Original Article

Effect of Laparoscopic Ovarian Cystectomy on Ovarian Reserve in Benign Ovarian Cysts

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Abstract

Background: Laparoscopic cystectomy is one of the common modes of treatment for benign ovarian cysts. The data related to the effect of cystectomy on ovarian reserve are limited. **Aim:** The aim of this study was to investigate the effect of laparoscopic ovarian cystectomy on anti-Mullerian hormone (AMH) levels in benign ovarian cysts. **Settings and Design:** It was a prospective clinical study conducted in a tertiary care hospital from March 2017 to August 2018. **Materials and Methods:** Seventy-two benign ovarian cyst patients who were admitted for cystectomy were enrolled in the study. Serum AMH levels were estimated in all the patients at baseline, 1 week, and 3 months after cystectomy. **Statistical Analysis:** Paired *t*-test was used to assess the differences in AMH levels before and after laparoscopic cystectomy. **Results:** AMH was significantly reduced after 1 week ($P < 0.05$) and 3 months ($P < 0.05$) of cystectomy compared to preoperative levels in both endometriotic and nonendometriotic cysts. The percentage of reduction in the AMH values measured on the 7th postoperative day was found to be greater with endometriotic cysts (54%) followed by mucinous cystadenoma (32%). On day 90, greater recoveries of the AMH values to the baseline AMH levels were observed with cystic teratoma (83% of the baseline AMH levels). **Conclusions:** Laparoscopic ovarian cystectomy reduces AMH levels immediately after surgery, and improvement in AMH level was observed after 3 months.

Keywords: *Anti-Mullerian hormone, cystectomy, ovarian cysts, ovarian reserve*

Introduction

Benign ovarian cysts, either asymptomatic or characterized by pelvic mass, pain, and abnormal uterine bleeding, are seen frequently in women belonging to the reproductive age group.[1] These cysts regress spontaneously or increase in size which has to be removed by surgery.[2] Type of surgery depends on several factors, including the size of the cyst, type of the cyst, age of the patient, and desire to conceive. In the past decade, laparoscopic procedures such as electrocoagulation or stripping of the cyst wall, fenestration, and drainage of the cyst have been widely used for the removal of benign ovarian cysts.[3]

Ovarian reserve refers to the reproductive potential of a woman and reflects the number of follicles left in the ovary at any given time.[4] Several investigators have reported that age, exposure to radiation, chemotherapy, smoking, genetic factors, and other systemic gonadotoxic medication can result in reduced ovarian reserve.[5] Previous investigators have documented that ovarian reserve has been assessed by several serum markers such as follicle-stimulating hormone/luteinizing hormone ratio, estradiol, and inhibin[6] in the past, but each of them had its own limitations.

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Anti-Mullerian hormone (AMH), which belongs to family of transforming growth factor-β, is produced by granulosa cells in the antral and preantral active follicles and is involved in the regulation of folliculogenesis.[4,7] Recent studies have shown that serum AMH is a better marker of ovarian reserve, since its levels are unaffected by menstrual cycle and the use of GnRH agonists or oral contraceptive pills.[8] Furthermore, it has been demonstrated that AMH can be used to assess ovarian response to the stimulation in assisted reproductive techniques,[9-11] as it corresponds well with antral follicular count.

Laparoscopic ovarian cystectomy is considered as the first-line surgical choice for ovarian cysts, as it has an advantage over open technique like lesser postoperative pain, lesser requirement of postoperative analgesia, shorter hospital stay, lesser rate of *de novo* adhesion formation, better cosmetic results with faster recovery time, and overall reduction of cost on the gynecologic health care.[12,13] Surgical excision of the ovarian cysts was reported to have a negative impact on ovarian reserve,[2,3] but there are limited data about the effect of laparoscopic cystectomy on ovarian reserve in endometriotic and nonendometriotic cysts. Hence, the present study was undertaken to investigate whether ovarian reserve is affected by laparoscopic cystectomy for benign ovarian cysts.

