

# Role of Laparoscopic Surgery in Endometriosis Associated Infertility— Literature Review

Ganeshselvi Premkumar

Department of Obstetrics and Gynaecology, University of Bristol, UK

Correspondence: Ganeshselvi Premkumar, 43, Larkspur Drive, Chandlers Ford, Hampshire. SO534HU  
premgunny@yahoo.com, 0(44)2380267400

## Abstract

*Background:* Endometriosis is a common disease of reproductive age group women. It was first described by Dr Sampson in 1925 as, “presence of ectopic tissue which possesses the histological structure and function of uterine mucosa”. There is controversy surrounding its pathogenesis and the mechanism by which it causes infertility. Laparoscopic surgery is often used to treat this condition. Controversy exists as to the benefits of such surgery in infertile women.

*Objective:* To explore whether laparoscopic surgery improves the chances of conception both by natural and assisted conception methods in moderate to severe endometriosis.

*Methods:* Retrospective review of English literature regarding role of laparoscopic surgery in managing endometriosis associated infertility using keywords - Endometriosis, Laparoscopy, Infertility, Pregnancy rate.

*Results:* A large prospective study by Adamson et al 1993 showed that laparoscopic surgery significantly increased the cumulative pregnancy rate which was confirmed by a further meta-analysis in 1994. A large retrospective analysis by Osuga et al 1997 reported that pregnancy rate is unrelated to the stage of endometriosis. Further studies in 2002 suggested that the laparoscopic surgery increases the pregnancy rates in the first 6-12 months post operation. Two randomized controlled trials demonstrated higher pregnancy rates after laparoscopic excision of endometriomata. Few studies showed the benefits of laparoscopic endometrioma excision before IVF like reduced oocyte retrieval risks, missing occult malignancy and worsening of endometriosis during ovulation stimulation outweighs the drawback of cost and surgical risk. In addition, studies have reported improvement of dyspareunia after laparoscopic debulking for rectovaginal endometriosis.

*Conclusion:* There are no large prospective randomized double blind controlled trials available to date in this area. In spite of heterogeneity among the available studies, current evidence suggests that laparoscopic excision or ablation, either by electrocautery or laser is beneficial in improving pregnancy rates, both by natural and assisted.

## INTRODUCTION

Endometriosis was first described in 1860 by Von Rokitansky and endometriosis is one of the most prevalent diseases in Gynecology. There is paucity of knowledge about its epidemiology. In addition there is also a lack of consensus on a precise definition and pathophysiology, but recent research suggests morphological differences between endometriosis and endometrium.

Endometriosis can be a chronic, debilitating gynecological condition among women of reproductive age causing pain and infertility.

The incidence of endometriosis remains unknown because of the poor correlation between its presence and symptoms. The pathogenesis and mechanism by which it causes infertility is poorly understood.

Over the last two decades, there has been a large increase in the number of infertile patients found to have endometriosis. It is uncertain whether this represents an increase, or simply a reflection of the more frequent use of laparoscopy. Endometriosis accounts for 10 to 15% of infertility. There is an increasing trend towards treating infertile with endometriosis surgically. This review explores the evidence available particularly addressing the use of laparoscopic surgery and its effect on the probability of pregnancy.

We reviewed the literature using all the available English databases, Cochrane register and articles which addressed the question “does laparoscopic surgery improve pregnancy rates in women with infertility associated with moderate-severe endometriosis?” The results are shown in Table 1.

## PATHOGENESIS

No single theory can explain the pathogenesis of endometriosis. Endometriosis is sometimes called the disease of theories. The Implantation theory was first described by Dr Sampson<sup>1</sup> in 1925. He proposed that retrograde menstruation regurgitates viable

endometrial cells through the fallopian tubes. These cells are capable of implantation and development. Dissemination to distant sites is possible by lymphatic and vascular spread. This theory remains the most popular and is supported by experiments that show that endometrial cells are viable both *in vitro*<sup>2</sup> and *in vivo*.<sup>3</sup> The exact mechanism of endometrioma formation is unknown. One possibility is the formation of an adhesion between the ovary and pelvic peritoneum and the progressive infolding of the ovary forming a pseudo cyst called an endometrioma.

