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ORIGINAL ARTICLE

Anti-Mullerian Hormone Level in Benign Ovarian Cyst before and After Laparoscopic Ovarian Cystectomy.

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ABSTRACT

cystectomy) can be performed either by laparotomy or laparoscopy. Recent studies have reported significant decrease in ovarian reserve, estimated by measurement of serum anti-mullerian hormone (AMH) levels drops significantly after ovarian cystectomy. The aim of this work was the comparison of anti-mullerian hormone level in benign ovarian cyst Before and after laparoscopic ovarian cystectomy.

Methods: This was prospective observational study in the period from August 2020 to December 2020. Included 34 women at Obstetrics and Gynecology Department, Zagazig University Hospital undergoing Laparoscopic Ovarian Cystectomy for benign ovarian cyst to evaluate the ovarian reserve by using AMH level determination, and at one and 3 months after laparoscopic cystectomy.

Results: There was significant higher reduction in AMH among younger than older age groups (49.7% versus 41.5%), bigger than smaller cyst size (51.5% versus 39.2%), higher reduction among patients with higher pre-operative Anti-Mullerian Hormone (≥ 5 ng/ml) than<5 ng/ml (50.6% versus 40.7%).

Conclusions: Decreased serum AMH may be contributed to decreased ovarian reserve after laparoscopic ovarian cystectomy. This can result from thermo-coagulation used for hemostasis during the operation.

Key words: Anti-mullerian hormone, Ovarian cyst, Laparoscopic

INTRODUCTION

An ovarian cyst is a fluid containing sac that is formed in the ovaries. In the United States, almost all of the women in reproductive age and about 18 percent of those who are in post-menopausal age have ovarian cysts [1].

Most of the ovarian cysts were benign in nature with very low chance of malignant transformation. Most common symptoms of these cysts such as chronic pelvic pain, dyspareunia, gastrointestinal and urinary symptoms are resulted from the pressure they apply to the nearby structures [2].

Management of these cysts is mandated when there is chance for malignancy (cysts larger than 10 cm and abnormal serum CA-125 levels) and intolerable symptoms. Surgical removal of the cysts is required for persistent ones measuring 5-10 cm which have not shown any shrinkage after expectant management for several cycles should be considered [3].

The operation of resecting an ovarian cyst (ovarian cystectomy) can be performed either by laparotomy or laparoscopy. Recent studies have reported significant decrease in ovarian reserve, estimated by measurement of serum anti-mullerian hormone (AMH) levels drops significantly after ovarian cystectomy [4].

This reduction was partially reversible three months after operation. Some other studies have reported no decrease in the serum level of AMH or damage to ovarian reserve after ovarian cystectomy [5].

The anti-Mullerian hormone (AMH) belongs to the β-class of growth factor transforming and falls from primary granulosa cells to small antral follicles and is associated with the small antral follicles. The anti-Mullerian hormone is the only

menstrual cycle independent ovarian marker. The AMH acts as an ovarian reserve marker provide many advantages over other markers; it is stable during the menstrual cycle and is fairly autonomous from the use of hormone therapy. AMH level decreases after surgical cyst excision [6].

The best and most efficient conservative laparoscopic technique remains a controversial issue in the literature. The debate is between excision and ablation of the capsule. The reported benefits in favors of surgery include a decrease in the recurrence of symptoms and signs and a reduction in the recurrence of the benign ovarian cyst. There are also some reports that show an increase in responsiveness to ovarian stimulation and cumulative pregnancy rate (PR) in randomized controlled trials [7]. Concern has been expressed over the risk of damaging ovarian reserve owing to excision of the capsule or to the use of electrocautery in surgically treating benign ovarian cyst. Ablation may have a higher risk of recurrence, but excision may result more significant damage to ovarian follicular reserve, which could compromise future ovarian response during in-vitro fertilization. [8].

This study aimed to the comparison of anti-mullerian hormone level in benign ovarian cyst before and after laparoscopic ovarian cystectomy.