Materials and Methods

This was a cross-sectional study conducted in a tertiary care hospital from March 2017 to August 2018. Seventy-two women in the age group of 25–39 years with benign ovarian cysts (size = 6–15 cm) posted for laparoscopic ovarian cystectomy were enrolled in the study. Pregnant women; patients with polycystic ovary syndrome, active pelvic inflammatory disease, suspected or proven genital or extragenital malignancy, premature ovarian failure, and history of previous adnexal surgery; and those who are on hormonal therapy for the past 3 months were excluded from the study. Ethical clearance was obtained from the institute ethics committee for human studies. Written informed consent was taken from each patient after explaining the study protocol. A detailed history was obtained from each participant, and all the patients underwent a detailed physical examination and an ultrasonography.

All the patients underwent a laparoscopic cystectomy procedure under general anesthesia. The study included a single operator, and the corresponding author did the laparoscopic cystectomy for all the patients. Pneumoperitoneum was created by inserting a Veres needle. Just below the umbilicus, a 10–12 mm trocar was inserted and the abdominal cavity was inspected by a laparoscope. Under the guidance of the laparoscope, additional ports were introduced in the right/left hypochondrium. The cyst wall was separated from the ovarian cortex to perform cystectomy. Hemostasis was achieved with the use of electrosurgical bipolar cauterization at the lowest possible settings to prevent the possible damage to the ovarian follicles. Cautery was set at low settings 40–60 watts. Intraoperative findings regarding size of the cyst, type of the cyst, and usage of cautery during surgery were noted. The specimens obtained were assessed by visual examination for any evidence of malignancy and later were sent for histopathological examination. Patients were monitored for 1 day after surgery and discharged if not associated with any postoperative complication. The blood samples were collected for the estimation of AMH by peripheral venepuncture 1 day before the surgery, 1 week, and 3 months following the surgery. Samples were centrifuged at 4000 rpm; serum was collected and stored at −40°C until the analysis. AMH was estimated by ELISA using reagent kits from Elabscience, USA.

Statistical analysis

The analysis was done by SPSS version 19 IBM, Newyork, USA. Continuous variables were described using mean and standard deviation. Categorical variables were described using frequency and percentage. Chi-square test was used to find out the association between categorical variables. Comparison of pre- and postoperative variables was made using paired and independent *t*-test. $P < 0.05$ was considered statistically significant.

Sample size calculation

The sample size required for the study is 60. The sample size was estimated using the statistical formula for comparing two dependent (paired) means with OpenEpi software (version 3.1). It has been calculated to detect a minimum change in the levels of AMH (mean 1.64 ng/ml with standard deviation of 2.08) at 5% level of significance and 80% power of the study. The estimated sample size is 60 in the study and it has been modified to 72 with an expected drop out of 20%.

Results

A total of 75 patients with benign ovarian cysts posted for laparoscopic ovarian cystectomy from February 2017 to June 2018 were recruited into the study. There was a loss of follow-up of three patients during the study period. Hence, the data of 72 patients were analyzed in our study.

Table 1 shows the clinical characteristics, type of ovarian cysts and CA-125 levels in benign ovarian cysts. The

Table 1: Clinical characteristics, type of ovarian cysts and CA-125 levels in benign ovarian cysts (*n*=72)

Parameters	Benign ovarian cyst (*n*=72)
Age (Years)	31.17±4.5
Body mass index (kg/m^2)	25.97±3.7
Parity	
P0	24 (33.3%)
P1	43 (59.7%)
Clinical symptoms	
Pelvic pain	47 (65%)
Dysmenorrhea	14 (19%)
Asymptomatic	11 (16%)
Type of cysts (Histopathology Findings)	
Endometriotic cysts	29 (40%)
Serous cystadenoma	14 (19%)
Mucinous cystadenoma	8 (11%)
Cystic teratoma	11 (16%)
Corpus luteal cysts	10 (14%)
CA-125(IU/ml)	8.46±3.63

Table 2: Effect of laparoscopic cystectomy on Anti Mullerian hormone (mg/L) levels in ovarian cysts

Laparoscopic cystectomy	Anti-Mullerian hormone levels (ng/ml) (*n*=72)
Preoperative levels	4.77±1.32
Post operative (after 1 week of cystectomy) levels	3.21±1.54*
Post operative (after 3 months of cystectomy) levels	3.64±1.32*