The coelomic metaplasia theory explains the unusual sites of endometriosis but evidence for it has yet to be established. Dr Meyer<sup>4</sup> proposed that coelomic epithelium undergoes metaplasia to become endometriosis. Endometriosis does not show the distribution with older age that is found in other organs that undergo metaplasia, e.g. squamous metaplasia in the lung.

Iatrogenic dissemination can occur during gynecological procedures, but it is not clear whether the rate of transplantation varies with the time of cycle. Recent work on pathogenesis showed immunogenetic defects, e.g. aberrant expression of factor. Steroidogenic Factor-1 activates the expression of the aromatase enzyme<sup>5</sup> and increased expression of cyclo-oxygenase-2 in the stromal cells.<sup>6</sup>

## HISTOLOGY OF ENDOMETRIOSIS

The natural history is that endometriosis evolves from type 1 to type 3 (Table 1). Type 1 may be more related to infertility and types 2 and 3 with chronic pain.

## ANATOMICAL DISTRIBUTION AND SYMPTOMS

The most common site of endometriosis is the ovary (44%). The other common sites are peritoneum, ovarian fossa, uterosacral ligaments, uterovesical fold and Pouch of Douglas. Endometriosis has also been found involving the bladder, ureter, lung, liver, diaphragms, scars and even brain.

The symptoms depend on the site. It can present as dysmenorrhea, dyspareunia, chronic pelvic pain, infertility, irregular heavy periods, cyclical rectal bleeding, tenesmus,

cyclical hematuria, cyclical dysuria, ureteric obstruction, cyclical hemoptysis, cyclical pain and swelling in the umbilicus or scars.

## PATHOGENESIS OF INFERTILITY IN ENDOMETRIOSIS

The nature of the relationship between endometriosis and infertility remains controversial. One recent study suggests that the presence of endometriosis alone where no other cause is found affects fertility.<sup>7</sup> But the mechanism by which minimal endometriosis affects fertility in such women is uncertain. It is accepted that moderate-severe endometriosis is likely to result in infertility because of adhesions disrupting the anatomical relationships between fallopian tube and ovary. Furthermore, severe dyspareunia and pelvic pain preventing regular sexual intercourse could also affect fertility.

## DIAGNOSIS OF ENDOMETRIOSIS

A clinical history of pelvic pain, particularly if related to the menstrual cycle always suggests a diagnosis of endometriosis. Examination may reveal tenderness or an adnexal mass. Ultrasound scanning, computerized tomography scan, and magnetic resonance imaging may assist in the diagnosis, but none are highly specific and a normal result does not exclude endometriosis.

However, endometriosis can only objectively be confirmed by visualization. This is mainly done by laparoscopy or laparotomy. Laparoscopy allows inspection of the entire pelvis and the extent of disease recorded using a classification system.

## STAGING OF ENDOMETRIOSIS

Since 1922, various classifications of endometriosis have been proposed. In the early 1900's the classification was descriptive. Huffmann<sup>8</sup> in 1951 was a pioneer in recommending treatment according to the stage of the disease. In 1973, Acosta<sup>9</sup> laid the foundations for a predictive classification. For the purpose of uniformity in practice, the American Fertility Society (AFS) proposed its first classification of endometriosis in 1979. As

