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Endometriosis in infertility; prevalence, clinical profile and diagnosis

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Abstract
Objective: To find out the prevalence of endometriosis amongst infertile women, the demographic & clinical characteristics associated with endometriosis.
Method: A prospective study conducted at the department of Obstetrics and Gynaecology, Index Medical college hospital &RC, Indore, M.P. From Nov 2015 to Oct 2016. All patients of primary or secondary infertility subjected to diagnostic hystero laparoscopy and chromopertubation test that were diagnosed to have endometriosis were included in the study. Women with PID, adhesions due to previous surgeries or infections were excluded. History, Physical examination. USG, Laparoscopy done, patient categorised and then statistically analysed. Chi Square test and Fisher Exact test has been performed to carry out P-value for categorical data. P-value <0.05 shows statistically significant difference.
Result: Out of 204 patients with infertility 90 (44.11%) patients had laparoscopic evidence of endometriosis. 63 (70.0%) had primary infertility and 27 (30.0%) had secondary infertility. The mean age of patients was 27± 3.6 years. Apart from infertility, the commonest complaints were dysmenorrhea (45.55%) followed by menstrual irregularity (18.88%), menorrhagia (12.2%), dyspareunia (8.8%) and chronic pelvic pain (5.5%). Abnormal USG findings were seen in 14.44% of cases. Presence of cysts/ endometrioma with ground glass appearance was seen in 13.33% of cases. Based on Revised AFS score (1985); STAGE 1 endometriosis was seen in 58 patients (66.44%); STAGE II in 19 patients (21.11%); STAGE III in 7 patients (7.77%); and STAGE IV in 6 patients (6.66%).
Conclusion: Endometriosis in infertile females is not uncommon & is increasingly being detected because of greater use of diagnostic modalities like laparoscopy in evaluation of infertility. Though most females are asymptomatic, dysmenorrhoea, chronic pelvic pain, restricted uterine mobility & adnexal tenderness raises the suspicion of endometriosis. Ultrasound had limited value for diagnosing and determining extent of endometriosis. Laparoscopy remains the gold standard for diagnosing and staging endometriosis.

Keywords: endometriosis, infertility, laparoscopy

1. Introduction

Endometriosis is defined as the presence of endometrial like tissue (glands and stroma) outside the uterus, which induces a chronic inflammatory reaction, scar tissue, and adhesions that may distort a woman's pelvic anatomy .Endometriosis is primarily found in young women, but its occurrence is not related to ethnic or social group distinctions. Patients with endometriosis mainly complain of pelvic pain, dysmenorrhoea, and dyspareunia. The associated symptoms can impact the patient's general physical, mental, and social well-being [1].

There is a wide spectrum of symptom severity, and the stage of endometriosis on laparoscopy correlates poorly with the extent and severity of pain. Some patients with minimal disease have debilitating pain, while other women with severe stage III–IV disease are asymptomatic [2].

It is postulated that women with endometriosis have increased amount of peritoneal fluid associated with increased peritoneal concentrations of prostaglandins, proteases and cytokines including inflammatory cytokines such as IL 1, IL 6 and TNF alpha, and angiogenic cytokines like IL 8 and VEGF [3]. These alterations have an adverse effect on oocyte, sperm, embryo and fallopian tube function [4].

Endometriosis is one of the most common conditions encountered in gynaecological practice. Classic studies have suggested that 25 to 50% of infertile women have endometriosis and 30-50% of women with endometriosis are infertile [5]. The true prevalence of endometriosis is difficult to quantify as very wide ranges have been reported in literature [6, 7]. Endometriosis is found in 45% - 82% of women with chronic pelvic pain and in 2.1%-78% of infertile women [8, 9]. Nevertheless, its prevalence depends on patient profile and diagnostic tools utilized. However, its prevalence is 6-21 times higher in infertile as opposed to fertile women [10, 11].

The role of Ultrasound in the clinical diagnosis of endometriosis is of limited value as it lacks resolution for visualizing adhesions and superficial peritoneal/ovarian implants. Hence laparoscopy is the mainstay in the diagnosis as it provides a visual proof of the minute endometriosis lesions and helps in staging of the disease [12].

