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Research Article

Potential impact of ovarian endometrioma on serum anti-Müllerian hormone level and antral follicle count

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ABSTRACT

Background: An endometrioma is a cyst formed when endometrial tissue proliferates in the ovaries. It affects women during their reproductive years and may result in persistent pelvic pain related to menstruation. The term "ovarian reserve" refers to the ovary's ability to produce an ovum that can be fertilized to achieve a successful and healthy pregnancy. Currently, the two techniques most frequently employed to evaluate ovarian functional reserve are serum anti-Müllerian hormone (AMH) level and antral follicle count (AFC). The aim of this study is to determine the possible effects of ovarian endometrioma on antral follicle count and serum anti-Müllerian hormone levels through a case-control study.

Methods: Out of 100 women, 50 had ovarian endometrioma, while the remaining 50 were selected as the control group. On the second day of the menstrual cycle, we conducted a thorough clinical examination and a complete history taking, including an ultrasound and measurements of serum anti-Müllerian hormone levels.

Results: Endometriomas were more common on the right side (46%), and those with endometriomas had lower anti-Müllerian hormone levels and total antral follicle counts.

Conclusions: When the volume of the endometrioma is high, the number of antral follicles is further decreased.

Introduction

The term "ovarian reserve" describes the ovary's capacity to release ovum that can be fertilized to result in a smooth and healthy pregnancy. The following tests are available for ovarian reserve evaluation: The following tests are used to measure ovarian vascularity, antral follicle count, ovarian volume, and basal estradiol: clomiphene citrate challenge test, basal follicle-stimulating hormone, anti-müllerian hormone, basal follicle-stimulating hormone, inhibin B, and gonadotrophin-releasing hormone stimulating test (1).

Only the ovary's microscopic antral follicles (AFs) and granulosa cells of the preantral (primary and secondary) stages produce the dimeric glycoprotein known as the anti-Mullerian hormone (AMH). Follicles with diameters of 2–6 mm migrate from the primordial to the primary stage, and then they reach the antral stages, which is when AMH creation starts (2).

There is a relationship between the number of small AFs and the measurement of the primordial follicle pool. Due to the aging-related decline in the quantity of AFs, AMH generation appears to decline and become negligible at and beyond menopause (3). Transvaginal ultrasound measurements of the basal antral follicle count (AFC) correlate highly with AMH levels (4). Unlike other biochemical indicators (5), it does not show intercycle variability and can be evaluated at any time during the cycle.

Transvaginal ultrasonography measures the number of antral follicles during the early follicular phase by averaging two measurements taken perpendicular to each other. The total AFC is calculated by adding the follicles in both ovaries. The ovarian reserve marker AFC has been in use for a long time. A count of 8–10 is thought to predict a normal response. AFC is defined by two diameters: 2.6 and 7-9 mm (6).

Regarding the size of AFs that accurately reflect ovarian reserve, opinions differ. It is discovered that while the number of AFs with a size of 3-6 mm decreases with age and is correlated with other indicators like FSH and CCCT, the number of AFs with a length of 7-9 mm stays constant (7); hence it would seem that the former is a more accurate indicator of ovarian reserve. Numerous measurements have demonstrated that the intercycle variability is relatively small. The two most popular techniques for determining ovarian functional reserve are AMH and AFC (8).

Chung and Han (9) found that while there is no evidence to support a lower rate of pregnancy and delivery in endometriosis-affected women, the development of a local proinflammatory microenvironment damages surrounding tissue by causing angiogenesis, vasodilatation, and congestion caused by inflammatory liquid, as well as the replacement of fibrous tissue with normal ovarian cortical tissue (10). In addition to distorting the surrounding anatomy and creating a more considerable distance between the normal ovarian tissue and the probe, an endometrioma and its associated local inflammation may lower the number of follicles. This could increase attenuation and make it more challenging to identify antral follicles [9]. For this reason, it is possible to underestimate ovarian reserve when endometrioma is present, which is less common following surgery when the pelvic geometry is more in line with physiologic values. Their explanation could be the difference in ovarian reserve measurements made before and after laparoscopy for endometriomas; AFC's higher ability to detect minuscule follicles during ovarian reserve tests could offset the ovarian reserve loss brought on by surgical intervention (11).