**TABLE 1: Histology of endometriosis**

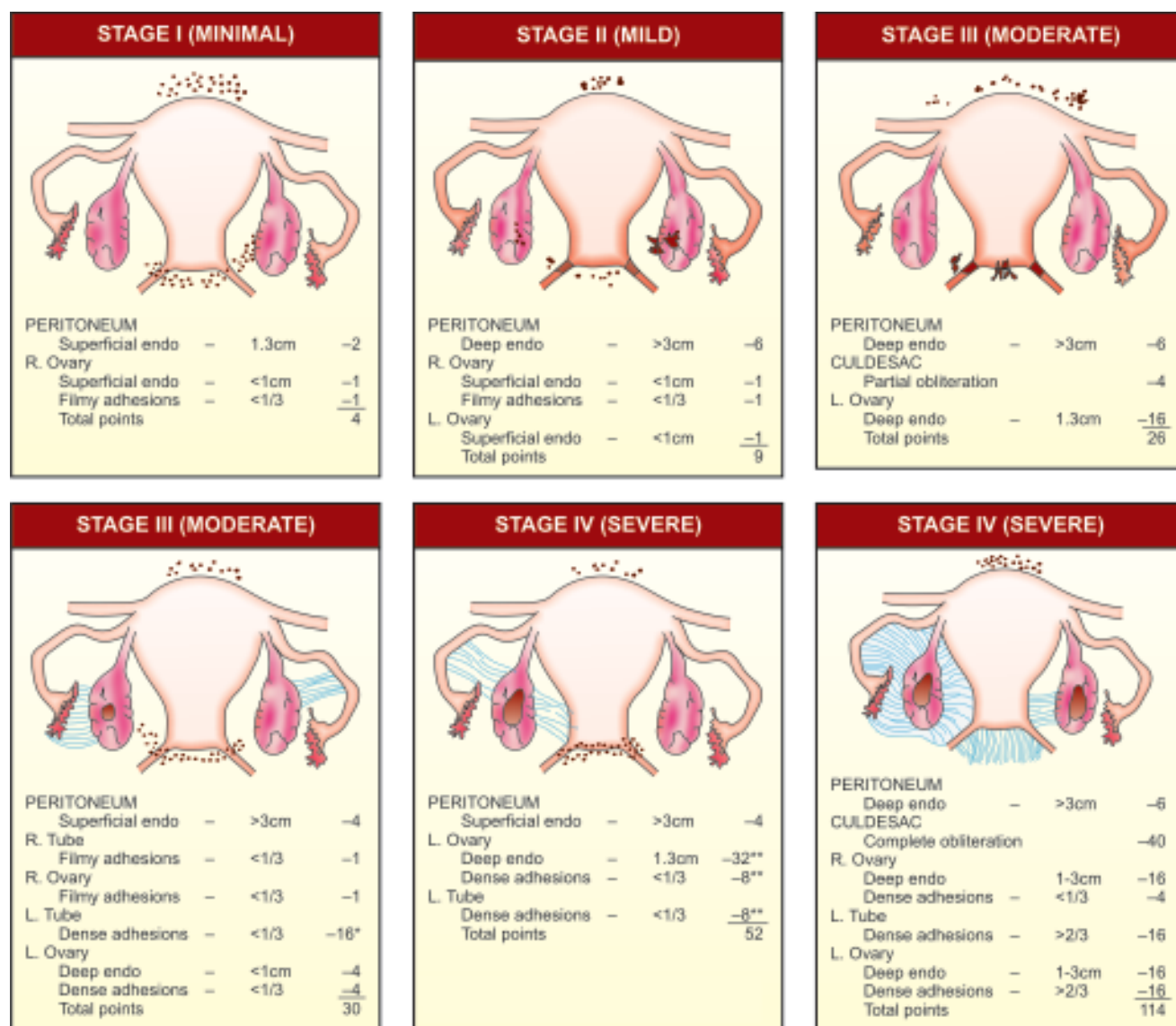
<i>Histological type</i>	<i>Histological appearance Macroscopic</i>	<i>Histological appearance Microscopic</i>	<i>Laparoscopic appearance</i>	<i>Response to treatment</i>
Type 1	Free growing implant or polyp	Surface epithelium and stroma, with or without glands	Hemorrhagic vesicles or spots	Hormone responsive
Type 2	Enclosed implant	Endometrial glands and stroma without surface epithelium	Papules or nodules	Proliferate in response to hormones
Type 3	Healed lesions	Glands only	Nodules or a scar	No response to hormones

