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ORIGINAL ARTICLE

Value of Laparoscopy in Diagnosis of Endometriosis in Unexplained Infertility Cases.

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ABSTRACT

Background: Endometriosis is a widespread gynaecological condition affect at least 11 per cent of women of reproductive age. The presence of endometrial tissue outside the endometrium and myometrium knownen as pelvic endometriosis. This study aimed to evaluate the value of laparoscopy in diagnosis of endometriosis in cases of unexplained infertility.

Methods: This was observational study that included 24 patients with unexplained infertility who underwent diagnostic laparoscopy at endoscopy unit at Zagazig University Hospital. In the period from July 2018 to January 2019 to diagnosis of endometriosis in unexplained infertility cases. **Results**: Endometriosis was diagnosed by means of laparoscopy in 24 patients included in this study, of which 9 patients (37.5%) had pelvic pain by regard local examination and while 15 patients (62.5%) were normal. endometriosis grade detected there was 1 patient (11.1%) showed endometriosis grade I, 2 patients (22.2%) showed endometriosis grade II, 2 patients (22.2%) showed endometriosis grade III and 4 patients (44.4%) showed endometriosis grade IV.

Conclusion: It is concluded that endometriosis is a common diagnosis in women with unexplained infertility and chronic pelvic pain. Laparoscopy is indicated when diagnosis is suspected, together with tissue sampling and histopathologic examination.

Key words: endometriosis, laparoscopy, unexplained infertility.

INTRODUCTION

Endometriosis is characterised as the presence of endometriotic and stromal glands outside the uterus. Histologically, three forms of endometriosis have been described: peritoneal, ovarian, and deep infiltrating endometriosis, which is defined as infiltrating the surrounding tissues by more than 5 mm**[1]**.

Superficial peritoneal endometriosis, ovarian endometriosis, and deep infiltrating endometriosis are three anatomical subtypes of endometriosis. Deep infiltrating endometriosis is characterised by nodules that locally invade pelvic structures, causing symptoms such as painful (deep dyspareunia) intercourse and painful (dyschezia) bowel movements**[2]**.

Patients with endometriosis-associated pain also show increased responsiveness within the painful abdominopelvic area to noxious and innocuous somatic stimuli ('hyperalgesia' and 'allodynia' respectively), so that a strong negative association is observed between patient-rated abdominopelvic pain severity (e.g. visual analogue scale) and pressure threshold (or 'force') **[3,4]**.

There are signs of painful cycles, chronic pelvic pain and infertility, but as these are not unique to the nature of endometriotic lesions or the severity of the condition, they are not appropriate for a definitive diagnosis**[5]**.

The most common medical intervention is suppression of menstruation[6,7]. Using mixed oral contraceptive tablets, progestin and GnRH agonists, often in combination with agents that change pain. For endometriosis, specific non-invasive diagnostic tests and more effective disease-modifying agents are needed for international recognition**[8]**.

The standard therapies have been progestin-based hormone therapy and gonadotropin-releasing hormone analogues, but many patients have undesirable systemic adverse effects in conjunction with one or both treatments**[9]**.

The diagnosis is usually delayed due to the lack of informative biomarkers, the sometimes early age of initiation of symptoms and the symptomatic overlap with other conditions. Definitive visual detection of lesions during surgery is estimated to occur between 5 and 10 years after the onset of symptoms**[10]**.

Interaction between cells of the endometrial tissue, the peritoneum, and the immune system is needed for the development of a lesion. In the presence of interferon-gamma (IFNG) and tumour necrosis factor (TNF)[11], longitudinal endometriosis-like lesions reveal a change from acute inflammation and tissue breakdown to tissue remodelling and repair status, with lesions showing proliferation, angiogenesis, neurogenesis and fibrosis under the influence of transforming growth factor B1 (TGFB1) **[12]**. There is growing evidence that non-coding RNAs (ncRNAs) mediate aspects of the complex dialogue between cells during endometriotic lesions in these diverse cytokine environments. For this cause, in recent years, the ability of ncRNAs to enhance our capacity to diagnose and treat endometriosis has been actively investigated**[13-15]**.

