Hum. Reprod. Advance Access published September 17, 2012
Human Reproduction, Vol.0, No.0 pp. 1–5, 2012
doi:10.1093/humrep/des316

human reproduction

ORIGINAL ARTICLE *Gynaecology*

Diagnostic delay for endometriosis in Austria and Germany: causes and possible consequences

G. Hudelist[1,2,†], N. Fritzer[3,*,†], A. Thomas[4], C. Niehues[5], P. Oppelt[6,2], D. Haas[6,2], A. Tammaa[1], and H. Salzer[1]

[1]Department of Obstetrics and Gynaecology/Endometriosis and Pelvic Pain Clinic, Wilhelminen Hospital, Vienna, Austria [2]Stiftung Endometrioseforschung, SEF, Germany, Austria, Switzerland [3]Department of Clinical Psychology and Psychotherapy, Institute of Psychology, Alps-Adria University of Klagenfurt, Klagenfurt, Austria [4]Department of Methodological Research, Institute of Psychology, Alps-Adria University of Klagenfurt, Klagenfurt, Austria [5]Median-Klinik am Burggraben, Bad Salzuflen, Germany [6]Department of Obstetrics and Gynaecology/Center for Endometriosis, General Hospital Linz, Linz, Austria

*Correspondence address. Department of Clinical Psychology and Psychotherapy, Institute of Psychology, Alps-Adria-University of Klagenfurt, Universitätsstraße 65, 9020 Klagenfurt, Austria; E-mail: fritzern@gmx.net

Submitted on April 13, 2012; resubmitted on July 17, 2012; accepted on July 19, 2012

STUDY QUESTION: What is the length of the diagnostic delay for endometriosis in Austria and Germany, and what are the reasons for the delay?

SUMMARY ANSWER: The diagnostic delay for endometriosis in Austria and Germany is surprisingly long, due to both medical and psychosocial reasons.

WHAT IS KNOWN ALREADY: Diagnostic delay of endometriosis is a problematic phenomenon which has been evaluated in several European countries and in the USA, but has not been reported for Germany and Austria.

STUDY DESIGN, SIZE, DURATION: A cross-sectional, questionnaire-based multicentre study was conducted in tertiary referral centers in Austria and Germany. From September 2010 to February 2012, 171 patients with histologically confirmed endometriosis were included.

PARTICIPANTS, SETTING, METHODS: Patients with a previous history of surgically proven endometriosis, internal diseases such as rheumatic disorders, pain symptoms of other origin, gynecological malignancy or post-menopausal status were excluded from the analysis. Patients with histologically confirmed endometriosis completed a questionnaire about their psychosocial and clinical characteristics and experiences. Of 173 patients, two did not provide informed consent and were excluded from the study.

MAIN RESULTS AND THE ROLE OF CHANCE: The median interval from the first onset of symptoms to diagnosis was 10.4 (SD: 7.9) years, and 74% of patients received at least one false diagnosis. Factors such as misdiagnosis, mothers considering menstruation as a negative event and normalization of dysmenorrhea by patients significantly prolonged the diagnostic delay. No association was found between either superficial and deep infiltrating endometriosis or oral contraceptive use and the prolongation of diagnosis.

LIMITATIONS AND REASONS FOR CAUTION: There was a possible selection bias due to inclusion of surgically treated patients only.

WIDER IMPLICATIONS OF THE FINDINGS: Several factors causing prolongation of diagnosis of endometriosis have been reported to date. The principal factors observed in the present study are false diagnosis and normalization of symptoms. Teaching programs for doctors and public awareness campaigns might reduce diagnostic delay in Central Europe.

STUDY FUNDING/COMPETING INTEREST(S): No competing interests exist.

Key words: diagnosis / endometriosis / diagnostic delay / reasons

[†] These authors contributed equally to this work.

Introduction

Endometriosis is one the most common gynecological disorders causing pain symptoms such as dysmenorrhea, dyspareunia, dyschezia and infertility. Tissue-destructive infiltrative growth of endometriotic implants and associated inflammatory response reactions has been linked with reproductive organ dysfunction and pelvic pain (Giudice, 2010). Endometriosis is a chronic and, in most cases, debilitating disease associated with a significant reduction of quality of life due to pain symptoms and/or infertility. In addition, several lines of evidence indicate that a significant number of women with endometriosis do develop comorbidities, such as depressive or anxiety disorders, over time thereby adding to the problem. Furthermore, a recent study by Simoens *et al.* (2011) demonstrated a high socioeconomic impact of endometriosis on health care expenses. Delaying the diagnosis of endometriosis clearly aggravates these problems.

