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Summary

To evaluate endometriosis patients' symptoms and relate them to fertility and different stages of endometriosis, 391 patients with endometriosis submitted to laparoscopy were studied. During laparoscopy 134 women were classified with stages I-II, 257 with stages III-IV. Pre-surgical symptoms (dysmenorrhoea, pelvic pain, and deep dyspareunia), recurrence of endometriosis, and pregnancy outcomes after laparoscopy were analysed in a long-term follow-up.

Pelvic pain, dysmenorrhoea and recurrence of disease after laparoscopy were more relevant in late-stage endometriosis ($P < 0.05$); infertility was the main indication to laparoscopy for early stages ($P < 0.05$). Admission for pelvic pain and severe dysmenorrhoea was prevalent in patients desirous of pregnancy before surgery who obtained a baby after ($P < 0.05$) while pain recurrence was more frequently observed in patients desirous of pregnancy but remain infertile. ($P < 0.05$). Symptoms of endometriosis may predict the stage of endometriosis. Painful symptoms of endometriosis may suggest diagnosis in late-stage of endometriosis, infertility in early stage.

Introduction

Endometriosis is a common, benign, oestrogen-dependent, disorder associated with pelvic pain and infertility. It is characterised by the presence of uterine endometrial tissue outside of the normal location, mainly on the pelvic peritoneum, but also on the ovaries and in the rectovaginal septum, and, more rarely, on extra-pelvic organs.

It has been estimated to affect 2.5–3.3% of all women of childbearing age

(Houston *et al.*, 1987), but its reported frequency differs widely depending on the type of population studied (Mahmood and Templeton, 1991).

This condition can cause severe pain and damage organs, frequently the reproductive organs. Typical signs and symptoms are chronic cyclic dysmenorrhoea, abdominal and pelvic pain, dyschesia (painful defecation), dyspareunia, irregular menstrual bleeding and, in approximately 4% of cases, painful urination (Martin DC, 1999). Endometriosis is identified as the cause of pelvic pain in 15–32% of women undergoing diagnostic laparoscopy for abdominal and pelvic discomfort (Mahmood TA *et al.*, 1991; Stovall DW *et al.*, 1997).

Most studies have indicated a weak association between the severity of the pain and the extent of endometriosis (Hurd WW, 1998). On the other hand, it has been suggested that the severity of pelvic pain is correlated with pelvic adhesions and deeply infiltrating endometriotic implants (Porpora MG *et al.*, 1999).

The present observational study evaluate patients' symptoms relating them to different stages of endometriosis and also to whether patients have fertile or infertile endometriosis. We report on a population in whom the presence of endometriosis was evaluated at laparoscopy. First, we investigated factors that may be related to either minimal/mild or moderate/severe endometriosis. Moreover, we evaluated whether data from the clinical history and symptomatology could predict the presence of endometriosis at laparoscopy.

Materials and Methods

The study was performed between 1995 and 2003 in our Department of Gynaecology Perinatology and Human Reproduction. We studied 391 consecutive women who underwent either diagnostic or operative laparoscopy. All cases were categorised as early (stages I and II) or late (stages III and IV)-stage endometriosis and 250 women, seeking pregnancy after surgery. In those, infertile group was defined after a period of at least 12 months without conception despite unprotected intercourse, not due to the male partner. Patients with previous pelvic surgery were not excluded.

Women completed a pre-operative questionnaire that collected demographic data and an assessment of pain using a visual analogue scale (VAS) for three components of endometriosis-related pain; dysmenorrhoea, non-menstrual pelvic pain, and dyspareunia. We used an 11-point VAS scale (0–10 cm), with zero representing no pain and 10 representing the worst pain imaginable. Patients who did not complete the initial questionnaire, were telephoned and asked to complete the questionnaire. Patients were followed-up after surgery for a very long period (range 1–11 years). Long-term follow-up was performed by telephone calls. Moreover 307 women accepted to submit to an ultrasonography follow-up. Recurrence of painful symptoms (dysmenorrhoea, pelvic pain and deep dyspareunia), course of infertility and recurrence of disease in patients with endometriosis were evaluated. Symptoms were evaluated on the basis of whether they were present or not and their degree of severity. The event dates considered were the date of operation and the date of reappearance of moderate or severe pain or the last menstruation before a positive pregnancy test.

