Endometriosis

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ABSTRACT

BACKGROUND: Endometriosis is a common mysterious and fascinating gynaecological condition with diverse clinical manifestations, highly variable and unpredictable clinical course with decreased quality of life. Despite extensive research, endometriosis is fraught with controversies.

METHODS: Review of pertinent literature on endometriosis, selected references, internet services through gynaecological search which have been critical in the understanding of this puzzling gynaecologic condition were included in the review.

RESULTS: Endometriosis most commonly afflict women in there late 20s and 30s.The classic symptom complex include dysmenorrhoea, dyspareunia, menorrhagia and infertility. About 30% of the patients are asymptomatic. The incidence of infertility amongst women suffering from endometriosis ranges from 30%-40%. The factors implicated in causing endometriosis-associated infertility are multiple and its management is shrouded in controversy, complex and imperfectly understood.

CONCLUSION: Inspite of diverse clinical manifestations, variable and unpredictable clinical course, there is a chance to improve pregnancy rates with improvement in assisted reproductive technology.

INTRODUCTION

Endometriosis is the ectopic implantation of endometrial tissue outside the uterine cavity and myometrium usually within the pelvis but rarely at distant sites like lung and heart [1-7]. It is a common fascinating gynaecological condition with diverse clinical manifestation with highly variable and unpredictable clinical course[8]. Endometriosis is a disease of reproductive age women, confronted with a lot of challenges despite extensive research yet fraught with controversies [1,8]. It most commonly presents with cyclic pelvic pain, infertility and decreased quality of life[8]. The management is individualized and depends on the patients age, symptomatology and reproductive desires[3,6,8].

INCIDENCE

The exact incidence is unknown[6,7]. Reported incidence has varied widely from country to country, but has increased due to widespread use of laparoscopy, increased awareness of the disease and changing social patterns like late marriages and limitation of family size[3,6.] The incidence range from 5-20%[3,6,9,10]. The prevalence of endometriosis in patients undergoing laparoscopy for chronic pelvic pain and infertility increases to 25% and 33% respectively[11-13.]

AETIOLOGY

Endometriosis is a disease of childbearing period. It is seen more among the affluent class and is frequently associated with infertility[8]. Familial tendency and genetic predisposition is seen in 15% of the cases. Several theories have been put forward to explain endometriosis, but no single theory can adequately explain the varied clinical and pathological presentations. The most widely accepted mechanisms explaining the development of endometriosis is the implantation of viable endometrium at an ectopic site[14]. The Sampson's theory of retrograde menstruation states that during menstruation endometrial tissue is deposited into the peritoneal cavity via the fallopian tubes. This theory is supported by the animal studies done by Telinde and Scott[16,17.] Sampson's theory is equally supported by findings of the frequent association of endometriosis with obstructive mullerian anomalies and frequent location of endometriotic lesions in the dependent portions of the pelvis[18,19.] However, retrograde menstruation alone could not explain why only 5 to 20% of women develop pelvic endometriosis, while menstrual reflux is a universal phenomenon.[20,21]

OTHER FORMS OF IMPLANTATION OF ENDOMETRIOTIC TISSUES:

- Iatrogenic implantation of endometrium in abdominal scar and episiotomy scar at the time of delivery resulting in endometriosis[22-24].
- Lymphatic and haematogenous dissemination of endometrium explains some cases of endometriosis with implants in lymph nodes or in distant sites like lung or extremities[25,26]
- Coelomic metaplasia of the peritoneal lining or growth of lesions from embryonic cell rests were suggested to explain development of endometriosis when endometrial implantation is not possible[27,28.] This

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theory can explain the occurrence of endometriosis in nearly all its distant sites and also in women without uterus[29], and the existence of endometriosis in males[30].

- Genetic basis for endometriosis: This is supported by increased incidence in women with a positive family history of the disease. In these women, endometriosis develops earlier in life with more severe form of the disease[6]. The inheritance pattern is probably polygenic or multifactorial[31,32.]

Other factors implicated in the occurrence of endometriosis are immunological, hormonal influence, vaginal and cervical atresia encouraging retrograde spill.

