Original Article

Evaluation of antimullerian hormone levels before and after laparoscopic management of endometriosis

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Abstract

Background: Serum antimullerian hormone (AMH) proposed to be a reliable marker of ovarian reserve; the aim of this study was to evaluate the influence and value of laparoscopic management in endometriosis as measured by serum AMH levels.

Materials and Methods: In this cross-sectional study, 33 infertile patients who referred to fertility - Infertility Center of Isfahan - with different stages of endometriosis managed by diagnostic operative laparoscopy and serum AMH levels were measured pre and one month postoperative laparoscopy. Main outcome measures were serum AMH levels in correlation with the type of infertility, stage of endometriosis, and type of surgery in infertile patients.

Results: 33 infertile patients enrolled in the study with mean age 28.9 ± 5 years, and thus did not show a significant difference. Mean serum AMH levels was 4.23 ± 3.75 ng/ml and 2.2 ± 2.47 ng/ml, respectively, in primary and secondary infertility groups before and one month after laparoscopy, which shows a significant difference ($P < 0.001$). Median AMH level changes in Cauterization (0.67 ± 0.76 ng/ml), endometrioma excision 2 ± 0.6 ng/ml, both 2.18 ± 0.81 ng/ml and shows no significant differences. Mean serum AMH levels were definitely decreased in minimal/mild and severe stage endometriosis before and 1 month after laparoscopy, (1.84 ± 2.06 ng/ml and 2.18 ± 3.45 ng/ml), respectively. Also serum AMH according to ovarian appearance and evolvement showed no significant differences after laparoscopy: (5.5 ± 1.4 ng/ml and 2.76 ± 0.96 ng/ml) and (3.37 ± 2.2 ng/ml and 1.84 ± 1.5 ng/ml).

Conclusion: Serum AMH levels clearly decreased 1 month after operative laparoscopy.

Key Words: Antimullerian hormone, endometriosis, laparoscopy, ovarian reserve

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INTRODUCTION

Endometriosis is a common gynecologic disorder in which the endometrial glandular epithelium and stroma are found outside the uterine cavity. Endometriosis affects 6% to 10% of all women in their reproductive years, and the mean age at time of diagnosis ranges between 25–35 years and it is presented in 9–50% of infertile women.[1] It is characterized by the presence of endometrial tissue growing outside uterine cavity and is found primarily on the ovaries, peritoneum, and rectovaginal septum.[2,3]

Ovarian endometriomas are associated with the most advanced stages of endometriosis and mostly encounter most of the ovarian cyst surgery, and it

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may be present in up to 17–44% of patients with endometriosis.[2] Ovarian endometriomas are usually associated with the symptoms of dysmenorrhea, chronic pelvic pain, dyspareunia, and reduced quality of life and infertility.

Possible mechanism of infertility among women with endometriosis includes anatomical distortion from adhesions or fibroids and the known presence of inflammatory mediators.[3]

Definitive diagnosis is made by direct operative visualization either by laparoscopy or via laparatomy and ideally with histological confirmation.[1]

Operative laparoscopy compared with laparatomy has been proved to be as the gold standard surgical approach for diagnose and treatment of endometriosis.[4] The diagnosis is staged laparoscopically from minimal to severe stages including ovarian endometrioma.[1,5]

The most common procedures for the treatment of ovarian endometriosis are either excision of the cyst capsule or electro-coagulation of the cyst wall. During excision the ovarian endometrioma is aspirated followed by incision and removal of the cyst wall from the ovary cortex with maximal preservation of the normal ovarian tissue.

