Original Article

Evaluation of Anti-Mullerian Hormone level as a marker of Ovarian Reserve and correlate it with Laparoscopic Surgery of Pelvic Endometriosis in Subfertile Patients

Abbasi S[a], Siddiqua SF[b], Alam MNA[c], Jesmin S[d]

Abstract

Background: *Endometriosis refers to the presence of endometrial glands and stroma outside the uterine cavity. About 10% causes of infertility are due to endometriosis. In women Anti-Mullerian hormone (AMH) level represents the ovarian follicular pool and has been suggested as the most reliable and reproducible marker to asses ovarian reserve. The gold standard approach of management of endometriosis with subfertility is laparoscopy. The objectives of this stydy are evaluation of AMH levels as a marker of ovarian reserve in subfertile patients with different stages of pelvic endometriosis, and correlate it with laparoscopic surgery.*

Methods: *This was a cross sectional observational study on 59 subfertile patients from January 2014 to January 2017 in Anwer Khan Modern Medical College Hospital (AKMMCH). Main outcome measured on the basis of measurement of AMH levels in correlation with the age, types of subfertility, stages of endometriosis, unilateral or bilateral ovarian involvement, size of the cyst, number of the cyst and the impact of different procedures during laparoscopy on AMH levels.*

Results: *Basal AMH levels significantly lower (p= 0.011 and p =0.001) before and after laparoscopy in primary subfertile patients than secondary subfertile patients and AMH significantly decreased (P<0.024) after laparoscopy in primary subfertile patients. AMH level significantly decreased (P<.001) after laparoscopic surgery of two ovaries. Mean serum AMH levels were decreased in moderate and severe stages of endometriosis after laparoscopy (3.01±.04 ng/ml and 2.15±.03ng/ml). Different surgical procedures of laparoscopy showed significant impact on serum AMH levels, in thermal cauterization (p=0.023) and excision plus cauterization (p=0.001) showed significant decreased of AMH.*

Conclusion: *Serum AMH level decreased in many patients after laparoscopy to such an extent from where future fertility is possible.*

Key words: *Anti mullerian hormone (AMH), Laparoscopy, Ovarian reserve, Subfertility.*

(BIRDEM Med J 2018; 8(1): 30-34)

Author Information

a. Dr. Sharmin Abbasi, Assistant Professor, Gynecology and Obstetrics, Anwer Khan Modern Medical College Hospital, Dhaka

b. Prof. Sehereen Farhad Siddiqua, Professor and Head Gynecology and Obstetrics, Anwer Khan Modern Medical College Hospital, Dhaka

c. Dr. Mohammad Noor A Alam, Associate Professor of Surgery, Ibrahim Medical College and BIRDEM General Hospital, Dhaka

d. Dr. Suha Jesmin. Associate Professor, Gynecology and obstetrics, Anwer Khan Modern Medical College Hospital, Dhaka

Address of Correspondence: Dr. Sharmin Abbasi, Assistant Professor, Gynecology and Obstetrics, Anwer Khan Modern Medical College Hospital, Dhaka, E-mail:

Received: August 6, 2017; **Accepted:** October 31, 2017

Introduction

Endometriosis is a condition during which functional endometrial gland and stroma situated outside the uterus most commonly in pelvic cavity. The hidden toll and extraordinary neglect of a disease that affects an estimated 176 million women around the globe, causing many to suffer a life of pain, debilitation and infertility[1]. One in 10 of reproductive age has endometriosis[2]. Endometriosis affects women in the prime of their life. The mean age of diagnosis between 25-35 years and in 10-50% patients with subfertility had endometriosis[3]. Patients with ovarian endometrioma ranges between 24-44% among endometriosis[4]. Sufferers present with dysmenorrhoea, dyspareunia, subfertility, chronic pelvic pain (CPP), followed by poor quality of life.