Several groups have investigated the prevalence of endometriosis and have observed numbers ranging from 1.9% (Ballard *et al.*, 2008; Seaman *et al.*, 2008) to 20.7% (Waller *et al.*, 1993). Nevertheless, the majority of studies conducted in the USA, UK, Norway or Italy have demonstrated that the length of the time interval from onset of symptoms to diagnosis is surprisingly long.

Hadfield *et al.* (1996) conducted a retrospective analysis of 218 women from self-help groups in the USA and the UK and observed a symptom to diagnosis interval of 11.7 and 7.9 years, respectively. Interestingly, these intervals have shown to be declining over time in the USA but appear to be stable in the UK (Ballard *et al.*, 2006; Nnoaham *et al.*, 2011).

Similar time periods (7 years) have been reported by Arruda *et al.* (2003) who performed a retrospective cohort study of 200 Brazilian women with endometriosis. However, this interval was shown to be dependent on the primary symptom since women with infertility took 4 years to be diagnosed with endometriosis, whereas 7.4 years elapsed from symptom to diagnosis in patients with pelvic pain.

The diagnostic delay does vary between countries from Europe, USA, Brazil and Asia. Nnoaham *et al.* (2011) recently investigated the impact of endometriosis on quality of life and work productivity in an international study including centers from Italy, Belgium, UK, Brazil, Spain, Ireland and China. Interestingly, the diagnostic delay ranged from 3.3 years in Guangzhou, China, to 10.7 years in Siena, Italy. To date, data on the length and causative factors for diagnostic delay in Germany and Austria are lacking.

The aim of the present work was to investigate the duration and possible causes of delay in the diagnosis of endometriosis in these two central European countries.

Materials and Methods

The present work was designed as a cross-sectional study conducted in Austria and Germany. From September 2010 to February 2012, 173 patients with histologically proven endometriosis were asked to take part in the present analysis designed as a multicenter study, which included tertiary referral centers for diagnosis and treatment of endometriosis in Austria and Germany. In all but four cases, laparoscopy was performed for treatment of endometriosis-associated symptoms such as pain and infertility. Four women underwent laparotomy for resection of deep infiltrating endometriotic disease. Only women with complete excision of all visible endometriotic lesions were included in the analysis. There were 171 patients with histologically proven endometriosis who completed a self-administered questionnaire, in her own language, within a maximum of 3 months after surgery. Patients with a previous history of surgically proven endometriosis, internal diseases such as rheumatic disorders, pain symptoms of other origin, gynecological malignancy or postmenopausal status were excluded from the analysis. Additionally, two patients who did not provide informed consent were excluded from the study (see Fig. 1).

The self-administered questionnaire consisted of 26 items evaluating demographic data, as well as medical, reproductive and obstetric history and information on feelings about menarche and dysmenorrhea during adolescence. Further items focused on the analysis of maternal and familiar attitudes toward menstruation, the use of hormonal and analgesic therapies and the number, type and quality of non-invasive and invasive investigations regarding the patient's complaints and symptoms. In addition, the type and number of contacts with medical doctors, the type and number of false diagnosis and the type and extent of surgical intervention were assessed.

Surgical reports were re-evaluated by an experienced gynecological surgeon (G.H.), and disease stage was documented using the revised American Fertility Society scoring system (Haas *et al.*, 2011) and the revised ENZIAN score for deep infiltrating endometriosis (DIE) (Tuttlies *et al.*, 2005) in order to discriminate superficial and deep infiltrating disease. The study was approved by the local Ethics Committee. Informed consent regarding the patients data was obtained from all women included in the analysis.

Data analysis

A self-administered questionnaire (26 items, partly closed questionnaire response format and partly 10-point rating scale) was analyzed using chi-square test and Fisher's exact test in the SPSS 16® software for categoric variables and independent *t*-test for equality of means to investigate associations between variables and study outcomes. A *P*-value of <0.05 was considered statistically significant.