Although the safety of this procedure in terms of residual ovarian function is uncertain and preserving the ovarian tissue is very important in young women who desire future fertility.[4]

Antimullerian hormone (AMH) belongs to the transforming growth factor –β family and is produced by the granulose cells of primary to small antral follicles and it is connected to the number of small antral follicles.[6] Antimullerian hormone is the only ovarian reserve marker that is menstrual cycle independent and it is not affected by oral contraception and GnRH agonists.[7]

Since endometriosis affects directly ovarian reserve that is defined as the functional potential of the ovary reflects the number and quality of the follicles left in the ovaries at any given time. Various tests and valuable markers of ovarian reserve such as serum AMH were studied in different recent studies to show its importance and impact in infertility in correlation with endometriosis through passing time, as it was shown by Alborzi *et al*.[8]

Since endometriosis is an important and complex issue in the infertility field and laparoscopy is the mainstay of diagnosis and treatment, and serum AMH levels is a reliable marker in correlation with endometriosis and infertility as reported in recent studies, it was so important to have a study evaluating AMH value before and after laparoscopic management of endometriosis to estimate ovarian reserve and future fertility and the female production rate.

MATERIALS AND METHODS

This cross-sectional study was conducted on 30 of three patients, who underwent diagnostic and operative laparoscopy for different stages of endometriosis as a cause of infertility in Fertility and Infertility Center of Isfahan in August 2012 to December 2013. Approval for the study was obtained from the review board of the Isfahan medical University and all participants gave informed consent.

Inclusion criteria to the study were: The presence of endometriosis as a cause of infertility confirmed during laparoscopy, age between 18 and 40 years, regular menstrual cycles, defined as a cycle length between 25 and 35 days, and no history of previous ovarian surgery. The exclusion criteria were: The presence of any endocrine diseases (diabetes, hyperprolactinemia, and thyroid diseases), previous history of chemo-therapy, the presence of pelvic inflammatory disease, hepatitis, other cause of infertility than endometriosis, history of previous ovarian surgery, and hormonal therapy received before.

All women underwent the operation under general anesthesia with a diagnosis of endometriosis in our institution during the study period. Laparoscopic pneumoperitoneum was induced by CO_2 insufflation with 10 mm trocar and telescope entries were made to intra-abdominal pressure reached 12 mmHg. One or two 5 mm trocars were inserted from supra inguinal regions under direct laparoscopic observation. The diagnosis is staged laparoscopically from minimal to severe stages including ovarian endometriomas. Small lesions of superficial peritoneal and ovarian endometriosis treated with laser coagulation under constant irrigation. Small endometriomas treated by electrocoagulation of the mucosal lining. Larger lesions greater than 5 cm in diameter treated with resection the wall of the cysts from the healthy surrounding normal ovarian tissue with using atraumatic forceps. Often the cyst ruptured during dissection of adhesions, the cyst contents were immediately drained with the suction cannula. Cauterization was done by bipolar cautery to avoid thermal destruction of ovarian follicles. When endometriosis is confirmed by laparoscopy 2 cc venous blood samples were obtained from the study group. Serum AMH levels were measured by

Enzyme-Linked Immunosorbent Assay (ELIAS), Diagnostic system laboratories, USA-Beckman Coulter. The minimal detectable concentration for AMH was 0.001 ng/ml and the maximum value detected is 21 ng/ml.

At the end of surgery approximately 50 ml Ringers Lactate solution was left in the peritoneal cavity. The patients were discharged from the hospital on the second postoperative day. All subjects were followed up postoperatively at 1 month and serum AMH levels were obtained.

Statistical analyses were performed with SPSS software version 20 for windows. Concentration of serum AMH levels were compared between each sampling point (preoperatively and 1 month postoperatively) using paired samples T-test and Fisher test.

Means were presented with SD $P < 0.001$ was considered statistically significant.

RESULTS

In this study, 33 patients enrolled with different stages of endometriosis as a cause of infertility to undergo diagnostic and operative laparoscopy. Diagnose of endometriosis was confirmed by laparoscopy in all of patients. Serum AMH levels were measured before and 1 month after laparoscopy.

The clinical characteristics of patients are described in Table 1. The mean age of the patients was 28.9 ± 5 years with the age range of 18-38 years. Thirty one patients (93.9%) have primary infertility, and two patients (6.1%) have secondary infertility, according to the T–test we do not have a significant difference between the age of our patients ($P = 0.11$). Serum AMH levels have significant difference before and 1 month after laparoscopy in patients with primary infertility, but was not seen in patients with secondary infertility ($P = 0.24$), Table 2.