Transvaginal ultrasound, MRI or transrectal ultrasound can help visualize endometriomas and deeply infiltrating endometriosis. Transvaginal ultrasound is likely superior to transrectal ultrasound in the majority of cases. MRI is particularly helpful in ultrasonographically-indeterminate

pelvic masses and diagnosing endometriosis of the ureters, bladder, and rectosigmoid. Imaging is inadequate for detection of pelvic adhesions or superficial peritoneal implants. No individual serum marker has yet been shown to be both sensitive and specific for diagnosis or monitoring of endometriosis [2].

For patients with pain in whom endometriosis is suspected, empirical Non-steroidal anti-inflammatory drugs (NSAIDs) or hormonal treatment (such as continuous oral contraceptive pills) is usually the first option. Patients with pain refractory to these treatments may benefit from diagnostic and operative laparoscopy, ideally with biopsy of at least one lesion to confirm the diagnosis. There are many options for the management of infertility (without pain) associated with minimal or mild endometriosis; these range from laparoscopic diagnosis and laparoscopic treatment to direct referral to an infertility center [2].

2. Materials and Methods

A prospective study conducted at the department of Obstetrics and Gynaecology, Index Medical college hospital & RC, Indore, M.P. From Nov 2015 to Oct 2016. After Clearance from Institutional Ethics Committee. This study aimed to determine the demographic, clinical and laparoscopic characterization of infertile women with endometriosis in addition to type of treatment administered.

Inclusion Criteria

All patients of primary or secondary infertility subjected to diagnostic hystero laparoscopy and chromopertubation test who were diagnosed to have endometriosis were included in the study.

Exclusion Criteria: Women with PID, adhesions due to previous surgeries or infections were excluded.

All patients included in the study were analysed with respect to the following characteristics.

- **Clinical Characteristics:** Points noted were age, type of infertility, duration of infertility, menstrual cycle – frequency and flow, association of symptoms like dysmenorrhoea, dyspareunia, chronic pelvic pain, urinary symptoms & their correlation to stage of endometriosis.
- **Physical Examination:** Findings were analysed with respect to presence of abdominal/adnexal masses, mobility of uterus and presence of adnexal tenderness.
- **USG FINDING:** Particularly to note endometriomas and probe tenderness.
- **Laparoscopic Findings:** Endometriotic lesions which were noted varied from dark blue, powder-burn black, red, white, yellow, brown or non-pigmented lesions. The size, depth and location of these lesions were noted to grade the severity of endometriosis. This laparoscopic staging was based on the revised AFS scoring [13] which categorized the finding into 4 stages.

Stage I

(Minimal) involved a few endometrial implants, most often in the cul de sac.

Stage II

(Mild) comprised of endometrial implants affecting one or both ovaries.

Stage II

(Moderate) involved moderate levels of endometriosis with implants in several reproductive areas & in one or both ovaries.

Stage IV

(Severe) involved wide spread endometriosis implants through the pelvic area.

2.1 Statistical Analysis

All collected data was entered into the SPSS version 20. Categorical data are expressed in frequency or percentage. Chi Square test and Fisher Exact test has been performed to carry out P-value for categorical data. P-value <0.05 shows statistically significant difference.

