Pain Symptoms in Endometriosis: Value in Disease Prediction and Staging

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Abstract

Background: Endometriosis is a chronic condition commonly presenting with pain symptoms and infertility. Endometriosis can only be diagnosed definitively at laparoscopy. In view of the absence of reliable tools that can establish the diagnosis in a non-invasive way, there is a strong need for clinical prediction.

Objective: To investigate the value of pain symptoms in prediction and staging of endometriosis.

Setting: Obstetrics and Gynaecology department, Cairo University hospital.

Materials and Methods: This is a cross-sectional study that included 50 women scheduled for laparoscopy for various indications. All cases underwent a preoperative clinical evaluation with meticulous analysis and grading of pain symptoms (dysmenorrhoea, dyspareunia, chronic pelvic pain). On laparoscopy, endometriosis was searched for and patients were categorized into 2 groups according to the presence or absence of endometriosis. Laparoscopic staging of endometriosis was then conducted according to the Revised American Fertility Society (AFS) scoring. The primary outcome measures were the relation of pain symptoms to the presence of endometriosis and the stage of the disease. The relation of pain to disease associated adhesions was also assessed.

Results: Laparoscopy was indicated as a part of infertility work up in 41 patients. Laparoscopic diagnosis of pelvic endometriosis was seen in 28 patients (56%). The frequency of endometriosis in infertile patients was 58.5% (24 patients). Stage I endometriosis was present in 5 patients, stage II was present in 8 patients, stage III was present in 10 patients and stage IV was present in 5 patients. The comparison of the presence and severity of both dysmenorrhoea & chronic pelvic pain between cases with and without endometriosis was statistically significant (p=0.02, 0.042 respectively). The presence and severity of dyspareunia was not statistically significant in women with and without endometriosis. The sensitivity, specificity, positive predictive value, negative predictive value and accuracy of dysmenorrhoea, were 93, 36, 65, 80, 68 respectively and those of pelvic pain were 71, 45, 63, 56, 60. The presence and severity of both dysmenorrhoea and chronic pelvic pain was not statistically significant between the different stages of endometriosis. Comparison of the presence and severity of pelvic pain between patients with and without adhesions was statistically significant (p=0.03).

Conclusion: The frequency of endometriosis in infertile women is 58.5%. Dysmenorrhoea and chronic pelvic pain are frequent symptoms in patients with endometriosis but are not related to the disease stage. There is a strong association between the intensity of chronic pelvic pain and the presence of endometriosis-associated adhesions.

Key Words: Endometriosis – Revised American Fertility Society Score (R-AFS score) – Dysmenorrhea – Chronic pelvic pain – Adhesions.

Introduction

ENDOMETRIOSIS is a chronic benign gynecologic condition defined by the presence of functioning endometrial glands and stroma outside the uterine cavity and musculature [1]. It is found predominantly in women of childbearing age and is most frequently associated with chronic pelvic pain, dysmenorrhea, menorrhagia and dyspareunia. Moreover, endometriosis represents a leading cause of infertility [2]. Nevertheless, typical endometriotic lesions have also been found in asymptomatic women [3]. Therefore, although the existence of a relationship between chronic pelvic pain symptoms and endometriosis is widely accepted by gynaecologists [4], the nature of this relationship remains poorly understood. Endometriosis is detected in 2-50% of cases during laparoscopy in women with no symptoms [5,6]. At the same time, various painful pelvic symptoms are frequent in the general population: a survey carried out in the USA revealed that 90% of women suffered from dysmenorrhea, 42% from deep dyspareunia and 39% from non-menstrual pelvic pain [7].

Definitive criteria to determine when the pain is actually caused by endometriosis are therefore lacking [8] and laparoscopy remains the gold standard for establishing the diagnosis. Since, an invasive procedure is currently required to establish the diagnosis, it would be very useful to identify patients at increased risk for endometriosis prior
to laparoscopy. Diagnosing endometriosis at an early stage, is in fact an essential part of the work-up for infertility. Women with even minimal or mild endometriosis may benefit from surgery [9], whereas women without endometriosis can be managed expectantly. Alternatively, the difficulties encountered with the surgical treatment of severe forms of endometriosis have led to the proposal of initial medical treatment [10]. It seems that, the best therapeutic strategy for endometriosis in a context of pain must be determined for each patient individually. It is thus essential, before considering aggressive surgery, to determine whether or not surgical or medical therapy will resolve the pain. If the characters of the endometriotic lesions responsible for pain, are identified, this will permit useful criteria to be proposed for therapeutic management of endometriosis.

It is the aim of the present study to investigate the relation of the pain symptoms and their severity with the actual presence of endometriosis and their relation to disease stage and endometriosis-associated adhesions.