RISK FACTORS: The risk factors are retroverted uterus, polymenorrhoea, familial (polygenic/multifactorial inheritance),[32] caffeine and alcohol consumption[8,33.] A reduced risk is associated with the use of oral contraceptives and life style exposures that lower oestrogen level such as smoking and exercise.[32,33.]

SITES OF ENDOMETRIOSIS

The most common sites are ovaries, the peritoneum of the anterior and posterior cul-de-sac, the uterosacral ligament, peritoneum overlying the bladder, sigmoid colon, back of the uterus, intestinal coils and appendix. Remote sites are limbs, central nervous system, lung and retina[8]. Endometriosis appear in the umbilicus following an operation in the laparotomy scars, in tubal stumps following sterilization operation, in the amputated stump of the cervix and in the scars of the vulva and perineum.

PATHOLOGY

On pathologic examination, endometriotic implants are composed of endometrial glands and stroma with haemosiderin-laden macrophages and occasional fibrotic elements[8,34,35]. The endometriotic foci involving the pelvic peritoneal surfaces are usually multiple. The classic appearance is usually that of a slightly raised spot with a dark red, bluish or brown discolouration adherent to the site where it is lodged[3,6,36]. The flamed-red lesions are considered to be the most active[1,8,36]. Powder-burnt areas are the inactive lesions seen scattered over the pelvic peritoneum[1,3]. Adhesions are common and the lesions are usually surrounded by dense fibrosis. Atypical lesions vary in appearance and are sometimes difficult to recognize[37]. Microscopic or hidden lesions are commonly present in peritoneal pockets[38]. In more extensive cases massive adhesions may involve pelvic or abdominal organs leading to the formation of large amalgamated masses and nodules[39].

Endometriomas are seen mainly within the ovary. These cystic structures have a fibrotic wall with a brown to yellow lining. Endometriomas (chocolate cysts) are usually small in size and rarely exceed 15cm in diameter, and contain thick brownish fluid caused by altered blood in the cavity[6,40], chocolate cysts of the ovaries represent the most important manifestation of endometriosis[3].

CLINICAL FEATURES

Endometriosis most commonly afflict women in their late 20s and 30s. This disorder may occur in adolescence[8]. The classic symptom complex include dysmenorrhoea, dyspareunia, menorrhagia and infertility. About 30% of the patients are asymptomatic[3].

DYSMENORRHOEA: This is the most common symptom. The pain begins before the onset of menstruation and ceases before the end of menstrual flow[3,8]. The pain is very variable from a dull ache to grinding or crushing pain, colicky pain or a bearing down pain and may be associated with backache. Pain of endometriosis is chiefly related to the location and not the extent of the lesion[3].

ABDOMINAL PAIN: Lower abdominal pain associated with endometrosis is common around menstruation[3]. Occasionally the pain suddenly becomes very severe, presenting as an acute abdomen necessitating immediate surgery. At laparotomy a ruptured chocolate cyst is observed[3,41].

DYSPAREUNIA: Endometriotic involvement of the cul-de-sac, the uterosacral ligaments, deep pelvic implants and lesions of the rectovaginal septum or a fixed retroverted uterus will result in noncyclic pelvic pain, backache and rectal pressure[3,42]. Movements of the cervix elicit tenderness. Dyspareunia and backache may be the result of this pathology. These patients are reluctant to attempt intercourse and this may add to the magnitude of infertility (25-50%)[3].

INFERTILITY: The incidence of infertility amongst women suffering from endometriosis ranges from 30% to 40%[3,6]. Factors implicated in causing endometriosis-associated infertility include anatomic distortion and fibrosis of the fallopian tubes in severe cases possibly interfering with motility and function[3,6]. It may inhibit ovulation and because of dyspareunia there is reduced frequency of sexual intercourse. Other causes of infertility are anovulation, luteal phase defects, luteinized unruptured follicular (LUF) syndrome, autoimmune factors, spontaneous early abortions, altered peritoneal fluid environment by prostaglandins or inflammatory cells, hyperprolactinaemia, corpus luteal phase defect and

tubal blockage[3,43].