Proper identification of possible risk factors or therapies for review relies on reliable diagnosis across clinical centres. The new gold standard for diagnosing endometriosis and determining its severity is known to be operative real-time laparoscopic results using standardised staging systems. Histopathological evaluation is recommended for diagnostic confirmation in compliance with recent recommendations, but its true meaning has not been sufficiently quantified because bias has been added to previous research by non-standardized and unblended evaluation. Current advice states that while positive histology can confirm endometriosis diagnosis, it is not excluded by negative histology**[5]**. This study aimed to evaluate the value of laparoscopy in diagnosis of endometriosis in cases of unexplained infertility.

PATIENTS AND METHODS

This was observational study that included 24 patients with unexplained infertility who underwent diagnostic laparoscopy at endoscopy unit at Zagazig University Hospital. In the period from July 2018 to January 2019 to diagnosis of endometriosis in unexplained infertility cases. **Inclusion criteria:** Women age between20 and 40 year. Infertility (at least 12 consecutive months of unprotected sex in failed attempts at pregnancy). Natural ovulatory cycles (regular 24-to-35-day cycles observed either biphasic basal-temperature curve or serum progesterone concentrations, or secretive shifts in endometrial biopsy). Partner semen sample containing at least 1.5 ml for semen volume, 39 million per ejaculate for total sperm count, 15 million per ml for semen concentration, 40 per cent for total motility, 32 per cent for progressive motility, 58% for vitality and 4% normal form for sperm morphology according to World Health Organization criteria (2012). Hystrosalpingiography (HSG) if it was performed we check it to assess uterine cavity and tubal patency. **Exclusion criteria:** Previous endometriosis surgical procedure. Medical treatment for endometriosis in the preceding 9 months. Ovulatory drug treatment or intrauterine insemination with partner sperm in the previous month. Other medical or surgical procedure for infertility in the preceding 3 months. Previous oophorectomy and salpingectomy. History of inflammatory pelvic disorder.

Written and informed consent was obtained from all participants and the study was accepted by the Research Ethics Committee of the Faculty of Medicine, Zagazig University. Study has been carried out on experiments involving human subjects in compliance with the Code of Ethics of the World Medical Association (Declaration Helsinki).

Method:

All patients were subjected to full history taken included medical history of chronic and acute disease, detailed personal history and detailed infertility history. Detailed infertility history; included duration of infertility , history of any surgery for patient or her husband the regulatory of menstruation, any symptoms for galactorrhea or hirsutism, any symptoms for hypo and hyperthyroidism, any history for (Hormonal assay, Hystrosalpingiogarphy, Endometrial biopsy and Post coital tests). Abdominal and endovaginal ultrasound was performed for all cases. The patients were examined generally, abdominally and locally.

Routine investigations were performed as Complete blood count (CBC) , blood group, Alanine transaminase (ALT), aspartate aminotransferase (AST), Serum creatinine and Coagulation profile .

Patients with unexplained infertility, referred to diagnosis (or lack of diagnosis) in patients in which all standard investigations, such as ovulation testing, tubal patency testing, and semen analysis, are usual.

CA125 was evaluated (a cell surface antigen found on coelomic epithelium , elevated in endometriosis and considered a usually marker for response to treatment and recurrence rather than a specific diagnosis tool , normal value range 5-35).

Laparoscope used for diagnosis of endometriosis in unexplained infertility cases and also for staging the grade of endometriosis also if present.

To ensure complete evaluation of the pelvis, inspection was carried out in a systematic manner in an anticlockwise manner starting from the right adnexa and the peritoneum of the right side of the pelvic wall (including the ovarian fossa) to the peritoneum of the anterior abdominal wall and vesical peritoneum, followed by the left adnexa and the peritoneum of the left side of the pelvic wall ending with the pouch of Douglas and uterosacral ligaments.

