

# Comparative clinical studies of fertility and infertility in women with endometriosis

Porównawcza analiza cech klinicznych występujących u płodnych i niepłodnych kobiet chorych na endometriozę

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## Abstract

**Objective:** To compare clinical characteristics of infertile and fertile patients with endometriosis.

**Material and methods:** We evaluated medical records of women who underwent surgical treatment of endometriosis (n=284) between January 1999 and December 2003. Our study included only cases of histopathologically proven pelvic endometriosis (n=269).

These patients were categorized into two groups named after infertile (n=45) and fertile cases (n=224). Clinical data were compared.

**Results:** Infertile patients are younger (t student.  $P=0.0000$ ), have lower weight (Wilcoxon test  $P=0.0150$ ), lower blood pressure — either systolic (Wilcoxon test  $P=0.0006$ ) or diastolic (Wilcoxon test  $P=0.0007$ ), separate noncystic endometriotic lesions occur frequently among these cases (Pearson chi-square  $P=0.000$ ).

**Conclusion:** Noncystic endometriotic implants are more strongly related to infertility than endometriomas. The relationship between blood pressure and infertility requires further investigation. endometriosis.

Key words: **endometriosis / infertility / endometrioma /**

## Streszczenie

**Cel pracy:** NPorównanie cech klinicznych występujących u płodnych i niepłodnych kobiet z endometriozą.

**Materiał i metody:** Ocenie poddano historie chorób pacjentek operowanych pomiędzy styczniem 1999 roku a grudniem 2003 roku, u których potwierdzono histopatologicznie endometriozę miednicy mniejszej (n=269).

Chorę podzielono na dwie grupy: kobiety niepłodne (n=45) oraz płodne (n=224). Porównano cechy kliniczne w obu grupach.

**Wyniki:** Niepłodne pacjentki są młodsze (t student.  $P=0,0000$ ), mają mniejszą masę ciała (Wilcoxon test  $P=0,0150$ ), niższe ciśnienie tętnicze krwi: zarówno skurczowe (t student.  $P=0,0006$ ) jak i rozkurczowe (t student.  $P=0,0007$ ). Wszczypty endometriotyczne występują częściej w grupie kobiet niepłodnych (Pearson chi-square  $P=0,000$ ) w przeciwieństwie do torbieli endometrialnych jajników.

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Sznurkowski J, et al.

**Wnioski:** Niecystyczne wszczepy endometriotyczne są silniej związane z niepłodnością niż torbiele endometrialne jajników. Związek pomiędzy ciśnieniem tętniczym krwi a niepłodnością towarzyszącą endometriozie wymaga dalszych badań. Otu bólowego miednicy mniejszej jest obserwowana szczególnie u kobiet bez współistniejącej endometriozy.

Słowa kluczowe: **endometrioza / niepłodność / torbiele endometrialne /**

## Introduction

Endometriosis is a pathologic condition commonly found in women of reproductive age. It was first described in 1860 by von Rokitansky [1] and since then has been defined as the presence of tissue resembling functioning endometrial glands and stroma outside the uterine cavity. A number of theories attempt to explain the etiology of endometriosis. Current theories regarding histogenesis include the transplantation of exfoliated endometrium [2, 3], coelomic metaplasia [4], and embryonic müllerian rests [5,6,7]. Despite over 130 years of endometriosis investigations, the disease remains enigmatic.

In numerous retrospective clinical studies, the revised classification of endometriosis proposed by The American Fertility Society (AFS) has been used. This system is based on a 40-point scale and includes four stages [8]. Minimal (stage I) and mild (stage II) disease are both characterized by scattered, superficial noncystic implants on structures with no associated adhesions. Moderate (stage III) disease is characterized by multiple implants or small endometriomas (<2cm) and/or minimal peritubal or periovarian adhesions. Severe (stage IV) disease is characterized by large ovarian endometriomas, significant tubal or ovarian adhesions, tubal obstruction, obliteration of cul de sac and major uterosacral involvement [9]. While classification strategies appear to correlate strongly with pelvic pain, the correlation between stage of disease and infertility is weak [10]. As pointed out recently by Schenken and Guzick, new measures or characteristics of the disease beyond those currently used are sorely needed [10].

