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Factors associated with recurrent endometriomas after surgical excision

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Abstract

Background Endometriosis affects women in reproductive age and causes a great impact on their lives. When affecting the ovary, excision represents the main management option. However, recurrence represents a challenging situation for patients and physicians. This study aimed to determine factors contributing to endometriomas recurrence after surgical excision.

Results This was a quasi-experimental study recruiting 60 patients with ovarian endometrioma. The mean age was 30.33 ± 7.95 years. The mean parity was 1.27 ± 0.69. The recurrence rate after excision was 11/60 (18.3%) after a mean follow-up period of 22.62 ± 4.96 months. None of the patients' characteristics or endometriosis-related characteristics were significant factors contributing to cyst recurrence (age, parity, history of infertility, preoperative endometrioma diameter, preoperative AFC, preoperative AMH, degree of pelvic pain, degree of dysmenorrhea, degree of dyspareunia, pelvic tenderness, and induration) (p value > 0.05).

Conclusion The patient's related factors and endometrioma characteristics did not predict its recurrence.

Keywords Endometrioma, Recurrence, Prediction

Background

Endometriosis is a gynecological condition which affects women of reproductive age, causing infertility, dysmenorrhea, and dyspareunia [1]. Surgical excision is the principal treatment, as medical options are of limited efficacy. Although effective, surgery is associated with multiple complications, with recurrence representing a challenging one reaching 40–45% after 5 years [2] and reoperation rates of 27% [3]. Additionally, fertility decline was noted to be more prominent after further interventions rather than after primary surgery [4]. This makes endometriosis a dreadful disease, and concerns about avoiding recurrence are paramount [5]. Several studies evaluated the role of adjuvant therapies in preventing recurrence as hormonal treatments [6]. Variable results were reported with a predilection toward the insignificant impact of hormonal treatment in preventing recurrence [7, 8]. Determining possible factors associated with recurrent endometriomas would influence treatment decisions and optimize treatment planes [9]. Accordingly, this study evaluated factors affecting endometrioma recurrence after laparoscopic excision.

Methods

This quasi-experimental study was conducted in the Obstetrics and Gynecology Department at Suez Canal University Hospital from November 1, 2020, to July 31, 2022. We recruited eligible patients during the study duration according to prespecified inclusion and exclusion criteria. Inclusion criteria: (a) unilateral endometrioma, (b) unilocular endometrioma 3–8 cm, (c) age 18–45 years, (d) regular cycles, (e) no previous history of ovarian operations, and (f) patients undergoing surgical excision of the endometrioma by laparoscopy. Exclusion criteria: (a) suspected or confirmed malignancy, (b) women within 2 years of menarche, (c) women on

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progesterone only or combined hormonal contraception, (d) women refusing to participate in the study, and (f) women preferring medication for the management of endometriomas.

Informed consent was obtained from all eligible study participants after adequately explaining the study procedures and aim. Eligible patients were subjected to the following:

1- Complete personal and medical history. Data about pelvic pain, dysmenorrhea, and dyspareunia were obtained and graded as mild, moderate, or severe.
2- The local gynecological examination, performed by the same researcher, focused on evaluating pelvic tenderness and induration and was graded into mild, moderate, or severe.
3- Ultrasound examination to diagnose ovarian endometrioma and measure its diameter [10]. The antral follicle count (AFC) of the affected ovary was evaluated on days 2–3 of the cycle by determining the number of follicles measuring 2–10 mm [11].
4- Routine preoperative laboratory investigations such as complete blood count, coagulation profile, liver function test, and anti-mullerian hormone (AMH) were withdrawn.
5- Patients were prepared for laparoscopic cystectomy. Any adhesions were lysed to free the ovary before excision. An incision in the endometrioma was done. Suction of the endometrioma contents was done. Stripping of the cyst wall from the ovarian tissue was done. Handling of the ovary was done using atraumatic grasping forceps. Bipolar cauterization was used to achieve hemostasis using pinpoint coagulations to avoid thermal damage to the ovary. Complete removal of the cyst wall was ensured [12]. No hormonal treatment was offered after the operation.
6- Initial follow-up visit was after 3 months. However, longer duration of follow-up was recommended to evaluate recurrences properly. Accordingly, further follow-up was done after at least 1 year of the operation. Recurrence was defined as cyst diameter > 10 mm [5].

Statistical analysis

Data were statistically described as mean and standard deviation, frequencies (number of cases), and percentages when appropriate. *P* value of less than 0.05 were considered statistically significant. All statistical calculations were done using the computer program SPSS (Statistical Package for the Social Science; SPSS Inc., Chicago, IL, USA), release 23 for Microsoft Windows. Comparison between patients with recurrent endometriosis and those without was done by the student *T* test. Multivariate and univariate regression analysis was performed to determine possible factors associated with cyst recurrence.

