

**THE STUDY OF RECURRENCE OF
ENDOMETRIOMA FOLLOWING OVARIAN
CYSTECTOMY IN HOSPITAL RAJA
PEREMPUAN ZAINAB II, KOTA BHARU OVER 5
YEARS (2014 to 2018)**

DR SITI SHUHADA BINTI HASAN

**Dissertation Submitted in Partial Fulfilment of
the Requirement for Degree of Master of
Medicine (Obstetrics and Gynaecology)**



UNIVERSITI SAINS MALAYSIA

2022

ACKNOWLEDGEMENT

Praise to Allah S.W.T. the Most compassionate and Most merciful, with His blessings, has helped me through the entire completion of this book. It is a great pleasure to acknowledge the help of several individuals, and without that help, could not have been written this book.

First and foremost, I would like to express my appreciation to my research supervisors, Dr. Ahmad Akram Bin Omar (Lecturer in Department of Obstetrics and Gynaecology, Hospital Universiti Sains Malaysia) and Datin Dr. Salwana Muhyiddin @ Che Kadir (Head of Department and Senior Consultant Obstetrics and Gynaecology, Hospital Raja Perempuan Zainab II) for all support and guidance until completion of this dissertation. Without their assistance and dedicated involvement in every step throughout the process, would have never accomplished this dissertation. I would like to thank you very much for your support and understanding over these past four years.

I am also grateful and much respects are devoted to lecturers, specialists and colleagues in Hospital Universiti Sains Malaysia and in Hospital Raja Perempuan Zainab II for their assistance. I am extremely thankful and indebted to all for sharing expertise and sincere and valuable guidance and encouragement extended to me.

I wish to express my sincere thanks to the staff nurses and attendant in the gynaecology ward and in clinics Obstetrics and Gynecology Hospital Raja Perempuan Zainab II, for providing me with all the necessary facilities for the research.

A special award to my beloved husband, Ahmad Hulaimi Bin Abdul Halim and my parents and in-laws for their tolerance of my absences, their unwavering support and encouragement and the faith in me and my task.

Last but not least, to all the patients to one and all, who directly or indirectly, have lent their hand in this venture.

Siti Shuhada Hasan

TABLE OF CONTENTS

TABLE OF CONTENTS	vi
LIST OF FIGURE.....	vi
LIST OF TABLE	vii
LIST OF ABBREVIATIONS.....	viii
ABSTRAK.....	ix
ABSTRACT.....	x
1.0 INTRODUCTION.....	11
1.1 EPIDEMIOLOGY AND RISK FACTORS.....	13
1.2 PATHOPHYSIOLOGY OF THE DISEASE	15
1.3 CLINICAL MANIFESTATION	16
1.4 INVESTIGATION.....	17
1.5 MANAGEMENT	19
2.0 LITERATURE REVIEW.....	22
2.1 RECURRENCE RATE OF ENDOMETRIOMA AFTER CYSTECTOMY.....	22
2.2 FACTORS ARE ASSOCIATED WITH THE RECURRENCE OF ENDOMETRIOMA AFTER CYSTECTOMY.....	24
2.2.1 AGE.....	25
2.2.2 DYSPENORRHEA , PELVIC PAIN AND DYSURUNIA.....	25
2.2.3 CYST SIZE.....	26
2.2.4 CA 125.....	27

2.2.5	ASRM SCORE.....	27
2.2.6	PREOPERATIVE MEDICAL TREATMENT.....	28
2.2.7	POSTOPERATIVE MEDICAL TREATMENT.....	29
2.2.8	TYPE OF INTERVENTION.....	30
3.0	JUSTIFICATION OF STUDY	31
4.0	OBJECTIVES	32
4.1	GENERAL OBJECTIVE.....	32
4.2	SPECIFIC OBJECTIVES.....	32
5.0	METHODOLOGY	33
5.1	STUDY DESIGN, SETTING AND DURATION	33
5.2	REFERENCE POPULATION.....	33
5.3	SOURCE POPULATION.....	33
5.4	STUDY PARTICIPANTS	33
5.5	SAMPLE SIZE CALCULATION	33
5.6	ETHICS AND CONSENT	36
5.7	INCLUSION AND EXCLUSION CRITERIA	36
5.7.1	INCLUSION CRITERIA.....	36
5.7.2	EXCLUSION CRITERIA.....	36
5.8	SAMPLING METHODS.....	36
5.9	STUDY METHOD.....	37
5.10	DATA COLLECTION	39