METHODS

This was prospective observational study performed in Obstetrics and Gynecology Department, Zagazig University Hospital during the period from August 2020 to December 2020 hospital was accepted cold patients in that period. The study included 34 women with diagnosis of benign ovarian cyst who underwent laparoscopic ovarian cystectomy and diagnosis of benign ovarian cyst was made by ultrasound imaging and CA125. Before enrollment, all participants were requested to sign informed consent forms.

Approval to conduct the study was obtained from the research committee of faculty of medicine, Zagazig University (IRB# 5975). An informed consent was written by every subject they were reassured about the study, the study procedures were free of any harmful effects on the participants as well as the service provided. The work was carried out for studies involving humans in accordance with the World Medical Association's Code of Ethics (Helsinki Declaration).

Inclusion criteria

Cases of benign ovarian cyst diagnosed by ultrasound imaging.

Exclusion criteria

History of suspected or proved ovarian malignancy. Previous adnexal surgery or surgery of ectopic pregnancy. Polycystic ovarian syndrome. Evidence of premature ovarian failure or premature menopause which is detected by FSH & LH assay. History of infertility due to endometriosis. Size of the cyst more than 15x15x15cm. Patients who had sonographic malignant criteria (The presence of a solid component and detectable flow by Doppler imaging within a cystic ovarian mass).

All participants were subjected to the following; Full history was taken from the women including (Personal history name, age. Family history: of medical diseases as hypertension or diabetes mellitus. The date of last menstrual period).

General examination: This included vital data signs (blood pressure, pulse and temperature).

Abdominal examinatio: Inspection, Palpation, Percussion & auscultation

Before the laparoscopy (investigations)

Diagnosis of ovarian cyst was made by ultrasound imaging using 2D ultrasound machine (SIMENS ACUSON X300 medical systems, endovaginal proper with frequency 7MHz). Criteria of benign cysts like as showing by ultrasound are (low echogenicity, a thin cyst wall, unilocular, and absence of internal papillary excrescences). Benign ovarian cyst including dermoid cyst, mucinous and serous cystadenoma were included. Those who had persistent cysts measuring 5-10 cm or intolerable symptoms of adnexal mass were candidate for laparoscopic ovarian cystectomy and were included in this study. Participants scheduled for laparoscopic ovarian cystectomy were examined and serum level of AMH, CEA, and CA 125 were measured before the operations.

Preoperative and postoperative follow up ultrasound evaluations were performed by the same gynecology resident using ultrasound device. Pre and postoperative measurements of AMH was performed by Diagnostic Systems Laboratories (DSL) Webster, Texas, United States active mullerian inhibiting substance/ AMH ELISA kit the same reference lab and reported in ng/ml values and detection limit of 0.006 ng/ml.

Laparoscopic maneuver:

Participants underwent laparoscopic ovarian cystectomy under general anesthesia. And complete aseptic techniques and on supine (supine position with abduction of lower limbs and with flexion of the thighs onto the pelvis of about 20°) position and pelvic laparoscopic operative design using a Verres needle passed through a 1cm umbilical incision, pneumo-peritoneum was induced by CO2 insufflation to maintain an intra-abdominal pressure of 12 -15mmHg. The initial

laparoscopic port was placed at the umbilicus with a 5–12 mm port. The pelvis was carefully surveyed, and the ovarian cyst was examined for any signs that may be suggestive of malignancy such as ascites, excrescences on the surface of the ovary, and implants noted on peritoneal, liver, or diaphragm surfaces. Five millimeter ports were then placed laterally. The surgeon obtained cell washings at this time for cytology. All cysts that were appeared benign cystectomy were performed. Cystectomy was then performed by incising the capsule of the ovary with scissor. The cyst is then enucleated carefully with traction and counter traction and dissection as needed (Figure 1). In case of intraoperative rupture occurs, particularly with a dermoid cyst, the peritoneal cavity was liberally be rinsed with normal saline or Ringer's lactate that has been shown to be safe. After the cyst was removed from the ovary, an endoscopic bag was then advanced through the umbilical 10–12 mm port, and the cyst is placed in the bag (Figure 2). The bag was then advanced up to the umbilical incision, and the port was removed while advancing the edges of the bag through the skin incision. The bag was then opened and triangulated to facilitate removal of the cyst intact and those which were small enough or with morcellation carefully avoiding any spillage out of the bag (Figure 3). Prior to removal, the cyst was drained while in the bag. Once the specimen was small enough, the bag was removed with the specimen through the incision.