Patients and Methods

This is a cross-sectional study that included 50 patients who attended the gynaecology outpatient clinic of Cairo University Hospital between April 2009 and July 2009. All patients were admitted and subjected to laparoscopic surgery, as an investigative procedure for different indications including infertility, sterilization, missed IUD or any other indication.

All patients gave a written consent. Initial assessment was carried out by taking a detailed history with stress upon type of infertility, menstrual and coital history, type and duration of pelvic pain. The women were asked about the severity of their pain symptoms and the symptoms were graded according to a verbal rating scale modified from the one devised by Biberoglu and Behrman [11]. Chronic pelvic pain was graded as absent, mild (limited to work), moderate (requiring irregular analgesic use), or severe (demanding regular analgesic use). Dysmenorrhea was graded as absent, mild (some loss of work efficiency/or in bed part of one day) or severe (in bed for one or more days/or incapacitation). Dyspareunia was graded as absent, mild (tolerable discomfort), or severe (demanding interruption of intercourse). All subjects had a pre-operative general examination followed by pelvic examination.

Patients with a previous clinical or endoscopic diagnosis of endometriosis were excluded from the study. Other exclusion criteria were previous abdominal surgery except appendectomy, a diagnosis of gastrointestinal, urological and orthopaedic diseases with potential pain irradiation to the pelvic area and known psychiatric disturbances.

Laparoscopy was done for all patients. Systematic assessment of the pelvic organs was done to determine the presence or absence of endometriotic lesions. The diagnosis of endometriosis was mainly visual, as biopsies were not always performed. If endometriosis was diagnosed, the extent of pelvic endometriosis was determined on the basis of the 1985 revised scoring system of the American Fertility Society (R-AFS) [12]. Surgeons were not blinded as to the nature of the symptoms at the time of staging. Patients were then categorized into two groups according to the presence or absence of endometriosis.

The primary outcome measures were the relation of pain symptoms to the presence of endometriosis and the stage of the disease. The relation of pain to disease associated adhesions was also assessed.

Data were statistically described in terms of mean ± standard deviation (± SD), frequencies (number of cases) and percentages when appropriate. Comparison of quantitative variables between the study groups was done using Mann Whitney U test for independent samples. Within group comparisons were done using Wilcoxon signed rank test for paired (matched) samples. For comparing categorical data, Chi square ($\chi^2$) test was performed. Exact test was used instead when the expected frequency is less than 5. A probability value ($p$ value) less than 0.05 was considered statistically significant. All statistical calculations were done using computer programs Microsoft Excel 2003 (Microsoft Corporation, NY, USA) and SPSS (Statistical Package for the Social Science; SPSS Inc., Chicago, IL, USA) version 15 for Microsoft Windows.

Results

This study comprised 50 patients submitted to video-assisted laparoscopy due to different indications. Laparoscopy was indicated as a part of infertility work up in 41 patients (82%). Laparoscopic diagnosis of pelvic endometriosis was seen in 28 patients (56%). Endometriosis was found in 24 patients with infertility (58.5%).

The mean age of patients with endometriosis was 26.8. For patients without endometriosis, the mean age was 29.
Table (1) displays the comparison of the different pain symptoms in women with and without endometriosis.

Dysmenorrhoea was present in 40 women (80% of the study population). Comparing the presence and severity of dysmenorrhoea between the two groups of the study population revealed that amongst cases with endometriosis dysmenorrhoea was absent in only 2 cases and present in 26 cases (93%); 14 presented with mild and 12 with severe dysmenorrhoea, while in cases without endometriosis this symptom was absent in 8 cases and present in 14 cases (64%) 10 presented with mild and 4 with severe dysmenorrhoea. This comparison was statistically significant ($p=0.02$).

Chronic pelvic pain was present in 32 cases of the study population (64%). By comparing the presence and severity of chronic pelvic pain between the two study arms, we found that amongst cases diagnosed with endometriosis pelvic pain was absent in 8 subjects and present in 20 (71%); 7 of whom presented with mild pain, 7 with moderate pain and 6 with severe pain, whereas in control subjects this symptom was absent in 10 women and present in 12 (55%); 10 of whom had mild, 1 had moderate and 1 had severe pain. This comparison was again statistically significant ($p=0.04$).

Dyspareunia was present in 27 women (54% of the study population). Comparison of the presence and severity of dyspareunia between cases with and without endometriosis was not statistically significant ($p=0.23$).

Accuracy of dysmenorrhoea and pelvic pain in diagnosing endometriosis was measured. The sensitivity, specificity, positive predictive value (+ve PV), negative predictive value (−ve PV) and overall accuracy of dysmenorrhoea and chronic pelvic pain in diagnosing endometriosis is given in Table (2).

Among laparoscopically diagnosed cases with endometriosis: five cases were classified as stage I, eight as stage II, ten as stage III and five as stage IV.