3. Results

A total of 204 patients with infertility were subjected to diagnostic hysterolaparoscopy & chromopertubation test during the period from November 2015 to October 2016. Of these, 90 (44.11%) patients had laparoscopic evidence of endometriosis. Sixty three patients (70.0%) had primary infertility and twenty seven patients (30.0%) had secondary infertility. The mean age of patients was 27± 3.6 years (Range: 18-39 years). Amongst the 90 patients studied, apart from infertility, the commonest complaints were dysmenorrhea (45.55%) followed by menstrual irregularity (18.88%), menorrhagia (12.2%), dyspareunia (8.8%) and chronic pelvic pain (5.5%). However, more than 50% of cases were asymptomatic. There was a statistical significant association between adnexal tenderness and restricted uterine mobility with staging of the disease ($p<0.01$). Abnormal USG findings were seen in 14.44% of cases. Presence of cysts/ endometrioma with ground glass appearance was seen in 13.33% of cases. This particular finding was found to be clinically significant as sonograpically detected endometriomas were confirmed laparoscopically. All 5 (100%) cases of stage IV endometriosis in our series had endometriomas in one or both ovaries. Based on Revised AFS score (1985); STAGE 1 endometriosis was seen in 58 patients (66.44%); STAGE II endometriosis in 19 patients (21.11%); STAGE III endometriosis in 7 patients (7.77%); and STAGE IV endometriosis in 6 patients (6.66%). [Table/Fig-1] shows the association of clinical signs and symptoms with stage of disease. [Table/Fig-2] shows the association of laparoscopy & USG findings with stage of disease. In our study, there was a definite correlation of USG and lap evidence of endometriosis with stage of disease. Although most patients of endometriosis in our study were asymptomatic, the presence of dysmenorrhoea, dyspareunia and chronic pelvic pain are clinically significant and should always anticipate the presence of subtle endometriosis in these patients. All patients of minimal and mild endometriosis were treated by fulguration /cauterization followed by three doses of GnRH agonist. Moderate and severe endometriosis were treated accordingly depending on laparoscopic findings i.e. Adhesiolysis, endometrioma cyst wall excision. This was followed by three doses of leupragon (3.75mg) at an interval of 28 days.

Table 1: Association of clinical presentations of endometriosis with staging

Clinical signs and symptoms	Stage 1 (of 58)	Stage 2 (of 19)	Stage 3 (of 7)	Stage 4 (of 6)	p-value
	N (%)	N (%)	N (%)	N (%)	
Menstrual Irregularity	12 (20.68%)	1 (5.26%)	1 (14.28%)	2 (33.33%)	0.40 (NS)
Dysmenorrhea	21(36.20%)	12 (63.15%)	4 (57.14%)	4(66.66%)	0.01 *
Dyspareunia	1 (1.72%)	2 (10.52%)	2(28.57%)	3 (50.00%)	<0.01 *
Chronic Pelvic pain	0 (0.00%)	1 (5.26%)	1 (14.28%)	3 (50.00%)	<0.01 *
Tenderness	1 (1.72%)	2 (10.52%)	4 (57.14%)	6 (100%)	<0.01 *
Adnexal mass	1 (1.72%)	1 (5.26%)	1 (14.28%)	4 (66.66%)	<0.01 *
Restricted Mobility	1 (1.72%)	2 (10.52%)	3 (42.85%)	5 (83.33%)	<0.01 *

(p <0.05 considered to be statistically significant difference Here, NS represents Non-Significant difference between these groups.)

Table 2: Association of ultrasonographic & laparoscopic findings with staging of endometriosis

Laparoscopic findings	Stage 1 (of 58)	Stage 2 (of 19)	Stage 3 (of 7)	Stage 4 (of 6)	p-value
	N (%)	N (%)	N (%)	N (%)	
Blocked tubes on laparoscopy	7(12.06%)	5 (26.31%)	3 (42.86%)	5 (83.33%)	<0.01 *
Endometrioma on Ultrasonography	0 (0.00%)	4 (21.05%)	3 (42.86%)	6 (100%)	<0.01 *
Endometrioma on laparoscopy	0 (0.00%)	1 (5.26%)	2 (28.57%)	6 (100%)	<0.01 *

(p <0.05 considered to be statistically significant difference Here, NS represents Non-Significant difference between these groups.)