After removal of the bag and specimen, the 10–12 mm laparoscopic port was replaced through the umbilical incision and the camera advanced through the port. The ovary was then carefully inspected for hemostasis. Bleeding from the bed of the cyst in the ovary in some patient required measures to obtain hemostasis. Hemostasis in the bed of the ovary at the site of the cystectomy has traditionally been accomplished with bipolar cautery. The edges of the ovarian capsule did not need to be re-approximated as is traditionally done with an open ovarian cystectomy. The procedure was completed by irrigation of the pelvis, and a careful survey of the pelvis for hemostasis with the intra-peritoneal pressure decreased to 5 mmHg. The port sites were then inspected for hemostasis. After all port sites are inspected for hemostasis, the CO_2 peritoneum was then allowed to escape through the umbilical port.

Care was taken to ensure that as much gas is expressed as possible to minimize postoperative discomfort for the patient and to avoid the bowel being pushed into the incision sites as residual gas escapes. The incisions were then closed with suture, Steri-Strips, or a skin adhesive. Fascial closure was recommended for ports 10 mm or greater in size prior to skin closure to prevent subsequent development of an incisional hernia.

After the surgery, participants were observed in hospital ward for 24 hours to avoid surgical complications or those associated with anesthesia. For all participants, operative and post-operative course were successful with no specific complication. Participants were evaluated at outpatient clinic at 1 month and 3 months after the surgery for measuring serum level of AMH and ultrasound evaluation of surgical outcome and recurrence of the primary cyst.

Statistical Analysis:Data were checked, entered and analyzed using SPSS version 23 for data processing.

RESULTS

The age of the studied group was (30.3±4.9) ranged from (23 to 38), (52.9%) of them was in the age group more than 31 years, their parity was (0.7±0.9) ranged from (nulliparous to para 3), (58.8%) of them was nulliparous, (41.2%) were multiparous and (11.8%) of the studied group were infertile (Table 1).

The ovarian cyst size in the study group was (69±1.6) ranged from (48 to 103) mm, divided equally to two groups less and more than 69 mm, most cysts were unilateral (70.6%) and (41.2%) of the studied group were dermoid cyst type (Table 2).

There was statistically significant higher reduction among younger than older age groups (49.7% versus 41.5%) with no statistically significant difference regarding parity and patients' complaint (Table 3).

There was statistically significant higher reduction among bigger than smaller cyst size (51.5% versus 39.2%) and also more reduction among dermoid than serous than mucinous cyst with no statistically significant difference regarding unilateral and bilateral cyst (Table 4).

There was statistically significant positive correlation between percent of reduction and AMH levels (pre- & post-operatively). But regarding age and cyst size, there was no statistically significant correlation (Table 5).

Table 1: Parity and patients' complaint among the studied group

Variable	**The studied group (34) mean ± SD (Range) Median**	
Age (years)	30.3±4.9 (23-38) 31	
Number of parity **P0-20** **P1-6** **P2-6** **P3-2**	0.7±0.9 (0.0-3) 0.0	
Variable	**NO (34)**	**%**
Parity Nulliparous Multiparous	 20 14	 58.8% 41.2%
Complaint Pain Infertility	 30 4	 88.2% 11.8%

Table 2: Characteristics of the ovarian cyst among the studied group

Variable	**The studied group (34) mean ± SD (Range) Median**	
The ovarian cyst size (mm)	69±1.6 (48-103) 69	
Variable	**NO (34)**	**%**
Ovarian cyst size: < 69 mm ≥ 69 mm	 17 17	 50.0% 50.0%
Ovarian cyst side: Unilateral Bilateral	 24 10	 70.6% 29.4%
Ovarian cyst type: Serous Dermoid Mucinous	 10 14 10	 29.4% 41.2% 29.4%