5.10	INTENDED STATISTICAL ANALYSIS	39
5.11	DEFINITION OF OPERATIONAL TERMS.....	40
5.12	STUDY FLOW CHART	43
6.0	MANUSCRIPT	44
	ABSTRACT.....	46
	INTRODUCTION	47
	METHODOLOGY	49
	RESULT.....	50
	DISCUSSION.....	56
	REFERENCES	61
7.0	APPENDICES.....	68
7.1	RESEARCH PROFORMA (Appendix 1).....	68
7.2	RESULTS (Appendix 2).....	71
7.3	ETHICAL COMMITTEE APPROVAL (Appenix 3).....	77
7.4	MEDICAL JOURNAL OF MALAYSIA (MJM) FORMAT (Appendix)..	79

LIST OF FIGURE

THESIS

	Page
Figure 1 Ttransvaginal ultrasound image of endometrioma	18
Figure 2 Classification of endometriosis	21

LIST OF TABLE

THESIS

	Page
Table 1 : Sample size calculation	33
Table 2 : Sample size calculation	34

MANUSCRIPT

Table 1: Recurrence case according to the demographic data	50
Table 2: Recurrence case according to preop assessment	51
Table 3 : Recurrence case according surgical and intraoperative intervention and postoperative treatment.	53
Table 4 : Time of diagnosis of recurrence endometrioma postoperative and cyst finding during diagnosis	54
Table 5 : Indication for surgical intervention	74

LIST OF ABBREVIATIONS

ESHRE	The European Society of Human Reproduction and Embryology
ASRM	American Society for Reproductive Medicine
CA 125	Cancer antigen 125
SD	Standard deviation
MRI	Magnetic resonance imaging
COCP	Combine oral contraception pills
GnRH α	Gonadotropin hormone-releasing hormone
GnRH	Gonadotropin hormone-releasing hormone
HRT	Hormone replacement therapy
TAHBSO	Total Abdominal Hysterectomy and Bilateral Salpingo Oophorectomy
OCP	oral contraception pills
HPE	Histopathological examinations
DNG	Dienogest
LNGIUS	Levonogestrel intrauterine system

ABSTRAK

OBJEKTIF: Untuk menentukan kadar berulang endometrioma selepas pembedahan sistektomi dan faktor risiko yang berkaitan untuk kes berulang endometrioma antara sosiodemografi, perincian mengenai penyakit dan data lain yang berkaitan .

KAEDAH KAJIAN: Kajian kohort retrospektif ini melibatkan semua pesakit ginekologi yang pernah menghadiri klinik Ginekologi Hospital Raja Perempuan Zainab II dan telah di diagnosis sebagai endometrioma. Data sosiodemografi, perincian mengenai penyakit serta perincian lain yang berkaitan diambil dari catatan kes. Data dianalisis yang digunakan bergantung pada normalitas data untuk mencari hubungan antara kambuhan endometrioma dan faktor risiko serta data sosiodemografi.

KEPUTUSAN: Seramai 29 pesakit mengalami endometrioma berulang semasa rawatan selepas pembedahan. Kadar berulang keseluruhan ialah 17.5% (n=29). Masa berulang adalah 9.2 bulan (julat 6 hingga 12 bulan) selepas sistektomi. Faktor risiko signifikan secara statistik dalam umur diagnosis, pengalaman dismenorea untuk data demografi, CA 125 dan melibatkan kedua-dua belah ovari adalah faktor penting dalam penilaian praoperasi. Laproskopik sebagai cara pembedahan, sis pecah semasa pembedahan, lebih tinggi dalam peringkat ASRM, rawatan selepas pembedahan dan tempoh rawatan berkorelasi dengan ketara dengan endometrioma berulang.

