

Frequency of endometriosis among infertile women and association of clinical signs and symptoms with the Laparoscopic staging of Endometriosis

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Abstract

Objective: The study aimed to determine the frequency of endometriosis in women who underwent diagnostic laparoscopy for evaluation of infertility and the association of clinical, ultrasonographic and laparoscopic findings of endometriosis with the laparoscopic stages of the disease.

Method: It was a retrospective study of women presenting to gynaecologic clinics of the Aga Khan University Hospital from January 1999 to December 2005 with primary complaint of primary or secondary infertility and were diagnosed with endometriosis through laparoscopy. Relevant demographic and clinical information was entered and analyzed in SPSS version 14.0.

Results: The frequency of endometriosis in women with primary complaint of infertility was found to be 16.8%. Statistically significant associations were found between staging of the disease and thin built ($p=0.007$) and restricted uterine mobility on pelvic examination ($p=0.035$). The patients' ultrasound and laparoscopic examination showed significant association with staging of the disease with the presence of cysts on ultrasound ($p\text{-value} < 0.0001$) and adhesions on laparoscopy ($p\text{ value} < 0.00001$).

Conclusion: The variability of the definition and inconsistency in diagnostic methods makes the prevalence of endometriosis difficult to determine and we might underestimate the true burden of the disease. Most of the signs and symptoms of endometriosis do not correlate with the severity (staging) of the disease. Hence, Laparoscopy remains the gold standard for diagnosis as well as staging of endometriosis (JPMA 59:30; 2009).

Introduction

Endometriosis is a common disease affecting women of reproductive age with a very diverse range of presentations that include pelvic pain, dysmenorrhoea, dyspareunia or subfertility.¹ Prevalence of endometriosis in general population is difficult to determine and is seen to affect approximately 33% women suffering from chronic pelvic pain and in 10% of adolescents and young adults with severe dysmenorrhea, largely estimated by laparoscopic visualization of the pelvic organs.^{2,3} However, the frequency in women presenting with infertility has been reported to vary between 20-50%.^{4,5}

Apart from causing personal discomfort and a variety of complaints affecting the young age group, endometriosis adds a huge economic burden being diagnosed by a surgical procedure and with complications like infertility, the management requires substantial costs.⁶ Additionally, it is a source of psychological stress not only on the woman with a poor health related quality of life but also on the male partner.^{7,8}

A definitive diagnosis of endometriosis can only be made via laparoscopy and is considered as the gold standard.⁹ Scoring systems available for disease severity staging are well established but have been seen to correlate variably with clinical presentations or infertility.¹⁰ The Revised American Fertility Society (AFS) scoring system is widely used but does not reflect symptom severity with accuracy, fecundity in infertile women with endometriosis or worse outcomes in terms of quality of life.^{11,12} Yet, it remains an imperative way of classifying the anatomical extent of the disease. Any possible association between this widely employed system and clinical or demographic variables can prove very beneficial to the physicians dealing with subfertility in women.

Data from Pakistan regarding the epidemiology of this disease is very scarce and cases are underreported.¹³ In a recent audit from a tertiary care hospital, endometriosis was reported as an uncommon morbidity affecting women.¹⁴ A recently conducted study on 50 patients over a period of two years from a local tertiary centre, showed 24% frequency of endometriosis in infertile women. A strong association of pelvic pain and dyspareunia with laparoscopic staging was observed.¹⁵

Considering the current burden of endometriosis, the diagnostic challenges faced by gynaecologists and the paucity of local data, the study aimed to calculate the frequency of endometriosis in women who underwent diagnostic laparoscopy for evaluation of primary/secondary infertility and to establish the association of clinical presentations of endometriosis with the laparoscopic stage of the disease.

Methods

This descriptive retrospective study was conducted at the department of Obstetrics and Gynaecology, Aga Khan University Hospital, Karachi, Pakistan for the period from January 1999 to December 2005. Medical records of all women presenting to gynaecologic clinics with primary complain of primary or secondary infertility and were subjected to diagnostic laparoscopy and dye test and were diagnosed to have endometriosis as the cause of infertility were included in the study. Women who had concomitant findings of other associated pelvic diseases like pelvic inflammatory disease and adhesions due to previous surgery or infection were excluded.