**P*<0.05 compared to baseline values

patients were in the age group of 26 – 36 years and their body mass index was between 21 – 30 kg / m2. Out of 72 patients, 67 were married (93.1%), while 5 women were unmarried (6.9%). Among 67 women who were married, 43 women had 1 or more children (59.7%) and 24 had infertility (33.3%). Around 65 % of the patients presented with pelvic pain, 19% had dysmenorrhea and 16% were asymptomatic. Post operative histopathology findings revealed that 29 patients (40.3%) had endometriotic cysts, 14 patients (19.4%) had serous cystadenoma, 11 women (15.3%) had cystic teratoma, 10 patients (13.9%) had corpus luteal cysts and 8 patients (11.1%) had mucinous cystadenoma.

Table 2 shows the effect of laparoscopic cystectomy on AMH levels in benign ovarian cysts. AMH was significantly reduced after 1 week ($p< 0.05$) and 3 months ($p< 0.05$) of cystectomy compared to preoperative levels.

The results were expressed as mean and standard deviation. AMH levels were compared between before and after cystectomy using paired t-test. A p value of less than 0.05 was considered statistically significant

Table 3 shows the effect of laparoscopic cystectomy on AMH levels in endometriotic and non endometriotic cysts. AMH was significantly reduced in both endometriotic and non endometriotic cysts after 1 week ($p< 0.05$) and 3 months ($p< 0.05$) of cystectomy compared to preoperative levels.

The results were expressed as mean and standard deviation. AMH levels were compared between before and after cystectomy in endometriotic and non endometriotic cysts using paired t-test. A p value of less than 0.05 was considered statistically significant.

Table 4 shows The changes in the AMH values were not related to the size of the cyst as shown by the results. The was no significant difference found in the baseline, day 7 and day 90 AMH values among the patients with different sizes of ovarian cyst.

No conception occurred during the study period.

Figure 1 shows the changes in the mean AMH value in the different types of cysts. It was noted that among all the cysts, the mean baseline AMH value was less in patients with endometriotic cyst. The percentage of reduction in the AMH values measured on the 7th postoperative day was found to be greater with endometriotic cysts (54%) followed by mucinous cystadenoma (32%). On day 90, greater recoveries of the AMH values to the baseline AMH levels were observed with cystic teratoma (83% of the baseline AMH levels).

Discussion

In the present study, we found that the laparoscopic cystectomy reduces serum AMH values in the immediate postoperative period. On further follow-up, it was found that there was an improvement in ovarian function as demonstrated by raised AMH levels.

Laparoscopic cystectomy is indicated in benign ovarian cysts with symptoms such as pelvic pain and dysmenorrhea or in those patients where the risk of malignant transformation is higher.[14] Earlier investigators have reported about a reduction in ovarian reserve after cystectomy.[1,15] AMH is widely established as a marker of ovarian reserve. In the present study, AMH levels were reduced within 1 week after cystectomy but recovered after 3 months of surgery. These findings were similar to a previous study by Chang *et al*. which demonstrated an initial fall in the AMH values postsurgery and a recovery of AMH levels to about 65% of the baseline AMH level at 3 months after surgery.[16] This study had limitations of small

Table 3: Effect of laparoscopic cystectomy on AMH levels in endometriotic and non-endometriotic cysts

Variable	Endometriotic cysts (*n*=29)	Non-endometriotic cysts (*n*=43)
Baseline Anti Mullerian hormone (ng/ml)	3.73±0.79	5.47±1.14
Anti Mullerian hormone after 1 week of cystectomy	1.96±0.90*	4.06±1.32*
Anti Mullerian hormone after 3 months of cystectomy	2.66±0.77*	4.37±1.20*

**P*<0.05 compared to baseline values

Table 4: AMH values in the different cyst sizes at baseline and after cystectomy

Cyst size	Baseline AMH (ng/ml)	Day 7 AMH (ng/ml)	After 3 months (ng/ml)	Statistical significance
5-8 cm	4.76±1.38	3.04±1.57	3.63±1.21	*P*=1.0
8-12 cm	4.55±1.26	3.17±1.53	3.49±1.48	*P*=0.91
12-15 cm	5.61±1.41	3.94±1.48	4.13±1.40	*P*=1.89