KESIMPULAN: Melihat keputusan secara keseluruhan, kami menyimpulkan pengenalpastian faktor risiko untuk berulang membantu doktor untuk memaklumkan pesakit. Pengesanan faktor risiko praoperasi akan membantu dalam kaunseling pesakit tentang prognosis di masa hadapan mereka dan manfaat kepada pakar bedah dalam memilih jenis pembedahan. Rawatan selepas pembedahan diperlukan sebagai pengurusan jangka panjang untuk mengawal penyakit. Kajian ini telah menunjukkan bahawa rawatan selepas pembedahan dan teknik pembedahan mempunyai kesan yang kuat ke atas berulang atau selang bebas penyakit.

ABSTRACT

OBJECTIVE: We sought to determine the recurrence rate of endometrioma after cystectomy and the associated risk factors for recurrence of endometrioma between sociodemographic, details regarding the disease and other related details.

STUDY METHOD: This retrospective cohort study involved all gynecology patients who had attended the Gynecology clinic Hospital Raja Perempuan Zainab II and were diagnosed as endometrioma. Retrieved sociodemographic data, assessment of the disease and other related details from the case notes. The test to analyze the data were depended on the variable and on normality of data to look for the association between the recurrence of endometrioma and the associated risk factors.

RESULT: 29 patients experienced of recurrence endometrioma in the present of post operative treatment. The overall recurrence rate was 17.5% (n=29). Recurrence time was 9.2 months (range 6 to 12 months) after cystectomy. Risk factors statistically significant in age of diagnosis, experience of dysmenorrhea ,CA 125 and bilaterality. Laparoscopic as surgical intervention, intraoperative cyst ruptured, higher in ASRM staging, post operative treatment and the duration of treatment were significantly correlated with recurrence endometrioma.

CONCLUSION: Looking at results overall, we concluded that identification of risk factors for recurrence helps clinicians to counsel patients regarding their future prognosis and benefit to surgeon in choosing type of surgical intervention. Post operative treatment is required as long term management to control the disease. This study has demonstrated that the post operative treatment and surgical technique have a strong impact on the recurrence or disease free interval.

1.0 INTRODUCTION

Endometriosis is the presence of endometrial tissue with glands and stroma outside the uterus similar to normal endometrium. Endometriosis is a chronic benign estrogen-dependent disease ⁽¹⁾.

Based on the locations of the lesions, the disease is classified as peritoneal, ovarian or deep infiltrating endometriosis. It can be found deposited throughout the pelvis, most commonly on the uterosacral ligament and ovaries. Ovarian endometriosis can lead to accumulated altered blood, causing an endometrioma or chocolate cyst. Ovarian endometriosis is the most common type, accounting 17% and 44% of all endometriosis. Occasionally, endometriosis affects vagina, umbilicus, abdominal wound scars, bladder, rectum and even the lungs ⁽¹⁾.

Ovarian endometriosis or endometrioma, is one of the most common manifestations among reproductive women with endometriosis. The European Society of Human Reproduction and Embryology (ESHRE) recommends that histology should be obtained to exclude malignancy when the diameter of ovarian endometriosis is more than 3 cm. Among types of endometriosis linked ovarian cancer, endometrioid and clear-cell are the commonest.

Although definite treatment of endometriosis is a hysterectomy with removal of the both ovaries, conservative surgery is preferred as the treatment of endometriosis and ovarian cyst when fertility still needs to be preserved ⁽²⁾.

Although endometriosis is a benign disease, its clinical spectrum varies widely, independent from its severity, endometriosis induces a chronic inflammatory process. As a result, the clinical spectrum might present dysmenorrhea, chronic pelvic pain, dyspareunia and infertility, even though most of the cases are asymptomatic.

Its prevalence is uncertain because depending on the population examined. Its incidence varies from 6 to 25%. It is observed primarily in patients of reproductive age, and its prevalence in this population is estimated to be 5–10%. Endometriosis causes the impaired quality of life (QoL) for women of reproductive age and has malignant clinical manifestation despite being a benign disease ⁽¹⁾.