Medical records of all subjects were reviewed for demographic and clinical information. Extracted clinical information was divided into three categories: 1) Presenting signs and symptoms with duration for which the patient had been actively trying to conceive, menstrual cycles, menstrual flow, dysmenorrhea, dyspareunia, chronic pelvic pain, urinary symptoms, history of previous surgery and previous treatment. 2) Physical examination findings including built of the patient, signs of hyperandrogenism, masses per abdomen and pelvic examination findings. 3) Ultrasound and laparoscopic findings.

Laparoscopic staging was based on the Revised American Fertility Society (AFS) scoring for endometriosis which divided the findings into four categories of severity. 1) Stage I (minimal) involved a few endometrial implants, most often in the cul-de-sac. 2) Stage II (mild) comprised of endometrial implants affecting one or both ovaries. 3) Stage III (moderate) had moderate levels of endometriosis with implants in several reproductive areas and in one or both ovaries. 4) Stage IV (severe) had widespread endometriosis implants throughout the pelvic area.

Data was entered and analyzed in SPSS version 14.0. Frequency of endometriosis based on laparoscopic diagnosis was calculated. Statistical associations using odds ratios (OR) were determined among the variables of clinical information with presence of disease and disease staging using the Chi-square test and univariate analysis using a significance level of less than 0.05.

Results

Out of all women presenting with complaints of primary/secondary infertility, a total of 796 women eventually underwent diagnostic laparoscopy and dye test. Of these, a total of 134 (16.8%) women were found to have endometriosis based on laparoscopic evidence. The mean age of patients was 29 ± 5.3 years (range: 16-47 years) and the majority of patients fell between ages 25 and 33 years.

The majority of patients in the study presented with

Table 1: Association of clinical presentations of endometriosis with staging.

| Clinical Signs and Symptoms | Stage I | | Stage II | | Stage III | | Stage IV | | p-value |
|------------------------------|-----------|------|-----------|------|-----------|------|----------|-------|---------|
| | N (%) | OR | N (%) | OR | N (%) | OR | N (%) | OR | |
| Menstrual Irregularity | 6 (8.7) | 1.00 | 5 (8.7) | 0.99 | 0 (0.0) | 0.00 | 1 (6.3) | 0.70 | 0.28 |
| Heavy Menstrual flow | 9 (13.0) | 1.00 | 12 (20.6) | 1.74 | 3 (10.3) | 0.77 | 1 (6.3) | 0.44 | 0.52 |
| Scant Menstrual flow | 8 (11.6) | 1.00 | 5 (8.6) | 0.72 | 0 (0.0) | 0.00 | 5 (31.3) | 3.47 | 0.46 |
| Mild Dysmenorrhea | 14 (20.2) | 1.00 | 14 (24.1) | 1.26 | 8 (27.6) | 1.25 | 1 (6.3) | 0.34 | 0.76 |
| Moderate Dysmenorrhea | 15 (21.7) | 1.00 | 9 (15.5) | 0.76 | 2 (6.8) | 0.29 | 5 (31.3) | 1.60 | 0.83 |
| Severe Dysmenorrhea | 16 (23.1) | 1.00 | 16 (27.5) | 1.26 | 8 (27.6) | 1.09 | 5 (31.3) | 1.50 | 0.62 |
| Deep Dyspareunia | 19 (27.5) | 1.00 | 15 (25.8) | 0.87 | 5 (17.2) | 0.47 | 2 (12.5) | 0.35 | 0.09 |
| Superficial Dyspareunia | 6 (8.7) | 1.00 | 4 (9.0) | 0.74 | 0 (0.0) | 0.00 | 1 (6.3) | 0.55 | 0.18 |
| Mild Chronic Pelvic Pain | 9 (13.0) | 1.00 | 8 (13.7) | 0.96 | 2 (6.9) | 0.46 | 0 (0.0) | 0.00 | 0.15 |
| Moderate Chronic Pelvic Pain | 10 (14.4) | 1.00 | 8 (13.7) | 0.86 | 5 (17.2) | 1.02 | 2 (12.5) | 1.02 | 0.97 |
| Severe Chronic Pelvic Pain | 9 (13.0) | 1.00 | 4 (7.0) | 0.48 | 2 (7.0) | 0.46 | 6 (37.0) | 3.42 | 0.23 |
| Urinary Complaints | 6 (50.0) | 1.00 | 2 (16.7) | 0.38 | 1 (8.3) | 0.37 | 3 (25.0) | 2.42 | 0.63 |
| Obesity | 16 (23.1) | 1.00 | 12 (20.6) | 0.71 | 7 (24.1) | 0.83 | 1 (6.3) | 0.17 | 0.13 |
| Overweight | 6 (8.7) | 1.00 | 4 (7.0) | 0.63 | 2 (7.0) | 0.63 | 2 (12.5) | 0.92 | 0.76 |
| Thin Built | 11 (16.0) | 1.00 | 4 (7.0) | 0.34 | 1 (3.4) | 0.17 | 0 (0.0) | 0.00 | <0.01 |
| Hyper androgenism | 7 (70.0) | 1.00 | 2 (20.0) | 0.32 | 1 (10.0) | 0.32 | 0 (0.0) | 0.00 | 0.06 |
| Palpation of Abdominal Mass | 3 (75.0) | 1.00 | 0 (0.0) | 0.00 | 1 (25.0) | 0.79 | 0 (0.0) | 0.00 | 0.34 |
| Tenderness | 8 (11.6) | 1.00 | 7 (12.1) | 1.25 | 6 (20.7) | 1.99 | 1 (6.3) | 0.74 | 0.56 |
| Nodularity | 4 (5.8) | 1.00 | 3 (5.2) | 1.07 | 3 (10.3) | 1.99 | 0 (0.0) | 0.00 | 0.93 |
| Fullness | 7 (10.1) | 1.00 | 8 (13.8) | 1.64 | 1 (3.4) | 0.38 | 3 (18.8) | 2.52 | 0.59 |
| Restricted Uterine Mobility | 1 (1.4) | 1.00 | 6 (10.3) | 8.59 | 2 (6.9) | 3.53 | 3 (18.8) | 17.67 | 0.03 |