Results

Patients and surgical findings

The mean age, presenting symptoms, demographic and clinical parameters of patients are depicted in Tables I and II. There were 171 patients who fully completed the questionnaire and underwent surgical resection with histological proof of endometriotic disease according to surgical and histological reports. As depicted, 85 of 171 (49.7%) women were diagnosed with superficial/peritoneal endometriosis, whereas 86 women (50.3%) also suffered from deep infiltrating disease. The mean age at the time of diagnosis was 32 (SD: 6.0) years.

The delay intervals from the onset of symptoms to first medical and gynecological consultation and according intervals from medical/gynecological consultations to final diagnosis are depicted in Table III. The median interval from the first onset of symptoms to diagnosis was 10.4 years (SD: 7.9). Within this, the interval from the first onset of symptoms to seeking medical help was 2.3 years and the interval from the first onset to gynecological consultation 2.7 years. The diagnostic delay for women with pelvic pain was 10.5 (SD: 7.9) years and 9.8 (SD: 8.7) years for patients with subfertility.

The total number of women with a false diagnosis was 127 of 171 (74.3%) and these diagnoses ranged from pelvic inflammatory disease (15/171, 8.8%) to psychosexual disorders (21/171, 12.3%) (Table II, Fig. 2).

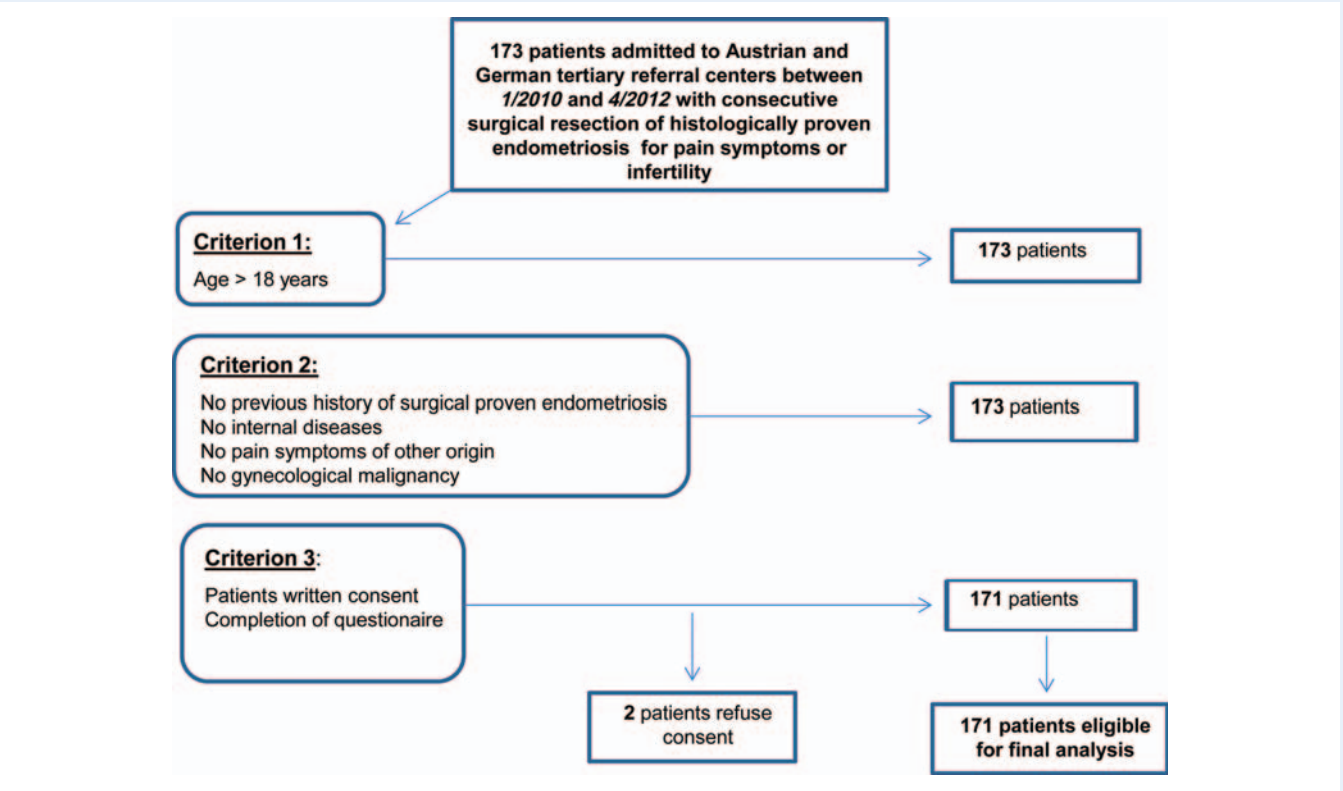

Figure 1 Flow chart of study participants.