1.1 EPIDEMIOLOGY AND RISK FACTORS

While the prevalence varies with the population being studied, approximately 10% of reproductive-age women globally have endometriosis. However, determining the prevalence of endometriosis in the general population is challenging because some women are asymptomatic. Those with symptoms can have varied and nonspecific presentations and definitive diagnosis typically requires surgery ⁽²⁾.

In a case-control Ballard et al. (2008) of over 5500 women from a national database, the prevalence of endometriosis varied from 1.2 to 1.5% , depending upon the inclusion criteria. The majority of endometriosis in symptomatic referral populations appears to be much higher. According to the journal by Dovey et al. (2010) endometriosis has been reported in up to 40% of adolescents with genital tract anomalies, up to 50% of women with infertility and up to 70% of women and adolescents with pelvic pain.

Regarding the risk factors, risk of endometriosis increased in null parity, prolonged exposure to endogenous estrogen (eg, early menarche (before age 11 to 13 years) or late menopause, shorter menstrual cycles (defined as ≤ 27 days), heavy menstrual bleeding, obstruction of menstrual outflow (eg, müllerian anomalies), exposure to diethylstilbestrol in utero, height greater than 68 inches, lower body mass index , exposure to severe physical and/or sexual abuse in childhood or adolescence, and a high consumption of trans unsaturated fat. Then, factors associated with a decreased risk of endometriosis include multiple births, extended intervals of lactation, and late menarche (after age 14 years) ⁽²⁾.

Regarding risk of endometrioma, a retrospective study was published by Kavoussi et al. (2017) revealed the incidence of ovarian endometrioma among women with peritoneal endometriosis with and without a history of hormonal contraceptive use less common in those women who had used oral contraceptive pills compared with women who had not (18 versus 49%).

1.2 PATHOPHYSIOLOGY OF THE DISEASE

Many theories regarding endometriosis have been postulated but the definite pathophysiology remains unknown.

According to the commonest theory of ectopic endometrial cells(Sampson's theory of retrograde menstruation), endometrial cells flow backwards through the fallopian tubes and into the peritoneal cavity during menses. When it happens, will disseminate the endometrial tissue and implant onto the peritoneal layer and cause peritoneal endometriosis. Endometriotic implants are very sensitive to the estrogen and progesterone stimulation as they will bleed as menstruation bleeding then irritating lead to pelvic pain and dysmenorrhea⁽²⁾.

Beside that, coeleomic metaplasia theory which embryologically, the coeleomic epithelium gives rise to the epithelium of the mullerian duct, the peritoneum and pleural cavities and ovaries. An unknown induction agent may stimulate endometrial differentiation of these tissues⁽¹⁾.

In addition,embolization theory which endometrial cells may spread via the lymph or blood vessels to ectopic sites.

1.3 CLINICAL MANIFESTATIONS

Usually patients with endometriosis classically present during their reproductive years with pelvic pain (including dysmenorrhea and dyspareunia), infertility, or an ovarian mass. However, women can also present with endometriosis that was incidentally diagnosed during surgery or imaging for other indications. While the peak prevalence of endometriosis occurs in women 25 to 35 years of age, the disease has been reported in premenarche girls and in 2 to 5% of postmenopausal women.

In addition, approximately 80% presented with pain, 25% with infertility, and 20% with an endometrioma (ovarian mass). Dysmenorrhea associated with endometriosis is dull or crampy pelvic pain that typically begins one to two days before menses, persists throughout menses, and can continue for several days afterward. Pelvic pain is usually chronic and described as dull, throbbing, sharp, and/or burning. Pelvic pain or pressures are also the most common symptoms associated with adnexa mass.