ABNORMAL UTERINE BLEEDING: A lot of abnormal bleeding has been documented with endometriosis e.g hypermenorrhoea, menorrhagia, premenstrual spotting and oligomenorrhoea. Polymenorrhoea is noted with ovarian involvement (10-30%).

CHRONIC PELVIC PAIN: Endometriosis is one of the causes of chronic pelvic pain. This pain is related to prostaglandin production in the lesions[3,43-46].

OTHER SYMPTOMS: Other symptoms related to specific organ involvement are sometimes seen, such as frequency, dysuria and rarely haematuria during menstruation. These may result from bladder or ureteral involvement. Obstruction of the ureter leads to hydronephrosis and renal infection[3,47]. Bowel symptoms are painful defaecation, diarrhoea and melaena around menstruation[48].

CLINICAL FINDINGS

Physical findings in endometriosis are not specific and do not correlate with disease severity confirmed at laparoscopy.

Speculum examination may reveal bluish or blackish puckered spots in the posterior fornix which may be tender to touch. The presence of the puckered spots is pathognomonic of endometriosis. Vaginal examination reveals a tender retroverted uterus. A fixed tender cystic mass or bilateral masses may be felt in the pelvis. The diagnosis is certain if the uterosacral ligaments and the pouch of Douglas are felt thickened and shotty with multiple small nodules palpable through the posterior fornix. Nodularity along the uterosacral ligaments and in cul-de-sac is also very suggestive[3,6]. These are described as cobblestone feel of uterosacral ligaments[3,6]. Deep lesions in the rectovaginal septum are better appreciated by a combined rectovaginal examination. This is important because they may be used during laparoscopy[6].

ENDOMETRIOSIS AND INFERTILITY: This is still controversial, complex and imperfectly understood[3,6,7]. For severe disease, there is distortion of pelvic anatomy resulting in interference with ovum pickup and tubal function by dense pelvic adhesions and loss of tubal motility favouring an obvious anatomic cause for infertility. However, in patients with mild endometriosis it is not easy to explain or demonstrate a clear association. Endometriosis is often associated with anovulation, abnormal follicular development, luteal insufficiency, and premenstrual spotting. Luteinization of the unruptured follicle is known to occur and hyperprolactinaemia with associated galactorrhoea are noted findings. However, no definite correlation between these endocrine events and the degree of endometriosis has been established[3,6].

DIAGNOSIS: This starts with taking a good and careful sexual, menstrual, gynaecologic and pain history and also by ruling out other causes of chronic pelvic pain[8,49].

PHYSICAL EXAMINATION is important and must include a careful abdominal, pelvic and rectovaginal examination. The presence of endometriotic implant will result in induration and tender nodularity of the uterosacral ligaments. Palpation of the ovaries and uterus to rule out enlargement and tenderness is important and also rule out cul-de-sac fixation.

CA 125 LEVEL: Glycoprotein and cell surface antigen is shown to be elevated more than 35U/ml in 89% cases of endometriosis and the level is directly proportional to the extent of the disease. The level is not specific, but is also raised in epithelial carcinomas of the ovary and a lot of nongynaecological conditions like abdominal tuberculosis, PID, chronic liver disease, adenomyosis, pregnancy, fibroids, in 2% normal women during menstruation, pancreatitis, and peritonitis. However, it may be used in assessing responsiveness of the disease to therapeutic interventions and an indication of recurrence of the disease in the follow up[3,6,8].

ULTRASOUND AND MRI: Ultrasound is not very useful in detection of endometriotic implants and can not differentiate these from other masses[50,51].

In contrast, endometriomas are diagnosed with excellent sensitivity and specificity[52,53]. The "ground glass" appearance of endometrioma on transvaginal ultrasound is suggestive of endometriosis. The role of Doppler studies is not well defined[54,55]. Magnetic resonance imaging gives identical picture as in ultrasound and is not more useful in the diagnosis of endometriosis.