4. Discussion

Endometriosis affects 2.5-3.3 percent of women of reproductive age [14] and is diagnosed in 20-68 percent of the women studied for infertility [15]. According to Tsuzi *et al*, worldwide endometriosis has been found up to 63% [16]. The true incidence of endometriosis is difficult to establish since endoscopy or laparotomy is required for a definitive diagnosis and the disease may still undoubtedly exist in patients who are asymptomatic. It is generally believed, the disease is relatively less common in India, Pakistan, Iran, countries of Middle East and black Africa [17]. Our study demonstrates a very high incidence of 44.11%. Therefore, we feel that the clinical impression of low incidence in Asian and black women may have been due to limited medical and diagnostic facilities available to these women. In our study, every alternative patient had evidence of endometriosis. The commonest sites of endometriosis were the uterosacral ligament (28 cases), Pelvic wall (24 cases) Pouch of Douglas (16 cases), ovarian fossa (13 cases), and endometrioma (9 cases). The other rare sites were uterovesical fold of peritoneum, bowel, round ligament, rectovaginal septum and diaphragm. One interesting point which we noted was that left side was more involved than the right though it was not found to the statistically significant. The mean age of patients was 27 ± 3.6years. This is in comparison to other studies which quote low prevalence of endometriosis in either extremes of age & high prevalence in women of reproductive age[18]. Seventy percent of cases were cases of primary infertility & 30 % of case was of secondary infertility. This finding is similar to other descriptive studies [19].

Commonest symptoms encountered in our study were dysmenorrhea (45.55%); irregular cycles (18.88%); menorrhagia (12%); dyspareunia (8.8%) and chronic pelvic pain (5.5%). However, other rare complaints which were noted were urinary complaints like dysurea and difficulty in defecation in one case of stage 4 endometriosis with frozen pelvis. Statistical significant association of symptoms and signs like dyspareunia, chronic pelvic pain, restricted uterine mobility and adenexal tenderness with staging of disease was noted. However majority of the cases (57.8%) were asymptomatic. We feel that, though none of clinical signs are decisive of endometriosis, positive clinical findings like tenderness on clinical examination, fixation or relatively decreased mobility of uterus or a fixed retroverted uterus or a pelvic mass should always raise the index of suspicion towards endometriosis. The final diagnosis is always by laparoscopy, the gold standard in diagnosis of endometriosis, preferably with histological confirmation [20].

Transvaginal ultrasound lacks adequate resolution for visualizing adhesions and superficial peritoneal/ovarian implants. But when the presence of endometrioma with a typical ground glass appearance is identified, it usually indicates that moderate to severe endometriosis is present. In our study, there was significant correlation between presence of cysts/endometriomas with ground glass appearance & severity of disease. Out of the 13 diagnosed cases of endometrioma by transvaginal USG, 6 cases were confirmed to have stage III and IV endometriosis on laparoscopy according to R-AFS score (1985).

Majority of the cases of our study had STAGE I endometriosis i.e. 58 cases (64.4%). Most of these patients were asymptomatic and this suggests an early presentation. STAGE II endometriosis was seen in 21.11% of case and STAGE-III in 7.7% & IV in 6.6% of cases each. All cases of stage IV endometriosis in our study (6 cases) had bilateral endometrioma & frozen pelvis with bowel adhesions. Tubal block was seen in almost 83.33% of case of stage IV endometriosis. Thus there were strong association of laparoscopic findings of endometrioma and blocked tubes. Since our study is a retrospective study, one of the important drawbacks is certain data could not be extrapolated like BMI. BMI & endometriosis by European & Western Studies suggested a positive association [21, 22].

All patients in stage I/II received medical management of 3 doses of leupragon (3.75mg) along with fulguration by monopolarcautery of endometriotic spots. Stage III/IV endometriosis underwent adhesiolysis & endometrioma cyst wall excision (based on individual findings) followed by 3 doses of leupragon at 28 days interval. Thus this study highlights the higher prevalence of endometriosis in our population particularly in asymptomatic infertile females. Laparoscopy is the gold standard for diagnosing endometriosis as recommended by ESHRE guidelines [23].

5. Conclusion

Endometriosis in infertile females is not uncommon & is increasingly being detected because of greater use of diagnostic modalities like laparoscopy in evaluation of infertility. Though most females are asymptomatic, dysmenorrhoea, chronic pelvic pain, restricted uterine mobility & adnexal tenderness raises the suspicion of endometriosis. Ultrasound evidence of endometrioma has strong correlation to severity of disease. But it is of limited value for diagnosing and determining extent of endometriosis. Laparoscopy remains the gold standard for diagnosing and staging endometriosis.

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