SPSS version 13 was used to record and statistically analyse data. Continuous variables are presented as mean \pm S.E.M. Tests of statistical significance of the difference in the frequency of symptoms in relation to disease stage and localisation were based on an unpaired Student's *t*-test, Pearson's chi-square test. $P < 0.05$ was considered significant in all comparisons.

Results

During laparoscopy 134 women were classified with stages I-II, 257 with stages III-IV. A total of 250 women were categorised into fertile and infertile groups. The mean age of the patients was 32.3 ± 6.3 years. Most of the patients ($n = 257$; 65.7%) had late-stage endometriosis diagnosed during laparoscopy. Symptom distribution among patients with early- and late-stage endometriosis is summarised in Table 1 which shows that pelvic pain, dysmenorrhoea and recurrence of disease after laparoscopy were more relevant in late-stage endometriosis than in those with early-stage endometriosis ($P < 0.05$); infertility was the main indication to laparoscopy for early stages ($P < 0.05$). Such symptoms as deep dyspareunia did not differ among different stages of endometriosis. Ca125 and Ca 19.9 showed a statistically significance difference between the stage I-II and III-IV.

In women seeking pregnancy symptoms characteristics were evaluated with reference to fertility status, previously defined, as shown in Table 2. The mean ages of patients with fertile and infertile endometriosis were 33.9 ± 7.7 and 33 ± 4.6 years, respectively ($P = \text{NS}$). Pelvic pain and severe dysmenorrhoea at the time of admission was prevalent in patients who conceived after surgery ($P < 0.05$) but pain recurrence was more frequently observed in patients who resulted infertile ($P < 0.05$).

Table 1: Symptoms distribution among patients with early- and late-stage endometriosis

Characteristics	Tot.	Stages		P
		I-II	III-IV	
Symptoms on admission	391	134	257	
Age (yr \pm SD)	32.3 \pm 6.3	31.6 \pm 5.6	32.6 \pm 6.6	NS
Ca 125 (mean \pm SD)	35.9 \pm 36.5	17.6 \pm 10.5	42.8 \pm 40.2	<0.05
Ca 19.9 (mean \pm SD)	24 \pm 44.7	12.8 \pm 10.9	27.9 \pm 51.1	<0.05
Infertility (n)	180/391 (46%)	79/134 (58.9%)	101/257 (39.3%)	<0.05
Pelvic pain (n)	143/391 (36.6%)	39/134 (29.1%)	104/257 (40.5%)	<0.05
Dysmenorrhoea (n)	220/391 (56.3%)	58/134 (43.3%)	162/257 (63%)	<0.05
Dyspareunia (n)	36/391 (9.4%)	25/134 (18.7%)	51/257 (19.8%)	NS
Pelvic pain VAS (yr \pm SD)	5.7 \pm 2.3	5.9 \pm 2.4	5.7 \pm 2.3	NS
Dysmenorrhoea VAS (yr \pm SD)	7.6 \pm 1.9	7.3 \pm 2.1	7.7 \pm 1.8	NS
Dyspareunia VAS (yr \pm SD)	4.6 \pm 2.3	4.6 \pm 2.1	4.6 \pm 2.4	NS
Pain recurrence (n)	113/391 (28.9%)	38/134 (28.4%)	75/257 (29.2%)	NS
Spontaneous pregnancies (n)	77/391 (19.7%)	32/134 (23.8%)	45/257 (17.5%)	NS
Recurrence of endometriosis (n) (Ultrasonography follow-up)	58/307 (18.9%)	8/99 (8%)	50/208 (24%)	<0.05

Table 2: Symptoms distribution among patients with fertile and infertile endometriosis after surgery.