primary infertility (74.6%). Complaints were noted in addition to infertility in 22.1% cases with chronic pelvic pain being the most frequent (42%), followed by dysmenorrhea (36.8%). Other complaints included menstrual irregularity (11.0%), oligomenorrhea (5.3%), lower back pain (5.3%), dyspareunia (2.6%) and other unusual complaints (5.3%). For patients who were actively trying to conceive ranged from 6 months to 24 years. Most of the patients had regular menstrual cycles (8.9%) while 20.9% women had a previous history of surgery.

Frequency of each stage of endometriosis were found to be 69 (40.1%) for stage I, 58 (33.7%) for stage II, 29 (16.9%) for stage III and 16 (9.3%) for stage IV.

Association between clinical presentation of endometriosis and staging via diagnostic laparoscopy and dye test has been summarized in Table 1. Statistically significant association was seen between stages of the disease and thin built (p=0.007) and restricted uterine mobility on pelvic examination (p=0.035).

Statistical associations determined between ultrasound and diagnostic laparoscopy and dye test findings and the staging of endometriosis are shown in Table 2. All the ultrasound and laparoscopic examination findings showed a significant association with staging of the disease. The strongest association was found with the presence of cysts on ultrasound (p- < 0.0001).

Table 2: Association of ultrasonographic and laparoscopic findings with staging of endometriosis.

| Ultrasound and Laparoscopic findings | Stage I | | Stage II | | Stage III | | Stage IV | | p-value |
|--------------------------------------|-----------|------|-----------|------|-----------|-------|------------|------|---------|
| | N (%) | OR | N (%) | OR | N (%) | OR | N (%) | OR | |
| Abnormal ultrasound findings | 34 (49.2) | 1.00 | 35 (60.3) | 1.57 | 22 (76.0) | 3.24 | 14 (87.5) | 7.21 | <0.001 |
| Cysts on Ultrasound | 15 (21.7) | 1.00 | 27 (46.5) | 3.14 | 16 (55.1) | 4.43 | 11 (68.7) | 7.92 | <0.0001 |
| Internal Echos | 6 (8.7) | 1.00 | 16 (27.5) | 4.00 | 9 (31.0) | 4.72 | 6 (37.5) | 6.30 | 0.001 |
| Endometriotic lesion on laparoscopy | 57 (82.6) | 1.00 | 53 (91.3) | 1.11 | 24 (82.7) | 1.00 | 13 (81.3) | 0.98 | 0.001 |
| Endometrioma on laparoscopy | 19 (27.5) | 1.00 | 31 (91.3) | 1.94 | 18 (82.7) | 2.25 | 11 (81.3) | 2.50 | 0.02 |
| Blocked tubes on laparoscopy | 18 (26.0) | 1.00 | 15 (26.0) | 0.99 | 10 (34.5) | 1.49 | 10 (62.5) | 4.72 | 0.01 |
| Adhesions on laparoscopy | 17 (24.6) | 1.00 | 39 (67.2) | 6.28 | 28 (96.5) | 85.65 | 16 (100.0) | N/A | <0.001 |

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.

