Incidence of Endometriosis in Unexplained Infertility during Diagnostic Laparoscopy

Thesis

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CONTENTS

LIST OF TABLES

LIST OF FIGURES

ABBREVIATIONS

ARTs : Assisted Reproductive Techniques.

BMD : Bone Mineral Density.

CA 19-9 : Cancer antigen 19-9.

CA125 : Cancer antigen 125.

COCs : Combination Oral Contraceptives.

COX : Cyclo-Oxygenase.

E1 : Estrone.

E2 : Estradiol.

FSH : Follicular Stimulating Hormone.

GnRH : Gonadotropin Releasing Hormone.

HOXA 10,11 : Homeobox genes essential for implantation.

IGF : Insulin-like Growth Factors.

IGFBP-4 : Insulin-like growth factor-binding protein-4.

IL : Interleukin.

IUI : Intrauterine Inseminations.

IVF : In-Vitro Fertilization.

LH : Luteinizing Hormone.

LUNA : Laparoscopic Uterine Nerve Ablation.

MMP : Matrix Metalloproteinases.

MPA : MedroxyProgesterone Acetate.

MRI : Magnetic Resonance Imaging.

N314D : allele of the gene for galactose-1-phosphate uridyl tranferase.

NK : Natural Killer.

NSAIDs : Nonsteroidal Anti-inflammatory Drugs.

OS : Oxidative Stress.

PAPP-A : Pregnancy-Associated Plasma Protein A.

PF : Peritoneal Fluid.

PGE2 : Prostaglandin E2.

PP14 : Placental Protein 14.

RANTES : Regulated on Activation, Normal T-cell Expressed and Secreted.

RASK : Retrovirus Assocciated Sequences Kirsten.

RNA : Ribonucleic Acid.

ROS : Reactive Oxygen Species.

SHBG : Sex-Hormone Binding Globulin.

SPRMs : Selective Progesterone-Receptor Modulators.

TCDD : Tetrachlorodibenzo-p-dioxin.

TIMP : Tissue Inhibitors of MMP.

TNF-α : Tumor Necrosis Factor alpha.

TP53 : P53 Tumor Suppressor gene .

TVS : Trans-Vaginal Ultrasound.

VEGF : Vascular Endothelial Growth Factor.

Abstract

The aim of the study: was to evaluate the incidence of endometriosis in cases of unexplained infertility undergoing diagnostic laparoscopy at kasr EL Aini Hospital.

Patients and methods: the study sample was 100 women in the child bearing periods with unexplained infertility who were planned to undergo diagnostic laparoscopy. Clinical assessment, laboratory investigations, imaging of the patients were collected**.**

Results: our study , no doubt ,has some limits due to the nature of the study, and needs confirmation with randomized clinical trials, but the results suggest that the presence of endometriosis negatively influences fertility outcome.

Conclusion: laparoscopy is the gold standard for definitive diagnosis of endometriosis. The incidence of endometriosis in unexplained infertility appears to range between 25% to 35%.

key words: endometriosis, infertility, laparoscopy.

Introduction

Infertility is defined as the inability to conceive after one year of unprotected intercourse of reasonable frequency. Unexplained infertility, by definition, has no pathophysiologic basis and it is a diagnosis of exclusion **(Tsuji et al, 2009)**.

Up to 25% of patients, who present for investigation in a reproductive medicine clinic, are diagnosed as unexplained infertility. The diagnosis is usually made after investigations showing normal semen parameters, ovulatory concentrations of serum progesterone in the mid-luteal phase, tubal patency, and a normal uterine cavity **(Hart, 2003).**

Endometriosis is defined as the presence of endometrial-like tissue outside the uterus ***(Kennedy et al., 2005)***.

The incidence of endometriosis, especially in association with infertility, has been a subject of debate, ranging from 1% to 71%. **Dokras and Olive (1999)** reported a 6% incidence in infertile women, while **Martin and Ling** reported that endometriosis was found in 1-8% of patients who are diagnosed surgically **(Martin and Ling 1999).** The figure for **Moghissi (1999)** was 10% of all premenopausal women. **Tsuji et al (2009)** stated that endometriosis is present in 20% to 40% of women who complain of subfertility, although it can be found in 5% of fertile women. The figures for **Burns and Schenken** are 30-50% of women with infertility and subfertility, but using laparoscopy for diagnosis; these figures decreased to 21-23% (**Burns and Schenken 1999**). On the

extreme**, Wenkel (1999),** using laparoscopy for diagnosis of endometriosis, reported an incidence of 71% of which 45-50% were asymptomatic.