Results

Sixty patients were recruited throughout the study duration. The mean age was 30.33 ± 7.95 years. The study population was either virgins or married/divorced/widowed equally. The mean parity of the married/divorced/widowed patients was 1.27 ± 0.69. The mean follow-up period was 22.62 ± 4.96 months (Table 1).

The recurrence rate after excision was 11/60 (18.3%). The mean endometrioma size after recurrence was 3.27 ± 0.17. There was no significant difference in the ovarian reserve either before or after surgery as represented by AMH and AFC levels between patients who had recurrent endometriosis and those who did not (*P* value > 0.05) (Table 2). There was no significant difference in the extend of dysmenorrhea between both groups (*p* value 0.575).

None of the patients' characteristics or endometriosis-related characteristics were significant factors contributing to cyst recurrence by multivariate analysis (age, parity, history of infertility, preoperative endometrioma diameter, preoperative AFC, preoperative AMH, degree of pelvic pain, degree of dysmenorrhea, degree of dyspareunia, pelvic tenderness, and induration) (*p* value > 0.05) (Table 3).

Discussion

After surgical excision, recurrence was noted in 18.3% of the participants. The recurrence rate after endometrioma excision was reported to be high. It ranged from 29 to 56% after 2 years, while after 5 years, it was 43% [13] without postoperative medical treatment. Another study reported a recurrence rate of 6.4%. This study conducted follow-up visits every 3 months of surgery, and the results were reported after a mean follow-up period of 22.62 ± 4.96 months, while they reported their

Table 1 Basic demographic data of the studied population (*N* = 60)

Age (years) (mean ± SD)		30.33 ± 7.95
Occupation *N* (%)	Not working	29 (48.33%)
	Working	31 (51.67%)
Residence *N* (%)	Urban	28 (46.67%)
	Rural	32 (53.33%)
Marital status *N* (%)	Virgin	30 (50%)
	Married/divorced/widowed	30 (50%)
Parity (mean ± SD)		1.27 ± 0.69
Mean follow-up period (months) (mean ± SD)		22.62 ± 4.96

Table 2 Ovarian reserve and endometrioma size between patients with recurrent endometriomas and those without

	Recurrent endometrioma 11/60 (18.3%)	No recurrence 49/60 (81.7%)	*P* value
Age	33.5 ± 6.9	29.6 ± 8.04	0.139
Parity	1.5 ± 0.6	1.2 ± 0.7	0.244
Preoperative endometrioma diameter	5.9 ± 1.6	5.3 ± 1.76	0.354
Postoperative endometrioma diameter	3.27 ± 0.17	0.07 ± 0.53	0.0001
Preoperative AFC	5.9 ± 1.6	5.2 ± 2.2	0.809
Postoperative AFC	3.9 ± 1.4	3.3 ± 1.7	0.469
Preoperative AMH	1.76 ± 0.4	1.8 ± 0.4	0.843
Postoperative AMH	1.5 ± 0.44	1.5 ± 0.43	0.649

Table 3 Multivariate analysis for the factors affecting recurrent endometriomas after laparoscopic excision

	Beta	95% confidence interval	*P* value
Constant	−0.108	−2.328–2.113	0.920
Age	0.008	−0.027–0.044	0.626
Parity	0.070	−0.297–0.436	0.694
Infertility	−0.221	−0.662–0.221	0.307
Endometrioma diameter	0.003	−0.137–0.143	0.961
AFC (preoperative)	−0.013	−0.131–0.106	0.822
AMH (preoperative)	0.086	−0.462–0.633	0.745
Degree of pain	0.122	−0.181–0.426	0.408
Degree of dysmenorrhea	0.105	−0.256–0.466	0.546
Degree of dyspareunia	−0.029	−0.284–0.227	0.815
Pelvic tenderness	−0.136	−0.431–0.160	0.347
Induration	−0.054	−0.351–0.243	0.706

results after 5 years. A large number of their participants received postoperative hormonal treatment in the form of oral contraceptives, Mirena for at least 1 year, Gonadotropin releasing hormone analogs (GnRHa) for 3–6 months, or GnRHa followed by Mirena. Only 3.4% of their studied population did not receive any hormonal treatment which might impact the recurrence rates after surgery [14]. Hormonal treatment leads to apoptosis of the ectopic endometrial implants either in the pelvis or de novo implants leading to decreased recurrences [15]. The current study provided no medical treatment after surgery. Immune cells and extracellular matrix metalloproteinase lead to the proliferation and survival of endometriotic cells, explaining recurrent endometriosis [16].