Fifteen patients (45.5%) have minimal/mild endometriosis, and 18 patients (54.5%) have severe endometriosis. Due to T-test we do not detect any significant difference between age and the stage of endometriosis, the age of patients was 28.2 ± 5.5 years and 29.6 ± 4.7 years, respectively, Table 1. All of patient with minimal/mild endometriosis and 16 patients with severe endometriosis had primary infertility (100% compared 88.9%); we conclude that there is no significant difference between infertility type and severity of endometriosis ($P = 0.45$) according to the Fisher test, Table 2.

The mean serum AMH level before and 1 month after operative laparoscopy was 4.23 ± 3.75 ng/ml and 2.2± 2.46 ng/ml, respectively [Figure 1]. As to T-paired test there was a significant difference before and after laparoscopy ($P < 0.001$). Also the mean difference of serum AMH levels before and 1 month after laparoscopy was 2.03 ± 2.87 ng/ml.

Table 1: Demographic characteristics of the participants

Number of patients	33
Age: Mean	28.9±5
Type of infertility (%)	
Primary	31 (93.9)
Secondary	2 (6.1)
Stage of endometrioses (%)	
Minimal/mild	15 (45.5)
Severe	18 (54.5)
Ovarian evolvement (%)	
Normal ovary	13 (39.3)
Endometrioma	20 (60.6)

Table 2: Comparison serum AMH levels before and after operation according to: Infertility type, severity, and ovarian appearance

	Before	After	Differences	*P*
Infertility				
Primary	4.4±3.81	2.31±2.5	2.09±2.9	<0.001
Secondary	1.64±0.31	0.54±0.48	1.1±0.62	0.42
P	0.32	0.33	0.64	-
Severity				
Mild-minimal	4.03±2.15	4.4±4.76	1.84±2.06	0.004
Severe	2.19±1.48	2.21±3.11	2.18±3.45	0.016
P	0.78	0.98	0.74	-
Ovarian appearance				
Normal	5.55±1.4	2.76±0.96	2.79±1.08	0.13
Abnormal	3.37±2.2	1.84±1.5	1.53±1.9	0.13
P	0.1	0.3	0.22	-
Surgical procedures				
Cauterization	4.7±4.5	2.87±3.5	1.85±1.8	0.004
Excision/aspiration	4.69±3.5	1.86±1.6	2.73±0.99	0.016
Both	2.12±1.8	1.47±1.7	2.03±0.5	0.038
P	0.32	0.48	0.32	-

AMH: Antimullerian hormone

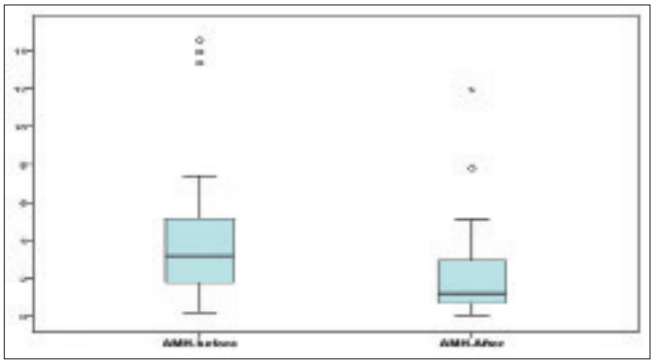

Figure 1: Serum AMH before and after laparoscopy

The mean value of serum AMH levels before and after operative laparoscopy definitely decreases in both minimal/mild and severe groups (1.84 ± 3.45 ng/ml and 2.18 ± 3.45 ng/ml), respectively. This difference did not depended on severity of endometriosis, Table 2.

The procedure was done during laparoscopy was 6.1% of patient cauterization, 39.4% endometrioma excision and 54.5% both excision and cauterization.