Methods

This case-control study was conducted at the Obstetrics and Gynaecology Department of Damietta Specialized Hospital between January 1st, 2021, and December 31st, 2022. Out of the 100 women, 50 had ovarian endometrioma, and the remaining 50 were chosen as controls.

Ethical consideration

Following participant selection, the following actions were taken: counseling, obtaining a written agreement to participate in the study, and explaining the protocol to each person.

1. The complete history taking covered age, parity, the type and duration of infertility, and additional medical or surgical history.

2. Comprehensive clinical evaluation, which included a comprehensive gynecological and general checkup.
3. Assessments:

– Ultrasonography: A multifrequency volume endovaginal probe-equipped Voluson 730 Pro machine (GE, Milan, Italy) was used for the ultrasound scan. If B-mode ultrasonography revealed the characteristic pattern of "a circular-shaped homogeneous hypoechoic mass of low-level echoes," ovarian endometrioma was diagnosed. Antral follicle counts (AFC) and the endometrioma volume were measured bilaterally. The formula used to compute the endometrioma volumes was height × length × breadth × 0.5233, and the results were represented in cm3. A 2D transvaginal ultrasound was used to count the antral follicles on the second day of the menstrual cycle.
– Serum Anti-müllerian hormone: it was measured on 2nd day of the menstrual cycle.

Statistical analysis of data

Utilizing an IBM-compatible computer, the Statistical Program for Social Sciences (SPSS) version 19 (SPSS Inc., Chicago, USA) was used to arrange, tabulate, and statistically analyze the obtained data. The frequency and percent distributions were computed for the qualitative data. The mean, standard deviation (SD), minimum, and maximum were calculated for the quantitative data. Using the independent samples (t) test, two groups were compared. Several variables were correlated using the Pearson correlation coefficient (r-test). P values less than 0.05 were deemed significant for every test. P values greater than 0.05 were considered insignificant for all tests.

Results

The present case-control study included 100 women of reproductive age; 50 of them had endometrioma, and 50 were control cases. The results of the present study are demonstrated in tables (1-4) and figures (1-2).

Table (1) shows that age and BMI were nearly comparable between both cases and controls (age: 27.4±4.2 Vs. 25.9±4.9 years and BMI: 30.4±4.5 Vs. 31±3.9 Kg/m2), while parity was high among controls than among endometrioma cases with a statistically significant difference.

In Table (2), most of our cases had primary infertility (64%). The mean duration of infertility is 3.85 years. Regarding endometriomas, most are right-sided (46%), with a mean volume of 104.2 cm^3.

In the present work, Table (3) shows that total antral follicle count was lower among patients with endometrioma (4.42±3.01) than the control group (16.14±3.11), with a highly statistically significant difference. Anti-müllerian hormone was reduced among cases (1.88 ng/ml) than the control (2.18 ng/ml), but the difference was not statistically significant.

Table (4) Figure (1) demonstrates that there was a moderate negative correlation (r= -0.42) between endometrioma volume and total AFC with a statistically significant difference, while there was no significant correlation between AMH with either total AFC or endometrioma volume.

According to the current study, there was no difference in the levels of AMH between cases with bilateral and unilateral endometriomas; however, there was a statistically significant difference in total AFC between cases with bilateral and unilateral endometriomas (Figure 2).