Recurrent endometriosis differed in its rate between studies. This was rendered to the variable factors contributing to its recurrence as the definition of recurrence depended on subjective pain sensation or clinical and radiological evaluation. Also, the type of endometriosis, disease severity, method of excision, surgical skills, and time to recurrence was reported [5]. The evaluation of recurrence depending on symptoms was higher than the sonographic evaluation, with a poor correlation between pain and actual recurrence [17]—the current study evaluated recurrence using ultrasound after 3 months of excision.

There was no difference in the endometrioma size before surgery among women with recurrent endometriosis and those without. Also, there was no difference in age, parity, extend of dysmenorrhea, and the ovarian reserve before and after surgery among both groups. This was evident in an earlier study where there was no difference in patients' age, parity, and BMI among those with recurrent endometriosis and those without. However, the extent of dysmenorrhea was increased significantly among those with recurrent endometriosis (p value 0.001) [14]. This difference would be related to the presence of concomitant conditions as adenomyosis which was not evaluated in our study population. it has been reported that dysmenorrhea was evident in women with adenomyosis due to associated deeply situated dense endometrial glands in the myometrium [18].

The current study demonstrated no significant risk factor associated with cyst recurrence. Another study done by Koga et al. 2006 demonstrated that previous history of medical treatment and endometrioma size predicted recurrence significantly [19]. An earlier study reported that younger age at surgery was associated with recurrent endometriosis. This was rendered to the increased estrogen concentration in younger women leading to preoperative hormonal treatment which results in atrophy and reduced size of the endometriotic lesions leading to missed removal in surgery [20]. It has been reported that risk factors contributing to endometriosis recurrence were heterogeneous among studies. The stage of endometriosis, adhesions, and size and number of endometrioma did not influence recurrence while previous surgery was significantly associated with recurrence. This was explained by the progressive and aggressive nature of the disease [21]. Another study concluded

that dysmenorrhea and ovarian cyst separations were associated with endometrioma recurrence [22]. Dysmenorrhea was rendered to the disease itself as a result of bleeding from focal endometriotic implants, release of inflammatory mediators, and direct irritation of the pelvic nerves and peritoneum [22]. While Selcuk et al. mentioned that deeply penetrating endometrial tissue in the ovary was significantly associated with recurrent endometrioma [23]. This was explained by decreased apoptosis and increased proliferation with deeply infiltrated endometriosis [22].

Other mechanical factors explaining recurrent endometriosis were regrowth of endometriotic lesions from residual loci [24], which was emphasized by the reappearance of endometriotic lesions at the same site after excision [25]. The use of laser ablation results in prevention of recurrence for at least 2 years, which elaborates the role of abnormal uterine contraction in the generation of ectopic endometrial implants [26, 27]. Lymph node involvement has also been reported as a possible cause of recurrence [28]. Immunological factors contribute to endometriotic spots' de novo or in situ regeneration. It has been reported that CD-16 expressing natural killer cells are abundant in the peritoneal fluid and blood of women with endometriosis and are not affected by surgical excision or hormonal therapy [29].

Variable results were rendered to multiple factors, including different surgical procedures adopted, different surgical experiences, different outcome measures, different types and stages of endometriosis between studies, different target populations, and the evaluation duration. Also, a possible bias in selection and recruitment, recall and data reporting, and inaccurate statistical analysis would contribute to the contradictory results. Incomplete removal of endometriomas because of extensive pelvic adhesions contributed to endometrioma recurrence. Additionally, different methodologies and power between studies are paramount [5, 14]. The presence of associated conditions as adenomyosis was associated with increased recurrence rates; however, this was not evaluated in the current study [30].

Strengths of the study

The study used the same technique of the surgical excision performed by the same surgical team. The recurrence rate was evaluated depending on recurrence in the same ovary. Recurrence was evaluated depending on ultrasound visualization of the cyst rather than depending on symptoms.

Limitations of the study

The follow-up duration was relatively small from 12 to 30 months. The sample size was small. Pregnancy rates after the intervention was not evaluated. It was performed in a single hospital which limits data generalization. We recruited women with unilocular endometriomas, while the involvement of women with multilocular cysts would be more informative.

Conclusion

The patient's related factors and endometrioma characteristics did not predict its recurrence.

Abbreviations

ANC	Antral follicle count
AMH	Anti-Mullerian hormone
rAFS	Revised American Fertility Society

Supplementary Information

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Additional file 1.

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Not applicable. The authors are compliant to respond to any post-publication queries regarding this study. Contact would be through the corresponding author.

Authors' contributions

KH Atwa: protocol/project development and manuscript writing/editing. OT Taha: data collection and analysis. EM El Bassuony: data collection and management and manuscript writing/editing. ZM Ibrahim: protocol/project development, manuscript writing/editing, data analysis, and manuscript writing/editing.

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Availability of data and materials

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Declarations

Ethics approval and consent to participate

All procedures performed in in the study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The study was conducted after the approval of our research ethics committee. Informed consent was obtained from all participants before recruitment.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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