Comparison of the presence and severity of dysmenorrhoea between different stages of endometriosis was not statistically significant ($p=0.16$) (Table 3). Similarly, comparison of the presence and severity of pelvic pain between different disease stages was not statistically significant ($p=0.5$) (Table 4).

Amongst cases diagnosed with endometriosis 18 (64.29%) had adhesions as well. All 18 patients were infertile by comparing the presence and severity of pelvic pain between patients with and without adhesions we observed that: amongst cases with adhesions, pelvic pain was absent in only 2 cases and present in 16 cases 2 of whom clinically presented with mild pain, 5 with moderate pain and 9 with severe pain, while in cases who had had no adhesions this symptom was absent in 6 of them and present in only 4, of whom 1 presented with mild pain, 2 with moderate pain and 1 with severe pain. This comparison was statistically significant ($p=0.038$) (Table 5).
Chronic pelvic pain:

<table>
<thead>
<tr>
<th>Stage</th>
<th>1 (40%)</th>
<th>2 (25%)</th>
<th>3 (20%)</th>
<th>4 (20%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>2</td>
<td>3</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Mild</td>
<td>0</td>
<td>2</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>Moderate</td>
<td>1</td>
<td>2</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Severe</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
</tr>
</tbody>
</table>

$p=0.5$

Table (5): Comparison of pelvic pain between endometriosis cases with and without adhesions.

<table>
<thead>
<tr>
<th>Adhesions</th>
<th>Present (n=18)</th>
<th>Absent (n=10)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic pelvic pain:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>2 (11%)</td>
<td>6 (60%)</td>
</tr>
<tr>
<td>Mild</td>
<td>2 (11%)</td>
<td>1 (10%)</td>
</tr>
<tr>
<td>Moderate</td>
<td>5 (28%)</td>
<td>2 (20%)</td>
</tr>
<tr>
<td>Severe</td>
<td>9 (50%)</td>
<td>1 (10%)</td>
</tr>
</tbody>
</table>

$p=0.038$

Discussion

Endometriosis remains a difficult clinical problem due to its variable presentation, costly diagnosis and management. The true prevalence of endometriosis in the general population cannot be determined as it is impractical to subject asymptomatic general population to a surgical procedure [13].

This study comprised 50 patients submitted to video-assisted laparoscopy due to different indications. Laparoscopic diagnosis of pelvic endometriosis was seen in 28 patients (56%). The present study found the frequency of endometriosis in infertile patients to be 58.5%. This is in agreement with Hemmings et al. [14] who reported an incidence of 55% and in contrast to Mehmud et al. [15] who reported a frequency of 24% in infertile women and G. Szendei et al. [16] who reported an incidence of 21%. Such a discrepancy may be attributed to the fact that >80% (n=41) of the patients included in this study were infertile (selection bias). Besides, in most studies, the diagnosis of endometriosis is based solely on visual criteria. There is consequently a risk that, depending on the indication for the laparoscopy, the surgeon will over- or under-diagnose endometriosis [17]. Indeed, visual diagnosis of endometriosis may fail in patients with subtle or atypical forms of peritoneal endometriosis [17,18] or in some patients with DIE (deeply infiltrating endometriosis) not associated with peritoneal or ovarian lesions. Use of precise and standardized macroscopic criteria may help to make the visual diagnosis of endometriosis more reliable [19]. Conversely, some authors recommend histological confirmation of all visible lesions [17]. In a study, visual diagnosis was confirmed by histology and only 54% of the excised lesions revealed endometriotic tissue [20]. These results emphasize the need for histological confirmation to obtain a diagnosis of endometriosis. Yet, such a criterion may be dependent upon the surgeon’s ability to excise lesions as well as the pathologist’s interpretation of the histologic finding, parameters that may vary tremendously. Furthermore, the clinical impact of such findings remains a matter of debate [14,21].

Dysmenorrhoea is the symptom most frequently reported by women with endometriosis [22]. In our study, we found that the frequency of dysmenorrhoea was 1.5 times higher in women with endometriosis than in controls. Amongst women with mild dysmenorrhoea the incidence of endometriosis was slightly increased. However, subjects with severe dysmenorrhoea had a 3 fold increased frequency of endometriosis. Previous studies have shown that dysmenorrhoea is more frequent in women with endometriosis than in the controls [5,23-25]. In the studies that used pain scales to assess the severity of dysmenorrhoea [26,27], the dysmenorrhoea scores were higher for women presenting with endometriosis than in the controls. C. Calhaz-Jorge et al. [28] reported that moderate and severe dysmenorrhoea was associated with a 2-5 fold increased risk for endometriosis. The causal association between severe dysmenorrhoea and endometriosis may be related to recurrent cyclic micro-bleeding in the implants but independent of the macroscopic type of the lesions or their anatomical locations [8,29]. Alternatively, dysmenorrhoea could be due to the cause of the endometriosis, rather than a consequence of existing lesions. This hypothesis has arisen from epidemiological studies addressing the aetiological aspect [30]. Endometriosis is indeed encouraged by the existence of obstructive pathologies affecting the genital tract [31] or by retrograde menstruation [32] both of which are known to cause severe dysmenorrhoea.