Endometriosis caused distortion of tubo-ovarion axis and relationship. It also caused immunological reactions and made subfertile environment. Regarding diagnosis we can get idea from clinical evalution and Ultrasound (USG) findings. But definitive diagnosis made by gold standard procedure -Laparoscopy[5]. The diagnosis is staged laparoscopicaly from minimal to severe stages including ovarian endometrioma. We commonly follow the procedure for excision of the cyst capsule or electro-coagulation of the cyst wall with maximal preservation of the normal ovarian tissue. Laparoscopic approaches will restore normal anatomy, reduce pain, prevent recurrence, and increase pregnancy rate (PR)[6]. Patients with endometrioma or pelvic adhesion as well as infertility would not benefit from medical therapy. Based on the current evidence, laparoscopic management appears to be the method of choice. Despite the improvements in technique and management of symptomatic patients with endometriosis, there is growing concern about negative impact on ovarian reserve due to inadvertent removal or destruction of the healthy ovarian tissue adjacent to the pseudo capsule of the cyst.

Anti Mullarian hormone (AMH) also called egg timer is a member of the transforming growth factor of â 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[7]. AMH is the only ovarian reserve marker that is absolutely menstrual cycle independent and it is not affected by oral contraception and GnRH agonists[8,9]. So, recently in many studies AMH was studied and showed its importance and impact in subfertility in correlation with endometriosis and it is better than other ovarian reserve markers like- FSH, LH, FSH: LH, E2, and AFC.

Methods

This is a cross sectional observational study, which includes total 59 subfertile patients with endometriosis, who underwent laparoscopy between January 2014 and January 2017 in Anwer Khan Modern Medical College Hospital (AKMMCH). Approval for the study was obtained from review board and the ethics committee of AKMMCH. All the recruited patients provided their informed written consents. Inclusion criteria were- Infertile patients with age between 25-40 years of age, had regular menstrual cycle, minimal to severe stages of endometriosis, unilateral or bilateral ovarian involvement, single or multiple endometriomas, presenting with subfertility and others symptoms of endometriosis. Exclusion criteria includes-presence of any endocrine diseases like-diabetes, hyperprolactinemia, thyroid disorder or adrenal disorder, previous adenexal surgery, suspected or proven ovarian malignancy, previous history of chemotherapy, hepatitis, PID, other causes of infertility than endometriosis.

All patients were examined physically at inclusion into the study and the findings were recorded in the data sheet. All women underwent the operation under general anaesthesia (G/A). Laparoscopic pneumoperitoneum was induced by CO2 insufflations with 10mm trocar and telescope entries were made into intra abdominal pressure reached 12mmHg. Two 5 mm trocars were inserted as lateral port under direct laparoscopic view. The pelvic cavity was explored and endometriosis was classified according to the revised American Society of Reproductive Medicine (ASRM) classification. Endometrioma was also visualized. Small lesions of superficial peritoneal and ovarian endometriosis treated with ablation or fulguration. Small endometriomas treated with electro coagulation of the mucosal lining. Large ovarian endometrioma >4 cm in diameter treated with resection of the wall of the cysts from the healthy surrounding normal ovarian tissue with using atraumatic forceps. Often the cyst ruptured during dissection, then the cyst contents were immediately drained with suction cannula. Minimal cauterization in the ovarian bed was done by bipolar cautery to avoid thermal destruction of ovarian follicles. All resected cyst walls and deep infiltrative endometriosis specimens were confirmed histopathologically. When endometriosis was diagnosed then venous blood samples obtained from study group and serum AMH level was measured by Enzyme – Linked Immunosorbent Assay (ELISA) and again measured one month postoperative of laparoscopy. Main outcome measures on the basis of measurement of AMH levels in correlation with the age of the patients, types of subfertility, stages of endometriosis, unilateral or bilateral ovarian involvement, size of the cyst, number of the cyst and different procedures of surgery during laparoscopy. The minimal detectable concentration for AMH was 0.92 ng/ml and maximum value detected was 12 ng/ml.