The idea that peritoneal endometriosis, endometriosis of the rectovaginal septum and endometrial cysts must be considered as three separate entities with different pathogenesis appears most frequently [11, 12, 13, 14].

Regarding these theses, it seems obvious that the results of previous clinical investigations based on the AFS classification must be verified by taking a new look at endometriosis based on morphological appearance of the disease. Only Stage I and II were homogenous in accordance with morphological appearance of endometriosis. Stages III and IV could be present in women with endometriomas and/or solid lesions, or in women with endometriosis of the rectovaginal septum.

The purpose of our study was to find differences between infertile and fertile patients with endometriosis comparing clinical features and morphological appearance of the disease.

## Materials and methods

Medical records of 284 women with histopathologically proven endometriosis were reviewed. These patients were diagnosed between January 1999 and December 2003 by direct visualization at laparoscopy (n=65), laparotomy (n=204) and wide resection of abdominal wall tumors (n=15). Histopathological examination was performed on all excised specimens.

We included in our study only cases with pelvic endometriosis (n=269) excluding women with scar endometriosis for lack of information about their abdominal organs.

Data on operative findings and the results of histopathological examination allowed us to distinguish three different types of morphological appearance of the disease: separate noncystic endometriotic implants (n=35), noncystic endometriotic implants with endometriomas (n=59) and separate endometriomas (n=175).

All patients (n=269) were categorized into two general groups named after infertile (n=45) and fertile (n=224) cases. Infertile cases were those who had primary (n=42) or secondary (n=3) infertility of at least 24 months duration. Fertile cases were those who had experienced one or more live births and had never before been treated for infertility.

For each record we collected information about the patient's age at the time of surgery, menstrual factors, parity, weight, height, blood pressure, the indication of surgical intervention, and the morphological appearance of the disease: cystic ovarian lesions referred to as endometriomas and/or noncystic endometriotic implants. Clinical data were compared.

Data normally distributed were analyzed using the Student t test. Otherwise, we used the Mann-Whitney test and Wilcoxon test. Proportions were then analyzed using Pearson's chi-square test. Statistical analysis was performed via Stata 8.0 for Windows Program. The differences are considered to be statistically significant if  $p < 0.05$ .

## Results

All patients in this study were Polish women living in Gdańsk. Of a total of 269 women with histopathologically proven pelvic endometriosis, infertility was recognized in 45 cases (16.7%). The mean age in this group was 29.9 (SD - 4.3 years), mean number of births was 0.43 SD - 0.9, mean weight was 59.0 SD - 9.3kg, mean height was 166.7 SD - 4.7cm, mean

Comparative clinical studies of fertility and infertility in women with endometriosis.

age at the menarche was 13.4 SD - 1.1 years, mean length of menstrual cycle was 24.8 SD - 10.0 days, mean duration of menstrual flow was 5.3 SD - 2.4 days, mean value of systolic blood pressure was 114.7 SD - 9.4mmHg, mean value of diastolic blood pressure was 73.4 SD - 8.8mmHg. In this group, we noted 23 cases with separate noncystic endometriotic implants (51.11%), 10 cases with noncystic endometriotic implants coexisting with endometriomas (22.22%) and 12 cases with separate endometriomas (26.67%).

Among infertile women with endometriosis, noncystic endometriotic implants were found more frequently (n=23, 51.11%) than endometriomas (n=12, 26.67%) (p<0.001, odds ratio 3.7, 95% confidence interval 1.4, 9.9).

In the remaining 224 fertile cases (83.3%) the indications for surgery were: pelvic pain syndrome (n=13), pelvic pain caused by persistent ovarian cysts (n=128) and non-symptomatic endometriomas found during gynecological/USG examination (n=83).

The mean age in this group was 36.8 SD - 8.5 years, mean number of births was 1.5 SD - 1.4, mean weight was 63.4 SD-12.7kg, mean height was 165.0 SD - 5.9cm, mean age at the menarche was 13.3 SD - 1.4 years, mean length of menstrual cycle was 25.5 SD - 7.8 days, mean duration of menstrual flow was 5.2 SD - 2.1 days, mean value of systolic blood pressure was 122.6 SD - 15.6mmHg, mean value of diastolic blood pressure was 79.5 SD - 11.1mmHg. In this group we noted 13 cases with separate noncystic endometriotic implants (5.8%), 49 cases with noncystic endometriotic implants coexisting with endometriomas (21.88%) and 162 cases with separate

endometriomas (72.32%). Among fertile women with endometriosis, endometriomas were found more frequently (n=162, 72.32%) than noncystic endometriotic implants (n=13, 5.8%) (p<0.000, odds ratio 155.3, 95% confidence interval 69.8, 345.2). The data distribution compared among fertile (n=224) and infertile (n=45) women with pelvic endometriosis is summarized in table 1.