On the other hand, we found that the presence and severity of dysmenorrhoea was not statistically significant between the different stages of endometriosis ($p=0.16$). No relation between the severity of dysmenorrhoea and R-AFS scoring
could be detected by; Fedele et al. [26]; Vercellini et al. [29]; Chapron et al. [33] and Mehmud et al. [15]. In contrast, Muzii et al. [27] and Milingos et al. [34] detected such a relation. C. Calhaz-Jorge et al. [28] observed that dysmenorrhoea was an important risk indicator for the presence of moderate to severe endometriosis (stage III and IV).

Unlike the case with dysmenorrhoea, we did not find the presence and severity of dyspareunia to be statistically significant between cases with and without endometriosis. This is in line with the data reported by Calhaz-Jorge et al. [28]. In contrast, Ballard et al. [25] reported that women with endometriosis have a significantly higher chance of experiencing symptoms related to sexual intercourse (including dyspareunia) than those without endometriosis.

Chronic pelvic pain (CPP) is pain of the lower abdomen or pelvis, of at least 6 months’ duration, occurring continuously or intermittently, which is not associated exclusively with menstruation or sexual intercourse [35]. The relationship between chronic pelvic pain and endometriosis is unclear because painful symptoms are frequent in women without this pathology and because asymptomatic forms of endometriosis exist. In this study, the frequency of endometriosis was 6-7 fold higher in cases with moderate to severe pelvic pain. Women with endometriosis have been reported to have increased risk of pelvic pain [25]. However, we did not find the presence and severity of chronic pelvic pain to be statistically significant between the different stages of endometriosis. This is in agreement with the data reported by G. Szendei et al. [16] and Vercillini et al. [21]. On the other hand, Calhaz-Jorge et al. [28] and Mehmud et al. [15] found a significant correlation between pelvic pain and R-AFS score.

It seems that the pain symptoms and the laparoscopic findings do not always correlate. The R-AFS score is primarily a staging instrument for infertility. Extensive superficial endometriosis and deep invasive peritoneal nodules may constitute advanced disease with profound clinical presentation and yet have R-AFS score of only mild disease. This may be the reason that many studies have found conflicting results on co-relation between symptoms and stages of disease [15].

Adhesions, which are often associated with endometriosis [36], can themselves also play a role in painful symptoms [37]. Besides, adhesions constitute a major cause of infertility in patients with endometriosis. We thus investigated the relation of pelvic pain to the presence of adhesions in endometriosis cases. Eighty nine percent of endometriosis patients with adhesions experienced pelvic pain and in half of them this pain was severe. This is in contrast to the fact that only 40% of patients without adhesions complained of pelvic pain which was mainly mild to moderate. It seems that increasing severity of pelvic pain is associated with the presence of adhesions. In fact, one histological study on structural features of adhesions in women with endometriosis has shown that periovarian adhesions contain endometrial and inflammatory cells which may generate painful symptoms [38]. In DIE, apart from glandular tissue, fibrosis can also affect the nerves in the sub-peritoneal pelvic space and thus may play an important role in the genesis of the pain [39]. The fact that pelvic cicatrization constitutes a major source of chronic pelvic pain has been proved by studies that noted improvement of the pain symptoms following surgical (adhesiolysis) and medical loosening of adhesions [40,41]. Indeed, the real impact of endometriosis on pain can only be assessed if the endometriosis has been completely treated [8]. However, Parazzini et al. [42] failed to detect a relation between endometriosis-associated adhesions and pelvic pain.

This study, however, is not without limitations. Our sample size was small and the diagnosis of endometriosis was visual and not always documented with histopathology.

Our data indicate that both dysmenorrhoea and chronic pelvic pain are frequent symptoms in patients with endometriosis but are not related to the disease stage. Furthermore, the detected accuracy of these symptoms in disease prediction suggests that their individual use may not be clinically reliable. Together with analysis of pain symptoms, simultaneous evaluation of other risk factors may be useful for the preoperative diagnosis of endometriosis e.g. in the context of infertility, the presence of such symptoms could encourage laparoscopic investigation [14,24]. The strong association between the severity of pelvic pain and endometriosis-associated adhesions implies the anticipation of possible intraoperative difficulties, and hence the consideration of initial medical therapy. Future studies with greater sample size are warranted to confirm this study results.

References


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