Statistical analyses were performed with SPSS system, version 18. Concentration of serum AMH levels were

compared between each sampling point (preoperative and one month post operatively) by using paired student t-test, and unpaired student t-test between groups. ANOVA test was done in one way analysis of variance. Data were presented as mean ± SD. P value less than 0.05 was considered statistically significant.

Results

The mean age of the patients were 28.06 ± 5.4 years. Patients older than 30 years of age had significantly lower baseline serum level of AMH when compared with those younger than 30 years. Patients with >30 years of old had significantly lower AMH levels (p=0.034) after laparoscopy.

Data were expressed as mean ± SD. Paired student t-test performed in before and after llaparoscopy. Unpaired student t-test performed between groups.* *significant

Table I. AMH level before and after laparoscopy according to parameter (n=59)

Type of infertility	Anti-Mullerian Hormone (AMH)		P value
	Before laparoscopy (Mean±SD)	After laparoscopy (Mean±SD)	
Primary subfertility	3.04±0.61	2.57±0.45	0.024*
Secondary subfertility	3.16±0.59	3.03±0.79	0.074
P value	0.011*	<0.011*	

Table II. AMH level before and after operation according to parameter according to staging of endometriosis (n=59)

Staging of endometriosis	Anti-Mullerian Hormone (AMH)		p value
	Before laparoscopy (Mean±SD)	After laparoscopy (Mean±SD)	
Mild/minimal	3.11±0.06	3.08±0.76	0.672
Moderate	3.05±0.89	3.00±0.08	<0.001*
Severe	2.63±0.06	2.15±0.07	<0.001*

In single bilateral involvement the p-value was (0.025) which was significant. In multiple bilateral involvements p-value was (0.036) which was significant.

Table III. AMH level before and after operation according to number and size of cyst in both ovaries (n=59)

Name of cyst	Anti-Mullerian Hormone (AMH)		p value
	Before laparoscopy (Mean±SD)	After laparoscopy (Mean±SD)	
Single/unilateral	3.21±0.92	2.07±1.26	0.660
Single/bilateral	3.17±0.58	2.41±1.03	0.025*
Multiple unilateral	3.06±0.39	2.86±0.01	0.107
Multiple bilateral	2.38±0.57	2.14±0.63	0.036*
Size ≤ 4cm	3.14±0.95	3.11±0.74	0.062
Size>4cm	3.02±0.66	2.98±0.92	0.283

Table IV. AHM level before and after operation according to surgical procedures (n=59)

ParameterSurgical procedures	Anti-Mullerian Hormone (AMH)		p value
	Before laparoscopy (Mean±SD)	After laparoscopy (Mean±SD)	
Thermal Cauterization	3.12±0.81	3.01±0.42	0.023*
Cystectomyl Complete Cystectomy	3.17±0.62	3.04±0.51	0.349
Pertial Cystectomy with adhesiolysis with ablation of lesion	3.03± 0.45	3.01±0.32	0.324
Aspiration of cyst with adhesiolysis	3.14± 0.85	2.03±0.24	0.241
Both (Excision +cauterization)	3.31±0.84	2.28±0.62	<0.001*
ANOVA test	0.104	<0.001*	

Discussion

This study has been conducted on patients with different stages of endometriosis underwent laparoscopy to assess the effects of the surgery on AMH. We found that significant decline in serum AMH levels from base line to 1 month postoperatively. This is consistent with other studies with follow-up periods of one month.[10] One month after surgery a significant decline in serum AMH levels were detected by Hirokawa et al.[11] and Iwase et al.[12] but not by Ercan et al.[13] and Litta et al.[14] Increased age as the independent risk factor for decreasing the ovarian reserve, could be responsible for decreased levels of AMH one month postoperatively. Jaduol and co-workers[15] performed a review to determine the effects of age on AMH.