there were inadequacies in staging adhesions and deep endometriosis, it was revised in 1985. But the revised AFS showed a very weak relationship between the severity of endometriosis and successful pregnancy outcome. Therefore, it was revised again in 1996<sup>10</sup> and remains the most widely used one. This classification depends on size, site and depth of lesion and point scores were given depending upon severity. Stage I (minimal), Stage II (mild), Stage III (moderate) and Stage IV (severe) (Fig. 1).

The revised AFS score enables easy and clear communication through standardized reporting, but has a number of significant drawbacks. It does not help in the comparison of different treatments and is also unable to predict

the disease progression, impact on future fertility and disease recurrence rate.<sup>11</sup> It has limited clinical relevance in the comparison of populations. This scoring system is prone to observational variation which impairs accuracy and reproducibility.<sup>12</sup> Most recently Kaloo et al<sup>13</sup> criticized the revised AFS as a poor indicator of severity as it does not consider bowel adhesions or multifocal nodular disease.

Currently, therefore, there is no ideal classification of endometriosis available that predicts fertility outcome or assists in the selection of treatment. An ideal classification would reliably correlate disease severity with symptoms and likelihood of conception. It might include a biological marker, as well as laparoscopic appearance.



\*Point assignment changed to 16, \*\*Point assignment doubled

Fig. 1: Shows revised AFS classification 1996. (Revised Endometriosis Classification: 1996, Reproduced with permission from Fertility and Sterility (1997), Volume 67, Number 5 by Schenken RS, Guzick DS)

## TREATMENT OF ENDOMETRIOSIS

Endometriosis can be treated medically and surgically by laparoscopy and laparotomy. Medical hormone treatment has no role in the treatment of endometriosis associated infertility in the absence of pain. This is because any hormonal treatment used to suppress endometriosis is contraceptive and does not improve pregnancy rates.

The treatment of choice will depend on the patient's age, symptoms and previous surgery and fertility requirements. After defining the severity and extent of disease, the choice of treatment should be made in conjunction with the patient. This should take into account the potential risks and complexity of surgery. In the infertile patient particular thought should also be given to alternative treatment such as IVF which may offer them a much better chance of conceiving than surgery.

Surgical treatment includes laser/diathermy ablation to endometriotic implant, adhesiolysis, excision of endometriotic cyst, cyst drainage and/or cyst wall ablation and uterosacral nerve ablation.

The advantages of laparoscopic surgery are quicker recovery time, shorter hospital stay, reduced physical and psychological stress, effective treatment of ovarian endometriomata and relief of pain. At the same time, it may enable a woman to achieve more than one pregnancy, without increasing the risk of multiple pregnancy associated with assisted conception treatment. The limitation of laparoscopy is the surgical intraoperative risk of injury to adjacent structures, infection and adhesion formation. Appropriate surgical skill is required and the availability of appropriate equipment. There is a 6.3% conversion rate to laparotomy associated with gynecological laparoscopy.<sup>14</sup> Therefore patients should be informed preoperatively about the chance of conversion to laparotomy depending upon intraoperative findings. Otherwise laparotomy is indicated only in cases of severe endometriosis with extensive dense adhesions along with deeply infiltrating endometriosis.<sup>15</sup>

Laparoscopic laser treatment or microsurgery during laparotomy increases this rate to 50%.<sup>16</sup> Few studies reported that laparoscopic excision of endometrioma before in vitro fertilization (IVF) reduces the risk of worsening endometriosis during ovarian stimulation, reduces the risk of infection during oocyte retrieval and allows histological diagnosis avoiding occult malignancy. It has therefore been advocated that the best management of endometriosis-associated infertility should be surgical.<sup>17</sup> If spontaneous pregnancy does not occur after surgery, IVF should be considered.<sup>18</sup> A study of laparoscopic treatment of endometriosis following multiple failed IVF has shown benefit in improving pregnancy rates in subsequent IVF cycles and spontaneously.<sup>19</sup> But this study has some limitations such as retrospective study, inadequate power, poor selection criteria for control and subject group and some women in the study had laparoscopic surgery after one cycle of IVF and

without enough explanation. In view of cost effectiveness between laparoscopy and ART, it was criticized that it needs to be considered as an individualized management plan which can't be generalized.