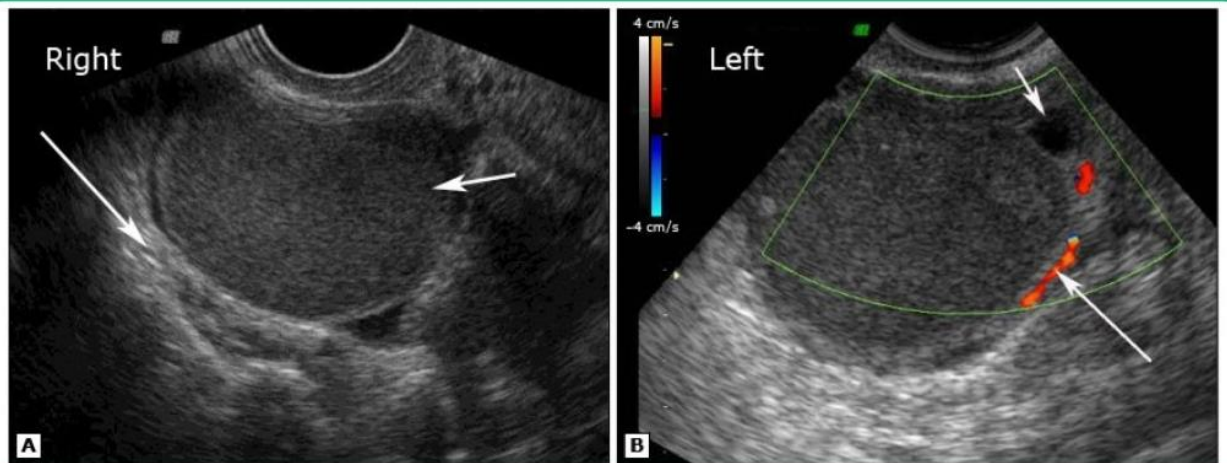
1.4 INVESTIGATION

To diagnose the endometriosis in general is guided by the patient symptoms, and physical examination findings. However there are no pathognomonic laboratory findings for endometriosis. Serum cancer antigen (CA 125) concentration can be elevated in women with endometriosis (ie, greater than 35 units/mL), although the role of serum CA 125 in primary diagnosis is undefined. However, serum CA 125 concentrations are not routinely ordered in women being evaluated or treated for endometriosis because other diseases, notably ovarian carcinoma, also elevate the serum CA 125 concentration.

Ultrasonography is useful in the diagnosis of fibroid and to screen and assess adnexal mass. The findings suggestive of pelvic endometriosis include ovarian cysts (endometriomas), nodules of the rectovaginal septum, and bladder nodules. These findings are typically seen with transvaginal ultrasound but can also be viewed with magnetic resonance imaging (MRI).

Endometrioma are generally easily classifiable on sonography appears as a unilocular or multilocular cystic mass on ultrasound, typically containing homogenous internal echoes. The ultrasound appearance of an endometrioma is often described as containing 'ground glass' internal echoes. The chocolate – colored fluid, or old blood contained in the cyst, has a classic appearance as in figure 1 below:

Endometrioma



(A) Transvaginal ultrasound image of the right adnexa showing an endometrioma. The homogeneous echo pattern of the cyst contents (ie, "ground-glass" appearance) is characteristic of an endometrioma (short arrow); the cystic nature of the endometrioma is also indicated by the post-cyst enhancement (long arrow).

(B) Transvaginal ultrasound with color Doppler image of the left adnexa showing a benign endometrioma of the left ovary viewed with color Doppler imaging. No flow within the cyst can be demonstrated; however, blood flow is demonstrated within the wall of the cyst in the ovarian tissue itself (long arrow). Also identified within the left ovary is a small follicle (short arrow).

Source : Uptodate

Figure 1 :Transvaginal ultrasound image of endometrioma

1.5 MANAGEMENT

The choice of treatment will depend on age, fertility plans, the severity of symptoms and site of the disease. Management can be dividing to three, conservative, medical treatment and surgical intervention.

For conservative treatment, women choose to use simple analgesia. This avoids hormonal preparations and is useful in women trying to conceive. In addition, patient support groups can provide valuable advice and counseling for women with endometriosis.

Medical treatment, aims to cause atrophy of ectopic endometrium. The COCP, progesterone or gonadotrophin-releasing hormone (GnRH) agonist may be used. All are equally effective at reducing pain associated with endometriosis. However, side effects limit their use. GnRH agonist are sometimes combined with add-back HRT. Symptoms recurrence is common with cessation of treatment as the primary biological mechanism is not addressed.