**P* value calculated using paired t-test

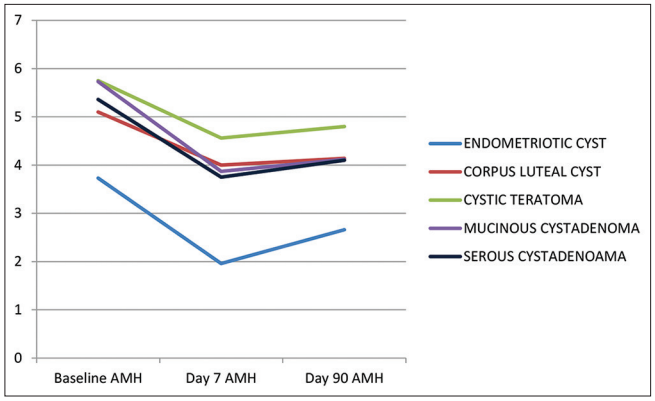

Figure 1: Comparison of anti-Mullerian hormone changes in different cyst types

sample size (n = 20) and the presence of endometriotic cysts in majority of the patients.

In the present study, the mean baseline AMH values were significantly low in the women with endometriotic cysts when compared to those with nonendometriotic cysts. These findings might be due to damage to the ovary caused by the presence of endometrioma before the surgery. When AMH levels were compared in endometriotic and nonendometriotic cysts, there was a reduction in AMH immediately after the surgery and significant recovery after 3 months of surgery. In the present study, the baseline AMH values were found to be lowest in the patients with endometriotic cysts, and these findings were in agreement with previous investigators.[16,17] Among all the cysts, a greater fall in the AMH levels in the immediate postoperative period was observed with endometriotic cysts (54%) followed by mucinous cystadenoma.[18] These findings were in contrast to the study done by Amooee *et al*. who found a greater reduction in the AMH values postoperatively with dermoid cysts compared to serous and mucinous cystadenoma.[1] In the present study on day 90, the AMH values raised significantly with nonendometriotic cysts compared to endometriotic cysts (79.8% vs. 71% of the baseline AMH values, respectively). Furthermore, we observed that, in cystic teratoma, the recovery of the AMH values after 90 days was around 83% of the baseline value. No conception occurred during the study period.

Different mechanisms were proposed to explain the reduction in the ovarian reserve following laparoscopic ovarian cystectomy. Endometriotic cysts lack a true capsule around the cyst, so a greater amount of surrounding ovarian cortex is lost while stripping the cyst wall during the cystectomy procedure. This results in a greater loss of ovarian follicles leading to a greater reduction in the AMH levels postsurgery for endometriotic cyst when compared to the nonendometriotic cyst.[19] Furthermore, inflammation and edema due to the surgery in the immediate postoperative period could be another reason for the initial fall in the ovarian reserve. The recovery of ovarian function can also be explained by the phenomenon of follicular cohort rearrangement.[16] The ovarian damage during the surgery activates the compensatory mechanisms, in which there are granulosa cell hyperactivation and primordial follicle recruitment and growth. Furthermore, the inflammation, ischemia, and edema of the ovarian cortex due to cystectomy resolve over a period of time increasing AMH levels.[19] However, the AMH levels on day 90, even though improved, did not reach the preoperative baseline values, indicating some amount of permanent damage to the ovarian tissue.

The strength of our study is prospective design and relatively longer follow-up of patients. The limitation of our study is less number of patients with each type of cyst to compare the effect of laparoscopic cystectomy on AMH levels between different types of cysts. We did not follow up to know how many conceived after the study

period. Furthermore, women with infertility were not analyzed separately. Other markers of ovarian reserve like antral follicular count were not analyzed.

Conclusions

Laparoscopic ovarian cystectomy for benign ovarian cysts resulted in a significant reduction of the ovarian reserve (AMH levels) in the immediate postoperative period and a gradual improvement was observed on postoperative day 90 indicating some amount of permanent damage to the ovarian follicles during surgery. Hence, patients with benign ovarian cysts have to be properly counseled and all the available management options to be considered before going for a surgical intervention, especially for young and infertility patients who desire future fertility and all the preventive measures, had to be taken intraoperatively to prevent damage to the healthy ovarian follicles.

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Conflicts of interest

There are no conflicts of interest.

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