A large randomized controlled trial revealed that laparoscopic ablation of endometriotic implants in minimal to mild endometriosis increased the cumulative pregnancy rate with a 95% confidence interval 1.28 to 3.24 and also the ongoing pregnancy more than 20 weeks with 95% confidence interval 1.18 to 3.22.<sup>20</sup> The investigators compared laparoscopic treatment with no surgical treatment. In contrast an Italian study<sup>21</sup> involving 101 women in 1999 reported no benefit from endometriotic ablation in improving pregnancy rate in minimal/mild endometriosis with a 95% confidential interval of 0.31 to 1.88 for pregnancy rate and for live birth was 0.32 to 2.28. But the Cochrane Systematic review in 2002<sup>22</sup> included these two studies and concluded that use of laparoscopic surgery to manage minimal/mild endometriosis associated infertility may improve reproductive outcome with 95% confidence interval of 1.05 to 2.57 for ongoing pregnancy and live birth rates.

A large prospective study by Adamson et al 1993<sup>23</sup> showed that laparoscopic surgery significantly increases the cumulative pregnancy rate. This was later confirmed by a metaanalysis by Adamson and Pasta in 1994.<sup>24</sup> Adamson in 1997,<sup>25</sup> proposed that surgery for endometriosis-associated infertility is more effective for severe than mild endometriosis and ideally should be carried out at the time of diagnostic laparoscopy. It has been proposed that pregnancy rate depends upon the presence of tubal adhesions and is unrelated to the stage of endometriosis.<sup>26</sup> Laparoscopic treatment therefore is ideal, because it preserves tissue integrity and reduces *denovo* adhesion formation.<sup>27</sup> In 1980's, various small studies supported the successful role of laparoscopic ablation and or resection of endometriotic lesions in treating both moderate/severe and extensive endometriosis. In a five year follow-up of women after laparoscopic surgery, Porpora et al 2002<sup>28</sup> reported a 65% pregnancy rate, with 23% of women conceiving in the first twelve months. After 12 months, the likelihood of conceiving was significantly decreased.

Two randomized controlled trials reported that laparoscopic ovarian cystectomy for endometriomata results in a better pregnancy rate than drainage alone.<sup>29,30</sup> When cystectomy for endometrioma is technically difficult, laparoscopic aspiration of cyst and destruction of cyst wall with laser or diathermy is an acceptable alternative.<sup>31</sup> The advantage of excision over ablation is that the cyst can be examined histologically and a diagnosis of ovarian cancer excluded. There is no advantage of repeating surgery within a short interval as this may reduce ovarian reserve.<sup>32</sup> A randomized crossover study involving 39 women followed up for 12 months reported reduction of chronic pelvic pain and dyspareunia after laparoscopic debulking for rectovaginal endometriosis thereby improving quality of life.<sup>33</sup>

**RESULTS**

Table 2 shows the various studies which looked for the effect of laparoscopic surgery on endometriosis associated infertility.

The studies in the Table 2 include observational studies, randomized controlled studies and non randomized studies which can be retrospective or prospective in nature.