It shows that infertile patients are younger (t-student. P=0.0000), have lower weight, lower blood pressure – either systolic (Wilcoxon test P=0.0006) or diastolic (Wilcoxon test P=0.0007), noncystic endometriotic implants occur frequently among infertile women with endometriosis as opposed to endometriomas (Pearson chi-square P=0.0000).

**Discussion**

In our research only 16.7% women with histopathologically proven pelvic endometriosis were infertile although others studies have observed infertility in 25% to 39% of endometriosis cases [15, 16]. This difference could be explained by the fact that we have included in the infertile group only those women who had primary or secondary infertility for at least 24 months.

The present study has demonstrated that infertile patients are younger (t-student. P=0.0000) than those with fertile endometriosis. No differences in mean age between the 41 fertile and 27 infertile endometriosis patients have been observed by H. Hassa et al [15], but a previous Polish study involving 384 women with endometriosis (170 infertile, 214 fertile) confirms our observations [17].

**Table I.** Data distribution among infertile and fertile endometriosis cases.

Feature	Infertile N=45	Fertile N=224	Method	p-value
The mean age at the time of surgery (years)	29.91	36.83	test Wilcoxon	0.0000
Mean weight (kg)	59.044	63.431	test Wilcoxon	0.015
Mean height (cm)	166.689	164.960	test Wilcoxon	not significant
Mean age at the menarche (years)	13.378	13.272	Test t-Studenta	not significant
Mean length of menstrual cycle (days)	24.822	25.491	Test t-Studenta	not significant
Mean duration of menstrual flow (days)	5.267	5.183	Test t-Studenta	not significant
Mean value of systolic blood pressure (mmHg)	114.667	122.545	test Wilcoxon	0.0006
Mean value of diastolic blood pressure (mmHg)	73.444	79.509	test Wilcoxon	0.0007
Separate endometriomas	26.67(%)	94.20(%)	TestPearson chi <sup>2</sup>	0.0000
Noncystic endometriotic lesions	51.11(%)	5.8(%)	TestPearson chi <sup>2</sup>	0.0000
Endometriomas plus noncystic endometriotic lesions	22.00(%)	21.88(%)	TestPearson chi <sup>2</sup>	not significant

Sznurkowski J, et al.

Our results showing that infertile endometriosis patients have lower blood pressure than older and heavier fertile cases could be explained by the fact that blood pressure rises with age and weight [18, 19]. The fact that endometriomas are found more frequently in older women is not a surprise, either. The incidence of endometriomata, like other ovarian tumors, increases with age. Surgical treatment is necessary even in non symptomatic cysts because malignant transformation has been widely reported in literature [20, 21, 22].

The observation that older fertile patients with endometriomas had never been treated for infertility before belies the previous thesis that endometriomas are the later sequelae of the disease, simply a manifestation of more advanced endometriosis. It shows instead that endometriosis is a clinically heterogeneous entity with differing subtypes strongly related to the morphological appearance of the disease.

Nisolle M, and Donez J [13] suggested that peritoneal, ovarian lesions, and nodules of the rectovaginal septum must be considered as different entities with different pathogeneses.

They support this thesis with results of immunohistochemical analysis showing the differences in proliferative activity and steroid receptor expression in peritoneal and ovarian endometriosis [12]. Nezath F.R. et al. in the comparative immunohistochemical study of noncystic endometriosis lesions and endometriomas suggest that different genes are involved in the development and maintenance of these two entities [14].

Our study confirms that noncystic endometriotic implants seem to be a clinically different entity than endometriomas.

We conclude that noncystic endometriotic implants are more strongly related to infertility than endometriomas. Rare infertile cases with separate endometriomas are older. Their fecundity could be decreased because of age. This question requires further random analysis.

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