Statistical analysis:

The data was statistically defined in terms of range, mean, SD, median, frequency (number of cases) and, where appropriate, percentages. The Mann-Whitney U-test for independent samples was used to compare the quantitative variables between the study groups. The χ2-test was conducted to compare categorical data. Where the predicted frequency is less than 5, an exact test was used instead. A P value below 0.05 has been found to be statistically important.

RESULTS

The mean age of studied patients was 30.0± 6.1 years with minimum age of 20 years and maximum age of 40 years (range 20 – 40). The mean duration of infertility in studied patients was 5.79± 2.72 years with minimum duration of 1 years and maximum duration of 10 years (range 1 – 10). The mean menstrual period in studied patients was 5.17± 1.27days with minimum period of 3 days and maximum period of 7days (range 3 – 7) table (1).

The description of general, abdominal and local examinations in studied patients. All studied patients (100%) had normal general, abdominal and examinations. As regard local examination, 9 patients (37.5%) had pelvic pain while 15 patients (62.5%) were normal table (1). The description of special habits, chronic diseases or acute diseases in studied patients. All studied patients (100%) had no acute or chronic diseases. As regard special habits, 2 patients (8.3%) were smokers while 22 patients (91.7%) were non-smokers table (1). The description of history of any surgery in studied patients. 8 patients (33.3%) had previous CS, 9 patients (37.5%) had previous abdominal surgeries (4 patients had appendectomy, 4 patients had cholecystectomy and1 patient had hernia repair) and 3 patients had other surgeries (Tonsillectomy and adenoidectomy) Table (1).

This study showed that the description of serum CA125 in studied patients. The mean serum CA 125 of studied patients was 81.42± 17.41 with minimum CA 125 of 48 and maximum CA 125 of 107 (range 48 – 107). Table (2)

This study showed that the description of laparoscopic findings in studied patients. 9 patients (37.5%) showed endometriosis, 8 patients (33.3%) showed adhesions and 7 patients (29.2%) showed no laparoscopic findings. Table (3)

This study showed that the description of endometriosis grade detected by laparoscope in studied patients. 1 patient (11.1%) showed endometriosis grade I, 2 patients (22.2%) showed endometriosis grade II, 2 patients (22.2%) showed endometriosis grade III and 4 patients (44.4%) showed endometriosis grade IV. Table (4)

Table (1): Demography of studied patients.

Variables		Studied patients (N = 24)
Age (years)	**Mean**	30.0
	±SD	6.1
	Min	20
	Max	40
	Range	(20 – 40)
Duration of infertility (years)	**Mean**	5.79
	±SD	2.72
	Min	1
	Max	10
	Range	(1 – 10)
Menstrual period (days)	**Mean**	5.17
	±SD	1.27
	Min	3
	Max	7
	Range	(3 – 7)
General examination	**Normal**	24 (100%)
	Abnormal	0 (0%)

Variables		Studied patients (N = 24)
Abdominal examination	**Normal**	24 (100%)
	Abnormal	0 (0%)
Local examination	**Normal**	15 (62.5%)
	Pelvic pain	9 (37.5%)
Special habits	**Smoker**	2 (8.3%)
	Non - smoker	22 (91.7%)
Chronic disease	**No**	24 (100%)
	Yes	0 (0%)
Acute diseases	**No**	24 (100%)
	Yes	0 (0%)
History of any surgery	**No previous surgery**	4 (16.7%)
	Previous CS	8 (33.3%)
	Abdominal surgery	9 (37.5%)

Table (2): Description of serum CA125 in studied patients.

Variables		Studied patients (N = 24)
CA 125	**Mean**	81.42
	±SD	17.41
	Min	48
	Max	107
	Range	(48 – 107)

Table (3):Description of laparoscopic findings in studied patients.