**TABLE 2: Laparoscopic surgery on endometriosis associated infertility**

Author	Sample size	Classification	Selection criteria	Intervention	Follow-up	Outcome			
						PR	LBR	MR	ER
Martin 1985 (abstract only)	50		Endometriosis, Other infer factors	Lap CO <sub>2</sub> laser	7-19 months	60%		(1)	(1)
Seiler et al 1986	90	Acosta	Moderate endomet	Lap electrocautery, Danazol	7 months	44% 39%			
Martin 1986 (abstract only)	115		Endometriosis, Other infer factors	Lap CO <sub>2</sub> laser	12-44 months	48%	69%	28%	1%
Donnez 1987	124	Acosta	Endometriosis Adnexal adhesion	Lap laser, adhesiolysis	18 months		52%	(3/124)	nil
Sutton et al 1990	56	rAFS	Endometriosis alone	Lap laser	1-6 years	80%	69%		
Adamson et al 1992	27	rAFS	Endometriosis Other infer factors	Laparoscopy, Laparotomy	2 years	29.6% 23.7%			
Dlugi et al 1992	74	rAFS	Endometriosis Other infer factors	Lap KTP laser	24 months	38%			
Hull et al 1992			Severe Endometriosis	Lap laser, Laparotomy	2 years	50%			
Adamson et al 1993	575	rAFS	Endometriosis Other infer Factors	Laparoscopy, Laparotomy, no or Medical treatment	> 3 years	82%			
Hughes et al 1993		Acosta rAFS	Endometriosis Endometrioma	Laparoscopy, Laparotomy					
Adamson and Pasta 1994		Acosta rAFS	Endometriosis Endometrioma	Laparoscopy, Laparotomy	3 years 52+/-9%	44+/-6%			
Beretta et al 1998	64	rAFS	Endometrioma >= 3 cm	Lap Excision, Lap coagulation	24 months	66.7% 23.5%			
Hemmings et al 1998	156	rAFS	Endometrioma >3cm Stage 3 and 4 endometr Laparotomy	Lap Excision, Lap ablate	36 months	60%			
Milingos et al 1998	64	rAFS	Endometrioma >= 3 cm	Lap cystectomy Adhesiolysis	2 year	53%			
Chapron et al 1999	30	rAFS	Endometriosis only	Lap resect, ablate	12 months	46%	(12)	(3)	
Maruyama et al 2000	186	rAFS	Endometriosis Tubal adhesion +/-	Lap excision, tubal adhesiolysis	18 months	27.6%			

Contd...

Contd...

Author	Sample size	Classification	Selection criteria	Intervention	Follow-up	Outcome			
						PR	LBR	MR	ER
Jones and Sutton 2002	39	rAFS	Moderate/severe endo endometrioma (2-25 cm)	Lap KTP laser, Diathermy	12 months	39.5%			
Porpora et al 2002	47	rAFS	Adnexal adhesion Tubal status	Lap excise, Ablate adhesiolysis	12-60 months	64.4%			
Elsheikh et al 2003	151	rAFS	Endometriosis	Laparoscopy, No or medical treat	2 year	53%			
Vercellini et al 2003		rAFS	Endometrioma	Lap cautery or laser Lap cystectomy	Variable	24-60%			
Alborzi et al 2004	100	rAFS	Endometrioma > 3 cm	Lap excision Lap fenestration and coagulation of wall	12 months	59.4% 23.3%			
Godinjak et al 2005	45	rAFS	Endometrioma	Lap cystectomy	1 year	35%			

PR—Pregnancy rate, LBR—Live birth rate, MR—Miscarriage rate, ER—Ectopic pregnancy rate (number): Number of cases in relation to sample size, rAFS—Revised American Fertility Society

## CONCLUSION

There is no large, prospective, randomized double-blind controlled trial that specifically addresses the question “does laparoscopic surgery in moderate-severe endometriosis improve pregnancy rates?” A better classification is needed which would correlate symptoms and fertility and aid selection of appropriate treatment. There is good enough evidence to suggest that endometriomata greater than three centimeters in diameter should be excised and examined histologically. In spite of heterogeneity among the available studies, current evidence suggests that laparoscopic excision or ablation either by electrocautery or laser improves pregnancy rates both by natural and assisted conception. Assisted Reproductive Techniques should be considered if conception has not occurred by 12 months after surgery.

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