Table I Demographic characteristics of 171 patients with endometriosis.

Variables	Mean	SD	%
Age at time of diagnosis (years)	32	6	
Number of children	0.4	0.7	
Number of spontaneous abortions	0.1	0.4	
Number of abortions	0.1	0.7	
Postsecondary education			27.5 (47/171)
Married or in partnership			84.2 (144/171)
Age onset of symptoms (years)	21.2	7.5	
Age first contact seeking medical consultation (years)	25.6	7.2	
Age first contact seeking gynecological consultation (years)	23.9	7.0	
Number of consulted gynecologists	3.4	2.8	

SD, standard deviation.

Relationships between relevant clinical, demographic and psychological variables and diagnostic delay are depicted in Table IV. Diagnostic delay was significantly longer in patients with a higher number of misdiagnosis compared with women with lower numbers of misdiagnoses [11.5 (SD: 8.2) versus 7.4 (SD: 6.3), $P < 0.01$]. An association between the patient's impression of not being taken seriously by the gynecologist and prolonged diagnostic delay was also observed [11.5 (SD: 8.0) versus 8.6 (SD: 7.5), $P = 0.02$]. A significant association was also found between women who understood their symptoms as 'normal' compared with patients without normalization of symptoms [11.3 (SD: 7.5) versus 8.5 (SD: 8.4), $P = 0.04$]. Furthermore, women with no or only few menstrual cramps during adolescence had a significant shorter diagnostic delay compared with the patients who suffered from severe cramps [9.0 (SD: 7.3) versus 11.6 (SD: 8.2), $P = 0.03$]. Patients whose mothers considered menstruation as a negative event also had a longer time to diagnosis [14.6 (SD: 6.6) versus 9.7 (SD: 7.9), $P < 0.01$] but there was no such effect for patients who themselves considered menarche negatively ($P = 0.28$). Additionally, no significant associations were found between the time interval for diagnosis of endometriosis and parameters such as use of hormonal ($P = 0.39$) or pain-relieving medication ($P = 0.11$), extent of disease (superficial endometriosis/DIE) ($P = 0.87$) and the main symptomatic complaints (pelvic pain/subfertility) ($P = 0.69$), Table IV.

Discussion

In the present study, we found an overall diagnostic delay of 10.4 years and a time interval of 7.7 years from gynecological consultation due to pelvic pain symptoms or subfertility until final diagnosis. This period lies above the upper range of European countries according to the previous studies reporting a median delay time of 8 years in the UK and Spain (Ballard *et al.*, 2006; Nnoaham *et al.*, 2011), 6.7 years

Table II Clinical characteristics of 171 patients with histologically proven endometriosis.

Variables	Mean	SD	n (%)
Hormonal therapy			127 (74.3)
Oral contraception pill/long cycle use (years)	0.8	2.1	58 (33.9)
Oral contraception pill/interval use (years)	3.4	5.2	85 (49.7)
Other hormonal therapy (LNG IUD, GnRH)			73 (42.6)
Pain relieving medication (years)	5.2	6.9	111 (64.9)
Pelvic pain symptoms			144 (84.2)
Subfertility			27 (15.8)
Superficial/peritoneal endometriosis			85 (49.7)
Deep infiltrating endometriosis			86 (50.3)
Number of patients with misdiagnosis			127 (74.3)
Pelvic inflammatory disease			15 (8.8)
Overactive bladder			18 (10.5)
Idiopathic subfertility			10 (5.8)
Irritable bowel disease			33 (19.3)
Chronic appendicitis			15 (8.8)
Stress-associated pelvic pain			57 (33.3)
Dysfunctional uterine bleeding			44 (25.7)
Lactose/fructose intolerance			21 (12.3)
Psychosexual disorders			21 (12.3)

SD, standard deviation; LNG, levonorgestrel; IUD, intrauterine device; GnRH, gonadotrophin analogue.

Table III Delay intervals for 171 patients with histologically proven endometriosis.