Comparison of two different cyst sizes d”4cm or >4 cm revealed that there was no significant difference in the baseline AMH levels. The size of endometrioma did not correlate with baseline and postoperative AMH levels in two others study.[16]

Patients with bilateral endometrioma had a lower baseline AMH level compared with unilateral cysts, which remained lower after one month of laparoscopy also. In the study by celik et al.[17] Shewu et al.[18] showed a significant lower baseline level in bilateral endometriomas and reported a more profound impact of bilaterility on the ovarian reserve, regardless of either conservative or surgical intervention. It should be kept in mind that the endometrioma itself can affect the ovarian reserve negatively. This study showed a significant decline in AMH levels in individuals with multiple bilateral endometriomas compared with single and multiple unilateral ones, thus representing bilaterality and multiplicity as more damaging factors. Few studies had evaluated the effects of bilateral and multiple presence of cysts on AMH[20] Kim et al[21] showed that in woman with advanced ovarian endometrioma, preoperative serum AMH values tend to be lower. Stage IV endometriosis appeared to be closely associated with decreased ovarian reserve, even before operation Even before the operation the ovarian reserve could be minimal secondary to advanced endometriosis.

In this study baseline serum AMH and 1 month after surgery levels of AMH significantly decreased. Shebl et al.[22] reported that AMH levels were significantly lower in patients with sever endometriosis. Lemos et al[23] concluded that serum AMH is more sensitive than other tests to evaluate ovarian reserve in different stages of endometriosis.

Yuh-Ming et al.[24] showed that patients undergoing bilateral cystectomy with cauterization had significantly lower AMH levels one month after surgery compared with patients with unilateral cystectomy or cauterization. This study supports our result.

In this study serum AMH levels showed a significant difference using different surgical procedures for endometriosis treatment during laparoscopy. Ecran et al. [25] proved that different procedures of surgery during laparoscopy had significant impact on AMH levels. Bicchiadaria et al[26] estimated the impact of laparoscopic

stripping of endometriomas on the ovarian follicular reserve. Serum AMH significantly decreased after the operation.

Conclusion

Serum AMH level decreases in many patients after laparoscopy to such an extent from where future fertility is possible. So, laparoscopy is the gold standard surgical procedure and serum AMH is more reliable and remarkable marker to assess ovarian reserve for the management of subfertile patients with different stages of endometriosis.

Conflict of interest: Nothing to declare.