LAPAROSCOPIC FINDINGS: Laparoscopy is the gold standard in the diagnosis of endometriosis[56]. Visualization of implant is crucial in making the diagnosis. The more classic power-burn implants and ovarian endometrioma or chocolate cysts represent both the appearance of the disease and its chronic nature[8,57]. Histologically, the presence of vesicular, petechial, haemorrhagic, polypoid and white lesions have correlated with endometriosis[58]. Laparoscopy remains the only definitive tool for assessment of the extent of endometriosis.

DIFFERENTIAL DIAGNOSIS:

(1) Chronic pelvic inflammatory disease (PID). Both endometriosis and PID produce pelvic pain, dysmenorrhoea, menorrhagia and subfertility.

Laparoscopic visualization of the pelvis will reveal the true pathology. Relief with hormonal therapy is another reasonably accurate test since endometriosis should respond while pelvic inflammatory disease does not[8].

(2) Uterine leiomyomas: They are painless except degenerated fibroids, and the uterus is not fixed. Laparoscopic visualization will differentiate the two.
(3) Ovarian malignant tumors with secondaries in the pouch of Douglas can be mistaken for endometriosis. The history, pain, the age of the patient and symptoms suggestive of endometriosis are against the diagnosis of cancer, but the physical signs, apart from tenderness, are very similar to those of an ovarian neoplasm.
(4) Rectosigmoid involvement will cause rectal symptoms which resemble the symptoms of rectal carcinoma[8]. Sigmoidoscopy and biopsy will give an accurate diagnosis.
(5) Gastrointestinal disorders; Rupture of chocolate cyst will mimick all possibilities of an acute abdomen. Laparoscopy will resolve the confusion.
(6) Chronic Pelvic Congestion Syndrome due to other causes must be excluded by ultrasound, CT and MRI.

CLASSIFICATION: The current classification is based on anatomic location and severity of endometriosis at operation. It does not take account of complaints like infertility or pain, however, it forms the acceptable basis for comparison of therapeutic outcomes. The classification described by American Fertility Society (1985) is based on the size and location of the endometriotic lesion and is classified as minimal, mild, moderate and severe. Points are assigned on the basis of distribution and invasiveness of peritoneal implants, ovarian disease, tubal occlusion, pelvic adhesions and cul-de-sac obliteration at laparoscopy.

Staging:

Stage I (minimal) Score 1-5 points:

- Small spots of endometriosis, but no clinical symptom.

Stage II (mild) Score 6-15 points:

Scattered fresh superficial lesions.

- No scarring or retraction.
- No adnexal adhesion.

Stage III (Moderate) Score 16-40 points:

- Ovaries involved with some scaring and retraction.
- Endometriomas not more than 2cm in size
- Minimal adhesions

Stage IV (Severe) Score > 40 points:

- Ovaries involved with endometriomas > 2cm
- Dense Peritubal adhesions and periovarian adhesions restrict mobility
- Uterosacral,ligaments thickened and involved
- Evidence of involvement of the bowel and urinary tract

The above classification helps in the prognosis and assessing the fertility rate in a woman afflicted with endometriosis[3,6,8].

TREATMENT: The options available for treating endometriosis are observation (expectant), medical therapy, surgical therapy and combination of surgical and medical therapy. The option applied in treatment of endometriosis depends on the patients age, her symptoms, future fertility, the stage of her disease, response to medical treatment, relief obtained with any previous conservative surgery and the attitude of the patient towards her problem[3,6,8,60]. The objective of the treatment should be to reverse and if possible, eliminate the disease process, alleviate symptoms, facilitate childbearing and enable the patient to lead a comfortable life [3,6,8]. For asymptomatic minimal endometriosis in a young woman, it is a good practice to observe (expectant management) the patient for 6-8 months and investigate for infertility[3,8,60]. Expectant management has the advantage of being cheaper and avoiding side effects of therapy[60].

Medical Management of endometriosis is based on assumption of the role of exogenous sex steroids, which influence endometriotic tissue in the same way that they influence the endometrium. Endometriosis proliferates as a result of increased oestrogen. Oestrogen deficiency and androgens result in atrophy of the endometrium and endometriotic deposits while progesterone and progestins result in arrest of the growth and development of a decidual reaction in both endometriosis and endometrial deposits. Traditionally, medical therapies applied for treatment of endometriosis are progestins and Danazol. Pseudopregnancy is obtained by the administration of high dose oral contraceptives in a continuous fashion. There is a high incidence of breakthrough bleeding responsive only to increasing oestrogen doses.