Variables	Mean (years)	SD
Onset of symptoms to first medical consultation	2.3	3.7
Onset of symptoms to first gynecological consultation	2.7	3.8
Gynecological consultation to final diagnosis	7.7	7.0
Onset of symptoms to final diagnosis	10.4	8.0

SD, standard deviation.

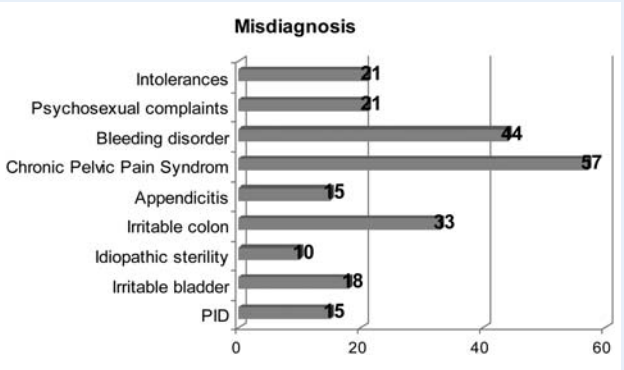

Figure 2 Misdiagnosis of 127 patients associated with the diagnostic delay.

Table IV Relationships between psychosocial/clinical characteristics and diagnostic delay.

Variable	Median (years)	SD	P
Mother regarded menstruation positive	9.7	7.9	<0.01*
Mother regarded menstruation negative	14.6	6.6	
Patient regarded menarche positive	9.9	7.1	0.28
Patient regarded menarche negative	11.2	8.7	
No/some menstrual cramps during adolescence	9.0	7.3	0.03*
Severe menstrual cramps during adolescence	11.6	8.2	
Normalization of pelvic pain/dysmenorrheal	11.3	7.5	0.04*
No normalization of pelvic pain/dysmenorrheal	8.5	8.4	
Misdiagnosis	11.5	8.2	<0.01*
No misdiagnosis	7.4	6.3	
Hormonal therapy use	10.8	7.7	0.39
No hormonal therapy use	9.6	8.6	
Analgesic medication use	11.1	7.9	0.11
No analgesic medication use	9.0	8.0	
Superficial/peritoneal endometriosis	10.5	8.0	0.87
Deep infiltrating endometriosis	10.3	7.8	
Subfertility	9.9	8.2	0.69
Pelvic pain	10.5	7.9	
Gynecologist took pain intensity not seriously	11.5	8.0	0.02*
Gynecologist took pain intensity seriously	8.6	7.5	

*$P < 0.05$; *t*-test for equality of means.
SD, standard deviation.

in Norway (Ballard *et al.*, 2006), 7–10 years in Italy and 4–5 years in Ireland and Belgium (Nnoaham *et al.*, 2011).

Several factors causing prolongation of diagnosis of endometriosis have been reported to date, including early onset of symptoms (Arruda *et al.*, 2003), normalization of pain by family doctors, intermittent use of contraceptives causing hormonal suppression of symptoms or the use of non-discriminatory examinations (Ballard *et al.*, 2006). Factors associated with diagnostic delay of endometriosis in the present analysis included false diagnosis, and the majority of patients (74.3%) received at least one misdiagnosis. Although the widespread use of oral contraceptives often causes alleviation of symptoms not necessitating enhanced diagnostic vigilance, only half of the patients were examined digitally (per vaginum) combined with transvaginal sonography (TVS) by their gynecologists. Although TVS is not

regarded as an obligatory examination in all Austrian and German outpatient gynecological clinics, TVS has been proved as a valuable tool for diagnosis of endometriosis, especially deep infiltrating disease (Moore *et al.*, 2002; Hudelist *et al.*, 2011). The widespread use of TVS in symptomatic women and enhanced diagnostic skills regarding the diagnosis of DIE may therefore reduce diagnostic delay in the gynecological primary care setting.

We also observed that a negative maternal attitude toward menstruation and the normalization of menstrual pain by patients caused further delay of diagnosis.