Table 3: Relation between reduction (AMH reduction) and patients' characteristics

Variable	Percent of AMH reduction	(range)	test	P-value
Age <31 years	49.7%	(31.3%-66.2%)	2.4	0.02*
≥31 years	41.5%	(26.7%-51.9%)		
Parity Nulliparous	46.6%	(29.1%-66.2%)	0.8	0.4
Multiparous	43.6%	(26.7%-56.3%)		
Complaint Pain	44.7%	(26.8%-61.9%)	0.9	0.3
Infertile	50.3%	(31.3%-66.2%)		

Table 4: Relation between reduction (AMH reduction) and ovarian cyst characteristics

Variable	Percent of AMH reduction	(range)	test	P-value	
Ovarian cyst size ≥69 mm	51.5%	(26.7%-66.2%)	3.9	0.001**	
<69 mm	39.2%	(26.9%-51.9%)			
Ovarian cyst side Unilateral	43.4%	(26.7%-61.9%)	1.6	0.1	
Bilateral	49.9%	(31.3%-66.2%)			
Ovarian cyst type: Serous cystadenoma	44.1%	(29.1%-50.4%)	19.8	0.001**	0.003*(1)
Dermoid	53.8%	(40.6%-66.2%)			0.009*(2)
Mucinous cystadenoma	34.8%	(26.7%-51.9%)			0.001**(3)

** Statistically highly significant difference (P ≤ 0.001), * statistically significant difference (P ≤ 0.05), (1) Serous versus dermoid, (2) Serous versus Mucinous, (3) Dermoid versus Mucinous

Table 5: Characteristics of the ovarian cyst among the studied group

Variable	percent of reduction r^	p	SIG
Age	-0.1	>0.05	NS
Ovarian cyst size	0.08	>0.05	NS
Preoperative AMH	0.4	0.004*	S
Postoperative one month AMH	0.5	0.003*	S
Postoperative three months AMH	0.3	0.02*	S

DISCUSSION

Many studies reported increased risk of ovarian damage and decreased serum AMH levels after laparoscopic cystectomy in women with benign ovarian cyst .Although some studies reported that laparoscopic surgery did not damage the ovaries, and laparoscopic cystectomy generally harmed the ovaries, resulting in decreased post-surgery ovarian reserve [7].

The age of the studied group was (30.3±4.9) ranged from (23 to 38), (52.9%) of them was in the age group more than 31 years, their parity was

(0.7±0.9) ranged from (nulliparous to para 3), (58.8%) of them was nulliparous, (41.2%) were multiparous and (11.8%) of the studied group were infertile. This was the same age group in Elsemary et al. [7] where a total of 60 patients were included in their study, with mean age of 28.24 ± 5.28 years. Among the patients, 41 (68.3%) had unilateral and 19 (31.7%) had bilateral benign ovarian cyst [7].

The present study showed that the ovarian cyst size in the study group was (69±1.6) ranged from (48 to 103) mm, divided equally to two groups less and more than 69 mm, most cysts were unilateral (70.6%), 10 women (29.4%) had serous, 10 women (29.4%) had mucinous and 14 women (41.2%) of the studied group were dermoid cyst type. this was in agreement with Amooee, et al. [1] whose study included 60, women with average age of 25.8 years. Ovarian cysts included in their study consisted of benign cysts including dermoid cyst (n=23), mucinous cystadenoma (n=11), and serous cystadenoma (n=26). Ovarian cyst diameters measured from 4.6-13 cm with mean size of 7.6 cm.

Similarly, Awad et al. [6] found that there were 9 (18%) simple cysts with focal inflammation of the fibrous wall and sloughed lining, 11 (22%) were endometriotic cysts, 12 (24%) were benign serous cyst, 11 (22%) were hemorrhagic retention cyst with fibrolytic wall and 7 (14%)were cystic teratomata.

