with moderate and severe endometriosis is clearly understood. It represents part of fallopian tube involvement in adhesion formation after treatment of active pelvic endometriosis. However, little is known about the prevalence of fimbrial pathology in the early stages of endometriosis.

The most widely accepted theory of endometriosis suggests that it occurs during retrograde menstruation, when fragments of menstrual endometrial tissue are refluxed into the pelvic cavity through fallopian tubes and stored for development of ectopic endometrial lesions [20, 21]. There are data on the correlation between the length of the fallopian tubes and infertility [22]. We can assume that retrograde menstruation is facilitated by the shorter length of fallopian tubes, which is confirmed by our study showing that among infertile women with endometriosis, the proportion of women with short fallopian tubes (length <8 cm) was significantly higher than among women without endometriosis.

It has been suggested that women with endometriosis exhibit diminished physiological utero tubal transport capacity compared to the control subjects [23], which may be due to tubal pathologies. Since fallopian tubes and uterine tissues have the same embryological origin [16,24], that may explain the link between endometriosis and the unusual appearance of fallopian tubes. In addition to endometriosis located in the fallopian tube, tubular abnormalities can also occur with the diagnosis of pelvic endometriosis elsewhere [25]. In our study, endometriosis showed a negative correlation with the normal appearance of fallopian tubes. The rate of adhesions and endometrial sites in the group of patients with endometriosis was significantly higher.

Causes of tubal dysfunction in endometriosis could be tube blockage, adhesion formation, or hydrosalpinx. All of these conditions of the disease are caused by inflammatory processes. They can co-exist, and are often interrelated, making it difficult to distinguish the exact contribution of each cause in the complete functional disorder of fallopian tubes. About 30% of women with endometriosis show any type of tubal pathology [26,27].

The prevalence of fimbrial pathology was significantly higher in infertile patients with early stages of endometriosis (50.2%) compared with infertile patients with no endometriosis (17.8%, $p < 0.0001$) [28]. According to our study, the normal appearance of fallopian tubes showed a significantly negative correlation with endometriosis, in particular, the rate of adhesions in both the left and right sides was higher. The incidence of individuals with both right and left fallopian tube lengths <8 cm was significantly higher in women with endometriosis; also, the frequency of individuals with a fallopian tube length >12 cm was signif-

icantly lower in women with endometriosis compared with controls.

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5. Conclusions

Infertile women with minimal or mild endometriosis have been shown to have anatomical and structural changes in the fallopian tubes and fimbriae compared to those without endometriosis. The presence of genital endometriosis (I;II stage) maybe associated with shorter fallopian tubes.

Author Contributions

LI, TV designed the research study, LI performed the research, LI, RG, LT analyzed the data, IT provided help and advice on statistical analysis, LI, AG, TV wrote the manuscript. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript.

Ethics Approval and Consent to Participate

All participants in the study signed an informed consent form.

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Conflict of Interest

The authors declare no conflict of interest.

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