The exact mechanism of endometriosis is still unknown, but several hypotheses have been proposed to explain its development including (1) retrograde menstruation, (2) metaplastic transformation of other tissues to endometrial tissue, (3) Coelomic metaplasia theory, (4) Vascular or lymphatic transport of endometrial tissue and (5) Immunologic theory. There is a growing evidence that factors such as the pollutant dioxin and genetic susceptibility play a role in disease aetiology ***(Moore and Kennedy, 2000)***.

Endometriosis can affect fecundity by anatomical damage to the pelvis, tubo-ovarian adhesions and impairement of tubal anatomy which impaires gamete transfer. In women with normal anatomy the cause may be related to impairment of ovulation, reduced response to ovarian stimulation, low embryo quality and impaired implantation ***(ASRM, 2004).***

Endometriosis should be suspected when there is dyspareunia, severe dysmenorrhoea, or unexplained abdominal pain. However, the symptoms experienced are poor indicators of the severity of disease. Pelvic examination may show tenderness, nodules of endometriosis on the uterosacral ligaments, or an enlarged ovary, which may be secondary to an ovarian endometrioma. The diagnosis of endometriosis is generally confirmed by laparoscopy. Preoperative ultra-sonography is helpful to diagnose the likely cause of a tender and enlarged ovary ***(Wingfield, 2000).***

Endometriosis is classified according to the revised American Society of Reproductive Medicine (ASRM) system. Using a point system, the classification is based on the amount of endometriosis and the number of adhesions during diagnostic laparoscopy **(ASRM, 1997).**

- Stage I (minimal): 1-5 points.
- Stage II (mild): 6-15 points.
- Stage III (moderate): 16-40 points.
- Stage IV (severe): more than 40 points.

(Kennedy et al, 2005).

Medical treatment of endometriosis includes estrogen - progestin combination, progestogens, gonagotropin releasing hormone (GnRH) analogue and danazol. In general, these agents inhibit growth of endometriotic implants by suppression of ovarian steroids and induction of hypoestrogenic state. The treatments are associated with a symptomatic improvement in 45- 65 % of patients; but the problem often recurs at a rate of 5- 15% in the first year **(Malik and Cunter, 2004).**

There is sufficient evidence in the literature to confirm that medical therapy should not be used for women with minimal/mild endometriosis and infertility. Not only does this treatment fails to improve fertility; but it acts as a contraceptive and delays conception ***(Wingfield, 2000)***.

For minimal or mild endometriosis, surgical ablation using laparoscopic laser treatment, bipolar coagulation of endometriotic deposits, or excision of the deposits has been shown to be more effective than expectant management. For severe disease the most cost/effective management is in-vitro fertilization (IVF) **(Filho et al, 2008).**

A number of therapeutic strategies may be considered in the management of unexplained infertility. Apart from expectant management, specific interventions may include natural cycle (non-medicated) intrauterine inseminations (IUI), IUI following ovulation induction/superovulation with clomophine citrate (CC), and/or exogenous gonadotropins, superovulation alone (with timed intercourse), and assisted reproductive techniques (ARTs), such as IVF **(Teirney and Prentice, 2002).**

Laparoscopy has become both the diagnostic and therapeutic tool for managing this disease. The primary goal is to remove all visible lesions and adhesions, thereby restoring normal pelvic anatomy. Various surgical techniques have been described, ranging from excision to ablation. In some instances, destruction of nerve pathways, thought to be carrying pain fibers from the pelvis, is also used (i.e, uterine nerve ablation and presacral neurectomy) **(Catenacci et al., 2009)**.

Aim of Work

This is a descriptive study to evaluate the incidence of endometriosis, in cases of unexplained infertility undergoing diagnostic laparoscopy at Kasr El Aini Hospital.

Endometriosis

Endometriosis is defined as the presence of endometrial tissue (glands and stroma) outside the uterus. The most frequent sites of implantation are the pelvic viscera and the peritoneum. Endometriosis varies in appearance from a few minimal lesions, on otherwise intact pelvic organs, to massive ovarian endometriotic cysts, that distort tubo-ovarian anatomy, and extensive adhesions often involving bowel, bladder, and ureter. It is estimated to occur in 7% of reproductive age-women in the United States and often is associated with pelvic pain and infertility ***(Comiter, 2002).***

Etiology

Endometriosis is an estrogen dependent disease. Some theories have been proposed to explain the histogenesis of endometriosis However, no single theory can account for the location of endometriosis in all cases ***(Giudice and Kao, 2004).***

1. Retrograde Menstruation

Sampson was the first to use the term endometriosis to describe these lesions. Before it was termed as adenomyosis or adenomyositis ***(Nixon and Hughsedon, 1963).***