References

1. Firtz CM, Speroff L. Endometrosis diagnosis and suitable treatment for the individual patient. In: Firtz CM, Speroff L, editors. Clinical gynecologic endocrinology and infertility. 8th ed. Pihaldelphia: Lippincott Williams and Wilkins Press; 2011.
2. D' Hooghe TM, Vercammen E, Hill JA. Berek and Novak's Gyncology. 15th ed. Philedelphia: Lippincott Williams and Wilkins Press; 2012. Endometrosis.
3. Giudice IL. Clinical practice Endometriosis. N Engl J Med. 2010; 362:2389–98.
4. Bulletti C, Coccia ME, Battistoni S, Borini A. Endometriosis and infertility. J Assist Reprod Genet 2010;27:441–47.
5. Bulletti C, Panzini I, Borini A, Coccia E, Setti PL, Palagiano A. Pelvic Factor infertility diagnosis and prognosis of various procedures. Ann NY Acad Sci 2008;1127:73–78.
6. La Marca A, Sighinolfi G, Radi D, Argento C, Baraldi E, Artenisio AC, et al. Anti-Mullerian Hormone as a predictive marker in assisted reproductive technology. Hum Reprod Update 2010;16:113–30.
7. Seifer DB, Baker VL, Leader B. Age-specific serum Anti Mullerian Hormone values for 17120 women presenting to fertility centers within the United States. Fertile Steril. 2011;95:747–50.
8. Hirokawa W, Iwase A, Goto M, Takikawa S. The post-operative decline in serum anti mullerian hormone correlates with bilaterality and severity of endometriosis. Hum Reprod 2011;26:904–10.
9. Iwase A, Zarei A, Alborzi M, Alborzi M. Mangement of ovarian endometrioma. Clin Obstet Gynecol 2006;49:480–91.
10. Ercan CM, Sakinci M, Duru NK, Alanbay I, Karasahin KE, Baser I. Antimullerian hormone levels after laparoscopic endometrioma stripping surgery. Gynecol Endocrinol 2010;26:468-67.
11. Litta, Arbo E, Scalco R, Weiler E, Rosa VC,cohort in infertile patients with mild/minimal endometriosis. Fertil Steril 2008;89:1064–68.
12. Jaudal, Duru NK, Karasahin KE, Coksuer H, Dede M, Baser I. Ultra sonographic evaluation and antimullerian hormone levels after laparoscopic stripping of unilateral endometriomas. Eur J Obstet Gyencol Reprod Biol 2011;158:280–84
13. Raffi F, Metwally M, Amer S. The impact of exicision of ovarian endometrioma on ovarian reserve: A systemic review and meta-analysis. J Clin Endocrinol Metab. 2012;97:3146–54.
14. Cleik, Dejarkom S, Petyim S, Dangrat C, Orachon D, Choavaratana R. Ovarian reserve evaluation by anti-mullerian hormone in women undergoing laparoscopic cystectomy of endometrioma. J Med Assoc Thai 2012;95:1389–95.
15. Shewu, Young Kim N, Jae Kim M, Yoon BK, Choi D. Effects of laparoscopic surgery on serum anti-Müllerian hormone levels in reproductive-aged women with endometrioma. Gynecol Endocrinol 2011;27:733–76
16. Iwasa,Chang HJ, Han SH, Lee JR, Jee BC, Lee Bi, et al. Impact of laparoscopic cystectomy on ovarian reserve: Serial changes of serum anti-Mullerian hormone levels. Fertil Steril 2010;94:343–49
17. Kim, Chang HJ, Han SH, Lee JR, Jee BC, Lee Bi, Suh CS, et al. Impact of laparoscopic cystectomy on ovarian reserve: Serial changes of serum anti-Mullerian hormone levels. Fertil Steril. 2010;94:343–49
18. Sugita A, Iwase A, Goto M, Nakahara T, Nakamura T, Kondo M, et al. One-year follow-up of serum antimüllerian hormone levels in patients with cystectomy. Fertil Steril. 2013;100:516.
19. Chang HJ, Han SH, Lee JR, Jee BC, Lee Bi, Suh CS, et al. Impact of laparoscopic cystectomy on ovarian reserve: Serial changes of serum anti-Mullerian hormone levels. Fertil Steril. 2010;94:343-49.
20. Hughesdon PE. The structure of endometrial cysts of the ovary. J Obstet Gynaecol Br Emp 1997;64:481-87
21. Shebl, Donnez J. Peritoneal endometriosis, ovarian endometriosis, and adenomyotic nodules of the rectovaginal septum are three different entities. Fertil Steril 1997;68:585–96.
22. Lemos, Momtahan M, Parsanezhad ME, Dehbashi S, Zolghadri J, Alborzi S. A prospective randomized study comparing laparoscopic ovarian cystectomy versus fenestration and coagulation in patients with endometriomas. Fertil Steril 2004;82:1633–37
23. Yuh-Ming, Hickey M, Maouris P, Buckett W, Garry R. Excisional surgery versus ablative surgery for ovarian endometriomata: a Cochrane Review. Hum Reprod 2005;20:3000–7.
24. Ecran, Foroughinia L, Kumar PV, Asadi N, Alborzi S. A comparison of histopathologic findings of ovarian tissue inadvertently excised with endometrioma and other kinds of benign ovarian cyst in patients undergoing laparoscopy versus laparotomy. Fertil Steril 2009;92:2004–7.
25. Raffei, Lousse JC, Jadoul P, Donnez O, Squifflet J. Laparoscopic management of endometriomas using a combined technique of excisional (cystectomy) and ablative surgery. Fertil Steril 2010;94:28–32.
26. Biacchiardi CP, Piane LD, Camanni M, Deltetto F, Delpiano EM, Marchino GL, et al. Laparoscopic stripping of endometriomas negatively affects ovarian follicular reserve if performed by experienced surgeons. Reprod Biomed Online 2011;23:740-46.