When the patient's mothers regard menstruation as a negative event and/or did not speak about this issue during adolescence, patients may adopt menstruation as a shameful topic. For this reason, dysmenorrhea may be regarded as normal or as 'part of being a woman'. Not surprisingly, this group hesitated much longer to communicate the issue or seek medical advice. The present study only included women with surgically confirmed endometriosis. Therefore, hospitalization was a precondition in order to fulfill this inclusion criterion. However, the sole inclusion of women with histologically proven endometriosis might also confer a selection bias since this population may not reflect the general population. As a consequence, the diagnostic delay in the general, non-hospitalized population might be longer than that observed in our patient cohort.

In conclusion, diagnostic delay in Austria and Germany is considerably long and is influenced by several causative factors. The results of the present study highlight the need for educational programs and training courses to enhance the diagnostic skills of present and future gynecologists and general practitioners. On the other hand, public awareness initiatives may help to increase the general knowledge of endometriosis as a main cause for menstrual pain and subfertility thereby lowering the barrier for affected women to seek early specialist advice.

Authors' roles

G. H.: chief scientist, preparation of the manuscript. N.F.: chief scientist, statistical analysis and data interpretation, preparation of the manuscript. A.T.: statistical analysis and data interpretation. C.N.: recruitment of patients. P.O.: recruitment of patients. D.H.: recruitment of patients. A.T.: recruitment of patients. H.S.: chief scientist.

Funding

No competing interests exist.

Conflict of interest

None declared.

References

Arruda MS, Petta CA, Abrao MS, Benetti-Pinto CL. Time elapsed from onset of symptoms to diagnosis of endometriosis in a cohort study of Brazilian women. *Hum Reprod* 2003;**18**:756–759.

Ballard K, Lowton K, Wright J. What's the delay? A qualitative study of women's experiences of reaching a diagnosis of endometriosis. *Fertil Steril* 2006;**86**:1296–1301.

Ballard KD, Seaman HE, de Vries CS, Wright JT. Can symptomatology help in the diagnosis of endometriosis? Findings from a national case-control study—part 1. *BJOG* 2008;**115**:1382–1391.

Giudice LC. Clinical practice. Endometriosis. *N Engl J Med* 2010; **362**:2389–2398.

Haas D, Chvatal R, Habelsberger A, Wurm P, Schimetta W, Oppelt P. Comparison of revised American Fertility Society and ENZIAN staging: a critical evaluation of classifications of endometriosis on the basis of our patient population. *Fertil Steril* 2011;**95**:1574–1578.

Hadfield R, Mardon H, Barlow D, Kennedy S. Delay in the diagnosis of endometriosis: a survey of women from the USA and the UK. *Hum Reprod* 1996;**11**:878–880.

Hudelist G, English J, Thomas AE, Tinelli A, Singer CF, Keckstein J. Diagnostic accuracy of transvaginal ultrasound for non-invasive diagnosis of bowel endometriosis: systematic review and meta-analysis. *Ultrasound Obstet Gynecol* 2011;**37**:257–263.

Moore J, Copley S, Morris J, Lindsell D, Golding S, Kennedy S. A systematic review of the accuracy of ultrasound in the diagnosis of endometriosis. *Ultrasound Obstet Gynecol* 2002;**20**:630–634.

Nnoaham KE, Hummelshoj L, Webster P, d'Hooghe T, de Cicco Nardone F, de Cicco Nardone C, Jenkinson C, Kennedy SH, Zondervan KT. Impact of endometriosis on quality of life and work productivity: a multicenter study across ten countries. *Fertil Steril* 2011;**96**:366–373.

Seaman HE, Ballard KD, Wright JT, de Vries CS. Endometriosis and its coexistence with irritable bowel syndrome and pelvic inflammatory disease: findings from a national case-control study—part 2. *BJOG* 2008;**115**:1392–1396.

Simoens S, Hummelshoj L, Dunselman G, Brandes I, Dirksen C, D'Hooghe T. Endometriosis cost assessment (the EndoCost study): a cost-of-illness study protocol. *Gynecol Obstet Invest* 2011;**71**:170–176.

Tuttlies F, Keckstein J, Ulrich U, Possover M, Schweppe KW, Wustlich M, Buchweitz O, Greb R, Kandolf O, Mangold R *et al.* [ENZIAN-score, a classification of deep infiltrating endometriosis]. *Zentralbl Gynakol* 2005;**127**:275–281.

Waller KG, Lindsay P, Curtis P, Shaw RW. The prevalence of endometriosis in women with infertile partners. *Eur J Obstet Gynecol Reprod Biol* 1993;**48**:135–139.