DRUG TREATMENT: This is aimed at causing atrophy of the ectopic endometrium with minimal side effects.

(1) Combined oral contraceptives: This regimen was termed pseudopregnancy because of induced amenorrhoea associated with its use. It is used in a continous fashion resulting in amenorrhoea, or in a cyclic fashion. The therapeutic effect is probably due to the progestin in the pill causing decidualization and then atrophy of the endometriotic lesions. However, high incidence of side effects and risk of thromboembolism limit their prolonged use. Oral contraceptives are a low-cost option for suppressive therapy and they seem to be effective in alleviating pelvic pain[61].

(2) Progestogens: These drugs exert an antioestrogenic

effect and the continous administration of progestogens result in endometrial atrophy[62]. Progestogens used for management of endometriosis are parenteral(medroxy-progesterone acetate), oral (medroxy-progesterone acetate, megesterol acetate, gestrinone, dydrogesterone and lynestrenol). The progestin most commonly used is medroxy progesterone acetate either orally 20-30mg daily or intramuscular 150mg every 3months. The side effects of progestins include abnormal bleeding, mood changes, depression, headaches, weight gain, bloating, nausea and a decrease of HDLs[6,63]. Progestins are an effective and inexpensive alternative for patients who do not tolerate Danazol, GnRH agonists or oral contraceptives[64-66].

(3) Danazol: This is an isoxazol derivative of 17& ethinyl-testosterone. It is midly anabolic, antioestrogenic and antiprogesteronal. It is very effective drug but expensive. The mechanisms of action are (1) Suppression of the hypothalamic-pituitary axis (2) Direct inhibition of ovarian steroidogenesis (3) Inhibition of several enzymatic processes and by competitive blockage of androgen, oestrogen and progesterone receptors in the endometrium[63]. It is administered in doses of 400 600mg daily for 6months starting on the first day of menses. Cessation of menses and serum oestradiol levels are good clinical and laboratory monitors of danazol therapy[63]. The side effects of Danazol are related to both its androgenic effect and to the resulting hypoestrogenic environment[6]. Danazol is associated with weight gain, mood changes, depression, oily skin, muscle cramps, headaches, oedema, altered appetite, acne, hirsutism, fatigue, decreased breast size, hot flushes, voice change and irregular vaginal bleeding. Others are abnormal lipoprotein changes (decrease in HDLs and an increase in LDLs), theoretical possibility of masculinization of a female fetus if the patient conceives[6,67].

(4) Gestrinone: Is a 19-nortestosterone derivative with progesterone agonist and antagonist effects. It results in amenorrhoea and endometrial atrophy. It has a long half life and it is given orally 2.5mg to 5mg twice weekly. 85-90% experience amenorrhoea[3]. The side effects are similar to those of Danazol but are much milder and better tolerated. There is no adverse effect on lipoproteins or liver function tests[68-70].

(5) GnRH Agonists: GnRH agonists are modified GnRH peptides with a longer half-life and greater potency[6,71]. Continuous administration of GnRH agonists downregulates the pituitary-hypothalamic unit, leading to decreased gonadotropin levels and induction of a reversible hypoestrogenic state or "medical oophorectomy". The native GnRH is a short-acting decapeptide that is secreted episodically into the pituitary portal circulation to regulate the release of LH and FSH. If the pituitary receptors are exposed to GnRH continuously, instead of in pulses, there is paradoxic downregulation of pituitary function, and LH and FSH levels decrease, leading to suppression of ovarian steroid production. Examples of GnRH agonist are leuprolide, goserelin, naferelin, buserelin, histrelin and tryptorelin. GnRH agonists are given in doses of 10-20mg intravenously, twice daily, or 200 to 400mg intranasally daily for six months. Discontinuation of GnRH causes recurrence of endometriosis within a year in 50% of cases[3]. GnRH-a treatment is associated with the side effects of hypoestrogenism. These include hot flushes, vaginal dryness, decreased libido, breast tenderness, insomnia, headache, fatigue, abnormal vaginal bleeding, depression, skin changes and reversible loss in bone mineral density. GnRH-a do not have adverse effect on serum lipoproteins[6,8,63].