	Tot. 250	Fertile group 74	Infertile group 176	P
Age (yr)	33.3±5.6	33.9±7.7	33±4.6	NS
Ca 125 (mean±SD)	37.4±37.7	45.3±36.2	33.8±38.1	NS
Ca 19.9 (mean±SD)	26.8±57.3	40.2 ± 89	19.9 ± 26.9	NS
Pelvic pain (n)	85/250 (34%)	34/74 (45.9%)	51/176 (29%)	<0.05
Dysmenorrhoea (n)	144/250 (57.6%)	54/74 (73%)	90/176 (51.1%)	<0.05
Dyspareunia (n)	52/250 (20.8%)	20/74 (27%)	32/176 (42.4%)	NS
Pelvic pain VAS (mean±SD)	5.8±2.4	6.1 ± 2.6	5.6 ±2.3	NS
Dysmenorrhoea VAS (mean±SD)	7.7±1.9	8.2±1.7	7.5 ±2.1	NS
Dyspareunia VAS (mean±SD)	4.9±2.3	5± 2.3	4.8±2.2	NS
Pain recurrence (n)	69/250 (27.6%)	12/74 (16.2%)	57/176 (32.4%)	<0.05
Pregnancy (n)	112/250 (44.8%)	18/74 (24.3%)	94/176 (53.4%)	<0.05
Recurrence of endometriosis during (Ultrasonography follow-up) (n)	39/236 (16.5%)	7/67 (10.4%)	32/169 (18.9%)	NS

Conclusions

It has been reported that there is a poor correlation between the extent of endometriosis and pain symptoms (*Hurd WW, 1998*). We disagree with this finding, because pelvic pain, dysmenorrhoea and recurrence of disease were significantly more relevant in late-stage endometriosis respect in early stage ($P<0.05$). The results from sub-analysis examining pain scores by stage suggest that pain is less frequent in early stages. We found that dysmenorrhoea remained the most common symptom of endometriosis, scores being higher than for the other parameters. Ca125, Ca19.9 level are significantly higher in III-IV stage than in I-II so we can consider that finding of pathologic marker is suggestive to suspect endometriosis.

Our study shows that infertility was the main indication to laparoscopy for early stages. In fact, since endometriosis is often without symptoms, many gynaecologists advise laparoscopy as part of the diagnostic study for all infertile women.

We investigated factors predisposing to recurrence of pain and endometriosis and the significant findings were that the group with advanced disease and infertile women were at significantly greater risk of re-operation.

Pregnancy seems to help prevent recurrence of pain and recurrence the disease demonstrated by pelvic ultrasonography. Admission for pelvic pain and severe dysmenorrhoea was prevalent among fertile patients with endometriosis ($P<0.05$) but pain recurrence was more frequently observed in patients with endometriosis related infertility ($P<0.05$).

Although conservative surgery at laparoscopy is nowadays considered the treatment of choice for symptomatic endometriosis stage III-IV (*Cook and Rock, 1991; Adamson and Nelson, 1997*), this approach does not seem to be highly effective in preventing recurrence of the disease (*Adamson and Nelson, 1997*). Specifically, ~20% of patients have recurrences over 5 years

following complete extirpation of endometriotic lesions (*Wheeler and Malinak, 1983; Redwine, 1991*).

Symptoms of endometriosis may predict the stage of endometriosis. Painful symptoms of endometriosis may suggest diagnosis in late-stage of endometriosis, infertility in early stage.

It could be important to identify endometriosis at an early stage in the work-up for subfertility. Whereas women without endometriosis can be managed expectantly or profit from intra-uterine insemination, women with minimal or mild endometriosis may benefit from surgery (*Marcoux et al., 1997*), and women with moderate or severe endometriosis need surgery or even IVF.

Laparoscopy is an invasive approach, clinical examination is still crucial in endometriosis diagnosis.

Studies shows that pain, and mainly severe dysmenorrhoea, represents so an important symptom of endometriosis that leads to the diagnostic suspicion of disease or recurrence in more severe stages.

Calhaz-Jorge *et al.* have recently published a cohort study indicating that the presence of endometriosis can be predicted from the medical history. The prevalence of endometriosis in subfertile women is related to race, BMI, irregular menstrual cycles, intensity of menstrual flow, dysmenorrhoea, chronic pelvic pain, obstetric history, oral contraceptive use and smoking habits (*Calhaz-Jorge et al., 2004*). These data should be used in the decision to perform laparoscopy at an early stage or a later stage in the work-up for subfertility.

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