Surgical intervention is based on their indication, include diagnosis of persistent pelvic pain that does not respond to medical therapy, evaluation of severe symptoms that limit function, and treatment of anatomic abnormalities, such as bladder lesions. Surgery, almost always laparoscopy, allows both definitive diagnosis and treatment ⁽²⁾.

Up to 70% of women with mild to moderate disease report symptomatic improvement after surgery. Benefits appear to be more long lasting than with medical treatment. Up to 90% of women continue to report symptomatic relief at 1 year. GnRH agonist use postoperatively significantly prolongs the pain-free interval. Laparoscopic ablation may also improve fertility rates.

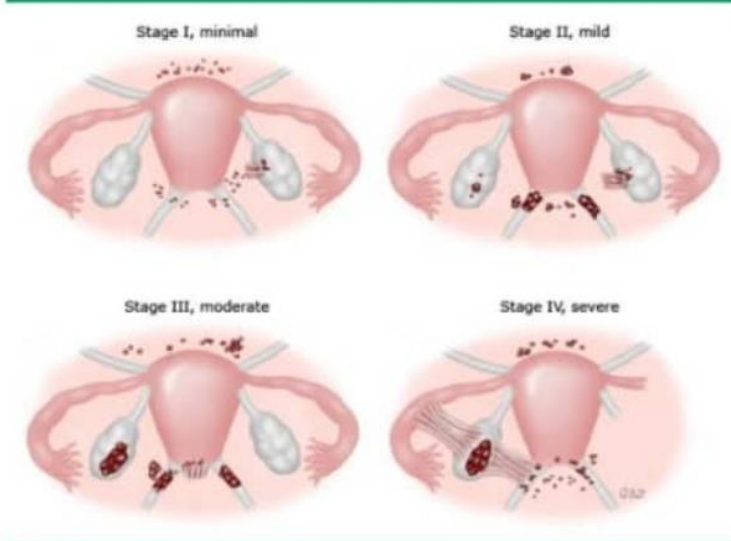
Endometrioma can be de-roofed and removed laparoscopically. The goals of endometrioma treatment are to relieve symptoms (eg, pain or mass), prevent complications related to the adnexal mass (eg, rupture or torsion), exclude malignancy, improve subfertility and preserve ovarian function⁽¹⁾. Therefore, one of the most important considerations is the patient's desire for fertility when determining the level of intervention needed to preserve the ovaries and their function. In this case, the surgical options available include excision of the cyst wall or drainage and coagulation of the cyst bed.

First line treatment for surgical intervention is cystectomy because cystectomy removes the endometriosis but leaves the normal ovary. Oophorectomy, or removal of the ovary with the cyst intact, is a definitive treatment mainly used in women who have recurrent cysts, have completed childbearing, are postmenopausal, or who have concerns for malignancy. Cystectomy preferably by laparoscopy, is preferred to cyst drainage or cyst wall ablation to treat pelvic pain or infertility. Aspiration alone is ineffective, 80 to 100% of recurrence rates have been reported at six months of follow-up. It has been observed that postoperative hormonal suppression can achieve a lower recurrence rate and better management of symptoms can. COCP (cyclical or continuous), should be considered in patients that do not wish to conceive after surgery.

TAHBSO are occasionally performed to alleviate symptoms. However, this operation is often technically difficult and should be a last resort, when all other treatment has failed and the women have completed her family ⁽¹⁾. Endometriosis is surgically staged according to the revised American Society for Reproductive Medicine scoring system ⁽²⁾:

- **Stage I** – Minimal disease is characterized by isolated implants and no significant adhesions.
- **Stage II** – Mild endometriosis consists of superficial implants that are less than 5 cm in aggregate and are scattered on the peritoneum and ovaries. No significant adhesions are present.
- **Stage III** – Moderate disease exhibits multiple implants, both superficial and deeply invasive. Peritubal and periovarian adhesions may be evident.
- **Stage IV** – Severe disease is characterized by multiple superficial and deep implants, including large ovarian endometriomas. Filmy and dense adhesions are usually present.