Median AMH level changes in these groups were 0.67 ± 0.76 ng/ml, 2 ± 0.6 ng/ml, 2.18 ± 0.81 ng/ml, respectively. By analysis with One Way ANOVA and repeated measures ANOVA we concluded that serum AMH levels according to surgical procedures did not show any significant difference with (P = 0.81) and (P = 0.76) respectively, Table 2.

Also, in our study we compared serum AMH before and after laparoscopic management according to ovarian appearance and evolvement. Twenty patients (60.6%) showed abnormal ovarian appearance during laparoscopy and 13 patients (39.9%) had normal appearance of ovaries, Table 1. Serum AMH showed no significant differences between the two groups (5.5 ± 1.4 ng/ml and 2.76 ± 0.96 ng/ml) before and after laparoscopy in group of normal ovarian respectively, and (3.37 ± 2.2 ng/ml and 1.84 ± 1.5 ng/ml) before and after laparoscopy in the group of abnormal ovarian appearance respectively [Table 2 and Figure 2].

Our study shows no difference between severity of endometriosis and mean serum AMH levels, Table 2. But serum AMH levels significantly decreased one month after laparoscopy in both minimal/mild and severe endometriosis (1.84 ± 2.06 and 2.18 ± 3.45 ng/ml), respectively.

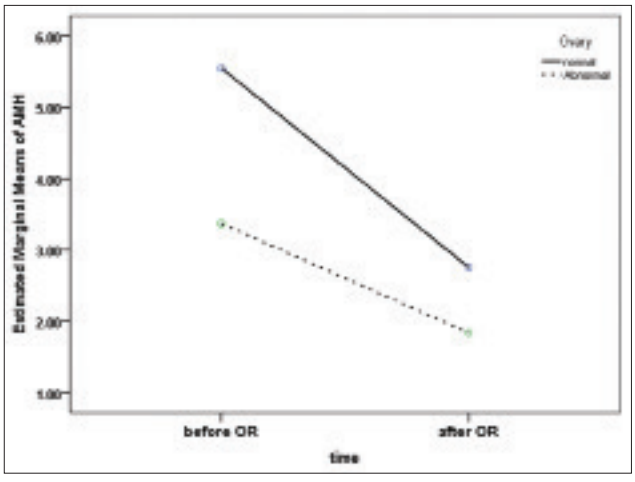

Figure 2: Serum AMH before and after laparoscopy according to ovarian appearance

DISCUSSION

This study is based on controversy between previous studies about changes of AMH levels after laparoscopic management of endometriosis. We attempt to evaluate the modifications of serum AMH levels as an ovarian reserve marker before and one month after operative laparoscopy in endometriosis.

As Lemos *et al.* reported that minimal/mild endometriosis is associated with a decrease in the follicular reserve and concluded that serum AMH is more sensitive than other test to evaluate ovarian reserve and its accuracy is limited and not in all infertile patients with endometriosis will be poor responder.[9]

Shebl *et al.* reported that AMH levels were significantly lower in patients with severe endometriosis than in the control group.[10] But our study shows no difference between severity of endometriosis and mean serum AMH levels.

Also, I and Hirokawa *et al.* documented a decrease of serum AMH levels 1 month after surgery of endometriomas from 3.9 to 3.3 ng/ml.[11] In agreement with aforementioned reports, we also found that patients with ovarian endometriosis had significantly lower serum AMH levels 1 month after laparoscopy.

Yuh-Ming *et al.* also discovered that patients undergoing bilateral cystectomy for endometrioma had significantly lower AMH levels 3 months after cystectomy compared with patients receiving unilateral cystectomy, the mean serum AMH level was significantly lower in patients treated with bilateral cystectomy than in patients treated with unilateral cystectomy, 1.4% of women (144 patients) enrolled in their study had ovarian failure one year after bilateral cystectomy.[12]

In our study, serum antimullerian hormone (AMH) levels did not show a significant difference using different surgical procedures for endometriosis treatment during laparoscopy. In our study only few numbers of patients had bilateral endometriomas.