Variables		Studied patients (N = 24)
Laparoscopic findings	**Endometriosis**	9 (37.5%)
	Adhesions	8 (33.3%)
	No finding	7 (29.2%)

Table(4):Description of endometriosis grade detected by laparoscope in studied patients.

Variables		Patients (N = 9)
Endometriosis	**Grade I**	1 (11.1%)
	Grade II	2 (22.2%)
	Grade III	2 (22.2%)
	Grade IV	4 (44.4%)

DISCUSSION

In our study laparoscopic diagnosis of endometriosis was reported in 37.5% of cases. 1 patient (11.1%) showed endometriosis grade I , 2 patients (22.2%) showed endometriosis grade II , 3 patients (22.2%) showed endometriosis grade III and 4 patients (44.4%) showed endometriosis grade IV . Biopsy was taken from suspected patients and the diagnosis of endometriosis was confirmed by histopathological examination. Therefore, meticulous histopathological confirmation is the first step in laparoscopic diagnosis and treatment of suspected endometriosis. Also in our study we included that in laparoscopy 33.3% of cases suffer from adhesions and no laparoscopic findings detected in 29.2% of cases.

Positive cases of endometriosis had a statistically significant range of menstrual disturbances including dysmenorrhea, whereas there was no significance as regards menorrhagia or dyspareunia. Dysmenorrhea should direct the attention to the possibility of endometriosis. Moreover, endometriosis was more common in patients with a history of previous surgery (e.g. cesarean section, myomectomy, and ovarian cystectomy), especially when uterine cavity was opened, which may be a predisposing factor. Another explanation is that some of these operations were originally performed to treat some

endometriotic lesions but patients did not have a confirmed diagnosis of endometriosis.

The most common pelvic pathology in our study was severe endometriosis by 44.4% , whereas in the study of **Bhandari et al.[16]** showed that most common pelvic pathology was minimal endometriosis by 24.2%. Also in this study laparoscopic findings showed that 48.4% of cases suffer from endometriosis, 17.8% adhesions and no laparoscopic findings in 47.9% of cases and this variation may be explained by long period of infertility.

In study of **Gajendra et al. [17]** showed that most common pelvic pathology was minimal endometriosis by 66.44% as in the study of **Bhandari et al. [16],** Whereas in our study the most common pelvic pathology was severe endometriosis by 44.4%. Also in **Gajendra et al. [17]** study laparoscopic findings showed that 44.11% of cases suffer from endometriosis and no laparoscopic findings in 55.89% of cases.

In study of **Gajendra et al. [17]** pelvic inflammatory disease was excluded which is similar to our study as in our study we excluded any history of PID , but also in this study they exclude any adhesions due to previous surgeries or infections.

Endometriosis was more common in patients with a history of previous surgery (e.g. cesarean section, myomectomy, and ovarian cystectomy), especially when uterine cavity was opened, which may be a predisposing factor. Another explanation is that some of these operations were originally performed to treat some endometriotic lesions but patients did not have a confirmed diagnosis of endometriosis. In our study 66.6% of cases of endometriosis had history of cesarean section .

Laboratory findings showed marked variance as regards CA125 between positive and negative cases, which could be considered a good noninvasive test for diagnosing endometriosis. In our study the mean serum CA 125 of studied patients was 81.42±SD 17.41, whereas in study of **Mohamed et al. [18]** mean serum CA125 was 28.3±SD 22.8.

In the study of **Mohamed et al. [18]** laparoscopic findings showed that 33% of cases suffer from endometriosis, 7% adhesions and no laboratory findings in 12% of cases.

CONCLUSION

It was concluded that endometriosis is a common diagnosis in women with unexplained infertility and chronic pelvic pain. Laparoscopy should be indicated when diagnosis is suspected, together with tissue sampling and histopathologic examination. Further well-controlled prospective randomized trials are required to compare the roles of laparoscopy and IUI in patients of unexplained infertility.

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