Examples of the classification of endometriosis



Original figure modified for this publication. Revised American Society for Reproductive Medicine classification of endometriosis: 1996. Fertil Steril 1997; 67:817. Illustration used with the permission of Elsevier Inc. All rights reserved.

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Source : Uptodate 2021

Figure 2 : Classification of endometriosis

2.0 LITERATURE REVIEW

2.1 RECURRENCE RATE OF ENDOMETRIOMA AFTER CYSTECTOMY

Hysterectomy with removal of both ovaries is a definite treatment for endometriosis, however, conservative surgery is preferred as the treatment of endometriosis and ovarian cyst when fertility is concern. However, the most concerning issue after conservative surgery is the recurrence of endometrioma ⁽⁶⁾.

The prevalence of endometriosis might differ according to the cohort of women, the recurrence rate also depends on the study group, the definition of recurrence, sample size, length of follow-up, the radicalism of the surgery, and the experience of the surgeon and postoperative intervention.

However, the definition of “recurrence” varied widely, from the recurrence of symptoms to the re-elevation of a tumor marker, CA125, to the ovarian morphological findings based on ultrasonography.

Many previous studies discussed the recurrence of ovarian endometrioma after laparoscopic excision, given requirements of reoperation (Busacca et al. (1999), Saleh and Tulandi (1999), Abbott et al. (2003)) or pain recurrence (Busacca et al., (1999) Abbott et al. (2003)). Busacca et al.(1999) evaluated 144 recurrences of endometriosis and found the 4-year recurrence rates as 24.6, 17.8, 30.6, 23.7% for ovarian, peritoneal, deep and peritoneal endometriosis, respectively. The rates of recurrence increase as time passed after the diagnostic surgery and 8 year recurrence rates are 42, 24.1, 43.4 and 30.9%, respectively ⁽⁵⁾. Similarly, Parazzini et al. (2005) reported that whereas the 2-year recurrence rates for stage I and II endometriosis were 5.7%, they were 14.3% for stage III and IV endometriosis.

Once meta-analysis or systematic reviews are taken into account, when 23 trials are analyzed, Vignali et al. (2005) expressed that the respective rates of recurrence for 3 and 5 years are 20.5 and 43.5% for the relapse of pain. However, the clinical recurrence rates after those periods of time were 9 and 28% ⁽³⁾.

In addition, a by Saleh et al. (1999) reported that the percentage of patients who experienced postoperative recurrence of cysts of at least 3 cm in diameter and required reoperation was 6.1% over 18 months and 23.6% over 42 months during their observation period.

Other than that, in research by Busacca et al. (2006) reported a cumulative recurrence rate of 11.7% over 48 months based on ultrasonography in 366 endometriotic patients who had cysts of at least 3 cm in size and underwent laparoscopic surgery. Most of the studies use the same definition of recurrence; however the rate ranges from 6.1% to 23%.

2.2 FACTORS ARE ASSOCIATED WITH THE RECURRENCE OF ENDOMETRIOMA AFTER CYSTECTOMY

Recurrence may occur due to the re-growth of residual endometriotic lesions that did not completely removed in the surgery, growth of microscopic endometriosis undetected at surgery or the development of de-novo lesions or a combination of these conditions.

Several risk factors have been evaluated to predict recurrence after cystectomy. Younger age, history of endometriosis surgery, bilateral ovarian involvement, nodularity in Douglas, advanced stage disease at initial surgery, postoperative higher American Society of Reproductive Medicine (ASRM) scores, completeness of the first surgery and medical treatment history are some of the evaluated risk factors for increased recurrence (Kikuchi et al. (006); Koga et al. (2006); Liu et al. (2007)).

This study, aimed to investigate pre and post operative factors that might influence the recurrence rate of endometrioma after cystectomy. Preoperatively, all patients should be assessed thoroughly include body mass index, marital history, years of infertility, obstetrics history, menstrual history, date of diagnosis and medical history was obtained gynaecological examination and transvaginal ultrasound, and routine laboratory tests were performed. Endometrioma was suspected if a homogeneous hypoechogenic ovarian cyst with a thick wall was visible on ultrasonography.