This study found that there was highly statistically significant reduction in AMH pre and post-intervention 4.1±1.01 versus 2.35±0.39 respectively with 45.4% percent of reduction) this was in agreement with Elsemary et al. [7] whose study reported that the serum levels of AMH decreased significantly 3 months postoperatively (4.12±3.4 versus .62±2.7 P < 0.001) and Awad et al. [6] who reported that AMH decreased after laparoscopy when compared with values before it (1.56±0.14 ng/ml versus 0.71±0.15 ng/ml).

The current results were also in consistent with Celik et al. [10] that measured the serum AMH until 6 month after cystectomy and noticed it gradually declined.

Also Chang et al. [11] reported that the serum AMH declined gradually after cystectomy after one month and that 65% preoperative level recovered 3 months later.

In contrast to our results, Lee et al. [12] and Biacchiardi et al. [13] showed no statistically significant decline in serum AMH level 3 months after the surgery

In this study the role of patients age, parity, complaint, cyst size, cyst type and bilaterally were compared with the changes of AMH level after laparoscopic cystectomy and the following result showed that there was statistically significant higher reduction among younger than older age groups (49.7% versus 41.5%), bigger than smaller cyst size (51.5% versus 39.2%), higher reduction among patients with higher pre-operative Anti-Mullerian Hormone (≥ 5 ng/ml) than <5 ng/ml (50.6% versus 40.7%) and also more reduction among dermoid than serous than mucinous cyst with no statistically significant difference regarding unilateral and bilateral cyst, parity and patients' complaint.

Elsemary et al. [7] found that Patients older than 38 years had significantly lower baseline serum level of AMH when compared with those younger than 38 years (1.56 ± 2.49 vs. 4.12 ± 3.48 ng/ml; P = 0.003). Both groups had significantly lower AMH levels (P < 0.001) 3 months after the operation. Women with large and small cysts (3 cm as a cut-off value) had no significant difference regarding the baseline level of AMH (4.01 ± 3.55 vs. 2.86 ± 2.58 ng/ml; P = 0.149). The decrease in AMH after the operation was similar between the two study groups. However, regarding AMH level between those with large and small cysts 3 months after the operation (P = 0.366), there was no significant difference. There were 19 (31.7%) patients with bilateral and 41 (68.3%) patients with unilateral benign ovarian cyst. The baseline AMH level was comparable between these two groups (3.29 ± 3.10 versus 4.21 ± 3.71 ng/ml; P = 0.074). The AMH level decreased significantly 3 months after the operation in those with unilateral (P < 0.001) and bilateral (P < 0.001) benign ovarian cyst. Those with single unilateral cysts had significantly higher baseline levels of AMH when compared with those with single bilateral cysts (4.21 ± 3.82 versus 2.59 ± 1.89 ng/ml; P = 0.006). Moreover, in those with multiple bilateral cysts, the baseline serum levels of AMH were significantly higher compared with those with single bilateral ones (4.49 ± 4.78 versus 2.59 ± 1.98 ng/ml; P = 0.026). The trend of reduction of AMH levels after the operation was similar in all groups.

Similarly to our results, Amooee et al. [1] study AMH before the operation showed a mean value of 3.77 ng/mL which declined to 1.87 (ng/mL 0.67-3.07 ng/mL) 1 month after the operation. This decline was significant with the p:<0.001. Measurement of AMH 3 months after the surgery revealed significant elevation to a mean level of 2.48 ng/mL (95% CI: 1.08-3.88 ng/mL) (p<0.001). Finally, regarding AMH level reduction within each type of ovarian cysts were significant (p<0.001). Long term recovery of ovarian reserve after ovarian cystectomy did not vary significantly

among serous and mucinous cystadenoma (p=0.48) but pairwise comparison of each type with dermoid cyst revealed significant difference in total recovery. Overall recovery was highest in mucinous cystadenoma (68%) and lowest in dermoid cysts (62%).

CONCLUSION

Decreased serum AMH may be contributed to decreased ovarian reserve after laparoscopic ovarian cystectomy. This can result from thermo-coagulation used for hemostasis during the operation.

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