The present study found the frequency of endometriosis in infertile patients to be 16.8% which is consistent with findings of various other studies done all over the globe.^{5,16-18} However, when compared to Mehmud et al. (2007), this estimate is modest.¹⁵ This difference could be attributed to a larger number of patients included and a longer duration of our study.

The mean age of 29 ± 5.3 years at presentation, the low incidence of the disease on either extreme of ages and higher prevalence of endometriosis in women of reproductive age is also in accordance with other studies.^{5,17,18} The highest frequency of endometriosis at the time of presentation was in stage-I of the disease suggesting an early presentation in majority of the cases. It is also indicated that an inverse association between severity of signs and symptoms and progressive staging of endometriosis exists, which is consistent with a study done by Vercillini et al.¹⁹

Three-fourth of the study cases presented with primary infertility and only a quarter with secondary infertility, a finding similar to other descriptive studies.²⁰ A significant number of patients in addition to infertility had other signs and symptoms consistent with endometriosis which included chronic pelvic pain, dysmenorrhea, menstrual irregularities and dyspareunia. This suggests that the patients coming to the clinic with infertility, added symptoms can prove a good guide to the diagnosis of endometriosis.

No statistically significant association was found between majority of clinical signs, symptoms and physical examination findings and staging of endometriosis except thin built and restricted uterine mobility. Recently, an association between presence of endometriosis and a low body mass index (BMI) done by European and western studies suggested a positive association.^{21,22} However, its association with severity based on staging has not been found in any other existing studies.

Both the clinical signs and symptoms of endometriosis may be nonexistent, minimal, or marked as a function of location and total mass of the disease. There are clinical signs that can increase the index of suspicion in patients with symptoms of endometriosis: thickness and feeling of nodularity in the posterior pelvic area; pain and tenderness during pelvic examination; fixation or relative

decreased mobility in the tubes or ovaries due to the presence of pelvic adhesions; presence of a uterus tilted backward and feeling of a pelvic mass. However, none of these clinical signs are decisive of the presence of endometriosis and final diagnosis can only be confirmed by laparoscopy.

The study assessed adequacy of ultrasound as a diagnostic modality for endometriosis. This method has been reviewed²³ but the rationale behind assessing in the study population in this study that was a large number of patients had financial constraints for laparoscopy. Significant associations were seen between abnormal ultrasound findings and the presence of endometriosis in this study. Sensitivity of ultrasound in the screening and diagnosis of endometriosis increases in direct relation with the increasing stage of the disease as shown by the increasing odds ratio for each progressive stage. This finding is consistent with a study conducted by Exacoustos et al.²⁴ Furthermore, significant associations were also seen between specific ultrasound findings; for example, cysts and internal echoes and staging of endometriosis. Therefore, ultrasound findings could have been a better screening as well as diagnostic marker for endometriosis but despite having a high sensitivity for endometriomas which usually gives a ground glass appearance, ultrasound fails to have a good specificity to prove as an efficient diagnostic method.

Strong associations were found between stage of the disease and laparoscopic findings like presence of endometrioma, pelvic adhesions and blocked tubes. Hence laparoscopic surgery remains the most definitive and accurate means of diagnosing and staging endometriosis as recommended by Kennedy S et al.⁹

Lack of positive association of clinical symptoms with staging is in contrast with Mehmud et al. (2007),¹⁵ while association of laparoscopic and ultrasonographic findings is a feature not studied before. Positive association of thin built and restricted uterine mobility is a novel finding this study.

Conclusion

Endometriosis with infertility is not an uncommon disease in women. Clinical symptoms and most clinical signs do not correlate with laparoscopic stage of the disease. Therefore it is difficult to predict stage or prognosticate the outcome based on clinical findings alone. Findings on laparoscopy as well as ultrasound have a significant association with the stage of disease. However, ultrasound remains a sound screening modality but cannot be used for definitive diagnosis and laparoscopy remains the preferred technique for diagnosis as well as staging of endometriosis.

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