Findings of our current study are in agreement with the above report thus it showed a significant reduction in serum AMH levels in patients with different stages of endometriosis one month after operative laparoscopy.

Ercan *et al.* proved that there was no significant serum AMH level decrease was noted 1 month after surgery for unilateral endometriomas. Also in another study, he showed that laparoscopic cystectomy for unilateral

ovarian endometriomas shown a decreased value of serum AMH levels in comparison to pre-operative period, also the value even decreased 3 month postoperatively.[13,14]

As we noted from Ercan *et al.* study, we can understand that not all studies concerned with this issue found a decrease in serum AMH levels after a specific and precise period of time laparoscopic endometriosis excision and endometriosis managements. Also Ercan found that the presence and size of endometrioma does not impair AMH levels and was no significant difference pre- and postoperation after laparoscopic endometrioma stripping surgery. Laparoscopic stripping surgery does not appear to cause damage in AMH secreting healthy ovarian tissue.[14]

Raffi *et al*. found that pre-operative AMH levels of 3.1 ng/ml or greater showed a significant postoperative fall in serum AMH and suggest a negative impact of excision of endometrioma ovarian reserve as evidenced by significant postoperative fall in circulating AMH.[15] And Suksompong *et al*. in a study found that median AMH levels was 2.11 ng/ml before surgery and reduced at first week post operation but did not reach a significant difference between the first week and the third month but it had a significant decrease after 1 month only.[16] In our study, we show a significant decrease of serum AMH levels 1 month after laparoscopy regardless of the initial value of serum AMH levels before laparoscopy.

Lee *et al*. in his study investigated the effects of laparoscopic cystectomy for endometrioma on ovarian reserve using serum AMH levels. They measured pre- and postoperative serum AMH levels at baseline and 1 week, 1 month, and 3 months after surgery. Mean levels of serum AMH decreased significantly immediately after surgery and remained for up to 3 months in both operation types.[17] In our study we didn't find any significant difference in AMH level decrease after surgical operations due to value of AMH prior laparoscopy.

Biacchiardi *et al*. estimated the impact of laparoscopic stripping of endometriomas on the ovarian follicular reserve. Serum AMH concentrations significantly decreased after the operation.[18]

Chang *et al*. also observed a significant decrease in serum AMH levels 3 months compared with one week after laparoscopic cystectomy of endometrioma, and it was significantly decreased in the endometrioma group and showed that serum AMH levels partially recovered 3 months after laparoscopy. He also reported in another study a statistically significant reduction of serum AMH levels at one week and one month after cystectomy from 2.7 to 2 ng/ml, and the rate of recovery was potentially correlated with pre surgical serum AMH.[19] In a recent study done by Sugita *et al*., he followed patients until 1 year after cystectomy of endometrioma and see a rise in AMH levels in comparison to 1 month after operation (1.9 to 2.1 ng/ml).[20]

More investigations should be done to confirm the association between decreased serum AMH levels and future reproductive rate. And much more studies have to concern the interval of time needed to show total recovery of AMH levels postoperatively and how long it would take.

Also, patients must be informed that after laparoscopy there is a decrease in ovarian reserve and since lower levels of AMH in infertile patients of endometriosis are at risk of premature ovarian failure syndrome it is impotent to counsel for future fertility potentials and outcomes and IVF/IUI must be initiated before laparoscopy.

And since different studies showed different and controversial results, longer periods are needed to see impact of laparoscopic management of endometriosis on ovarian reserve.

This study had some limitations such as high cost of AMH test and no cooperation to follow-up patients enrolled in the study for longer period of time.

- High cost of AMH test
- No cooperation to follow-up patients enrolled in the study for longer period of time.

CONCLUSION

In this study, we show that serum AMH levels clearly decreased after operative laparoscopy for different types of endometriosis in infertile women regardless of surgical procedures.

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