GnRH-a with Add-Back Therapy: This is a strategy to prevent or reduce bone loss. Add-back therapy combines GnRH-a with hormone replacement therapy (HRT) with the purpose of preventing the short and long-term consequences of the hypoestrogenism induced by these drugs (vasomotor symptoms). The steroidal agent selected, the dose used and the timing of administration can influence the efficiency of the combination[6,63,72]. The use of oestrogen/progestin combination add-back therapy would be excellent for vasomotor symptoms and can help preserve bone density but it might decrease the efficiency of GnRH agonists in controlling endometriosis[6]. Preliminary studies using biphosphonates and norethindrone showed a beneficial effect in preserving bone mass. After discontinuation of these multidrug therapies, significant recurrence rates were reported as with other medical lines of management[43,68].

Other Modalities: The antiprogesterone mifeprostone (RU486) was shown to have a beneficial effect on endometriosis[73,74]. Current medical treatment of endometriosis depends on suppression of ovarian function and induction of endometrial atrophy.

Letrozol, an aromatase enzyme inhibitor is useful in reducing pain and implants in severe cases.

Reasons for failure and recurrence following medical therapy:

(1) There is impaired drug supply to the fibrotic capsule.
(2) The ectopic endometrium responds less to hormones as compared to normal endometrium.

SURGICAL TREATMENT: Surgical therapy is the most common treatment modality used in endometriosis[6]. Recently, laparoscopic methods replaced most laparotomies for endometriosis, except in advanced stages and larger lesions[3,6,75].

OBJECTIVES OF SURGERY[63]:

- To remove or destroy implants
- To relieve symptoms
- To maintain or restore fertility
- To avoid or delay recurrence of symptoms.

INDICATIONS FOR SURGERY[63]:

(1) Pelvic pain that has not responded after 3months of NSAIDs and/or oral contraceptive therapy.
(2) Adnexal mass suspicious of being an endometrioma.

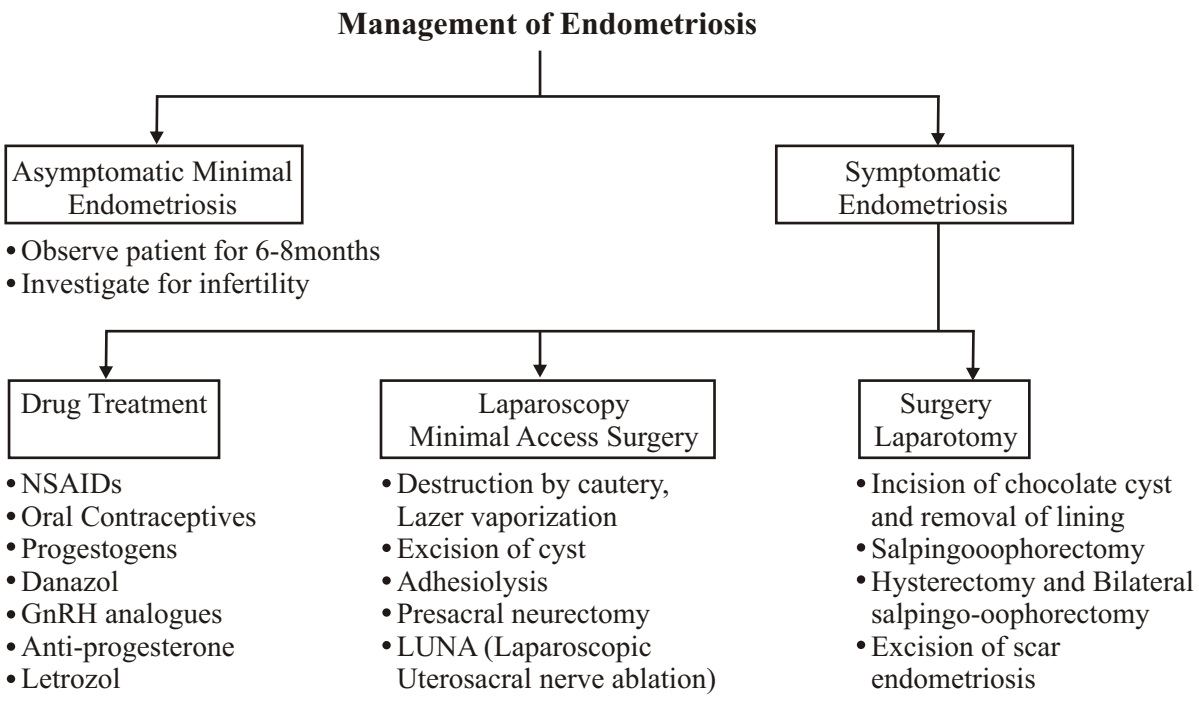
Surgical Principles in the treatment of endometriosis[63]:

- Knowledge of disease and treatment modalities.
- Informed consent
- Experienced surgeon (There may be need for gastrointestinal surgeon or urologists).
- Adequate facilities, personnel and equipment.
- Appropriate patient selection.
- Proper patient position, careful evaluation and maximum exposure.
- Use of magnification.
- Minimum tissue trauma
- Excellent haemostasis
- Removal of all diseased tissues
- Avoidance of foreign body material
- Confirmation of tissue pathology.

Surgical intervention can be conservative or radical. Radical surgery is performed on the patients who no longer desire fertility. The surgery is hysterectomy with or without bilateral salpingoophorectomy. Excision of all visible disease is recommended. Conservative surgical therapy is designed to restore normal pelvic anatomy and remove all visible deposits of endometrial implants. The introduction of endoscopic techniques (minimal invasive surgery) has resulted in decreased morbidity, hospitalization and hospital cost. In the procedure of conservative surgery, careful attention should be given to identification of ureters, pelvic vessels and bowel. Adhesions should be excised to reduce the chances of endometriotic deposits on these fibrotic structures. Endometriomas should be excised or ablated and patient followed with medical therapy.

The management of infertility associated with endometriosis is not clearly defined. In severe endometriosis, restoration of normal pelvic anatomy with careful maintenance of haemostasis and meticulous surgical technique is important. There is need to minimize raw surfaces with adhesion protection barriers. Patients with refractory infertility and concomitant endometriosis are successfully treated with assisted reproductive technology like gamete intrafallopian transfer (GIFT) and Invitro-fertilization/embryo transfer (IVF/ET) after all other aetiologies for infertility have been ruled out.

Illustration of Endometriosis Management[3,63]



MALIGNANT CHANGE IN ENDOMETRIOSIS

Malignant change in endometriotic lesions is rare and when it occurs, it is associated with disease involving the ovary. In a review by Hilli et-al[76], the occurrence of malignant transformation in extraovarian endometriosis is extremely rare. 90 percent of carcinomas are endometrioid clear-cell carcinomas which represents 5% of all carcinomatous and sarcomatous neoplasms of mullerian origin[76]. Finally, that malignancy arising in extra-ovarian endometriosis appears to parallel that in the endometrium[76]. The incidence is thought to be extremely rare, with the study done by Fathalla giving an incidence of 1 in 150 endometriomas[77].

PROGNOSIS

Adequate counseling of patients with endometriosis requires a detailed knowledge of the disorder. The initial operative staging is of primary importance to obtain adequate information on which to base future decision about therapy[7]. The patients symptoms and desire for childbearing dictate appropriate therapy. Longterm concerns must be more guarded in that all current therapies offer relief but not cure[7]. The course of endometriosis in any individual is impossible to predict at present, but with improvement in future treatment options, prognosis will be better[7].

CONCLUSION

The natural course of endometriosis is not clearly defined inspite of the classic symptom complex, about 30% of the patients are asymptomatic, but in some cases it is progressive. With improved ART, the pregnancy rates in endometriosis [even in severe cases] seem to be similar to tubal factor infertility. IVF/ET should be utilized after an adequate trial of less- invasive procedures[6,63].

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