Table 1. Demographic data of studied groups

Variable	Cases (n= 50)	Control (n= 50)	*t*	P
Age (years) Mean±SD Range	27.4±4.2 20-35	25.9±4.9 20-35	1.59	0.11
BMI (Kg/m^2) Mean±SD Range	30.4±4.5 22-37	31±3.9 24-35	0.73	0.46
Parity Mean±SD Range	0.7±0.1 0-2	1.03±0.14 0-4	3.7	0.001*

*: significant

Table 2. parameters of infertility and endometriomas among studied cases (group 1)

Variable	Finding
Period of infertility Mean±SD Range	3.85±1.7 1-8
Type of infertility (No., %) Primary Secondary	32 (64) 18 (36)
Site of endometrioma (No., %) Right Left Bilateral	23 (46) 12 (24) 15 (30)
Endometrioma volume (cm^3) Mean±SD Range	104.2±91.7 2.1-333

Table 3. Antral follicle count among studied groups

	Cases (n= 50)	Control (n= 50)	*t*	P
AFC				
Mean±SD	4.18±3.03	16.14±3.11	19.2	<0.001*
Range	1-14	12-25		
AMH (ng/ml)				
Mean±SD	1.88±0.96	2.18±0.79	1.7	0.087
Range	0.25-3.8	0.9-4.5		

*: highly significant

Table 4. Correlation between serum Anti-müllerian hormone, endometrioma volume, and antral follicle count among studied cases (group 1)

	Total AFC		AMH	
	r	P	r	P
AMH	0.075	0.607	-	-
Endometrioma volume	-0.42	0.002*	0.123	0.393

*: significant

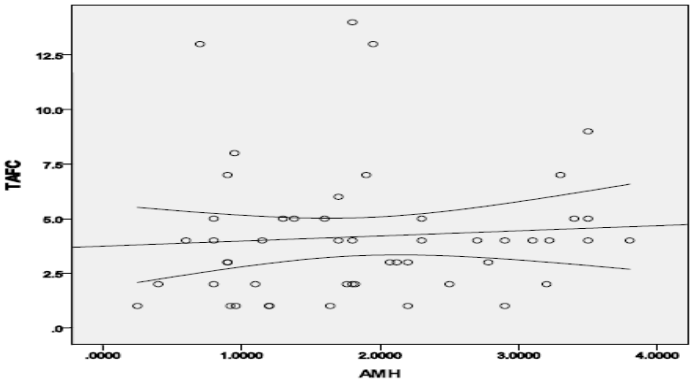


Figure 1. Correlation between antral follicle count and Anti-müllerian hormone among studied cases

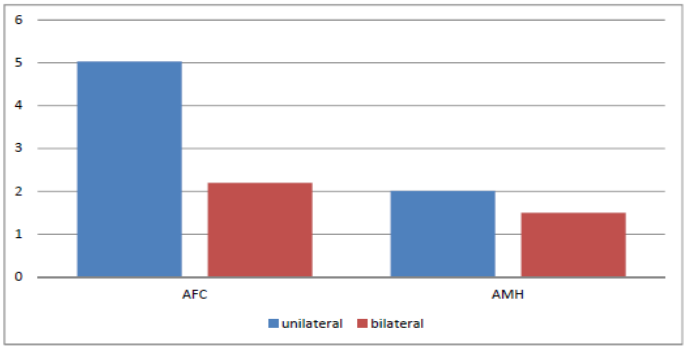


Figure 2. Relation between site of endometrioma with AMH and total AFC

Discussion

The aim of this work is to determine the possible effects of ovarian endometrioma on the antral follicle count and serum anti-Müllerian hormone through the present case-control study.

In the present work, age and BMI were nearly comparable between both cases and controls (age: 27.4±4.2 Vs. 25.9±4.9 years; P: 0.11) and (BMI: 30.4±4.5 Vs. 31±3.9 Kg/m^2).

These results rule out the impact of age or weight on the study's parameters. Their findings differed slightly from those of Streuli et al. (12), who found no difference in mean age between the study and control groups (31.9±5 among cases versus 32.1±5.9 among control). The BMI of women in the study group was marginally lower, 22±3.7 for cases compared to 23.4±4 for controls.

As predicted, parity was higher in the control group than in the cases, with a statistically significant difference (P: 0.001). It should be mentioned that every single one of our patients had primary or secondary infertility.

Numerous scientific explanations have been proposed for the frequently observed correlation between endometriosis and infertility. These consist of insufficient ovarian reserve, a peritoneal fluid containing higher levels of cytokines due to local and systemic inflammation, pelvic adhesion-induced mechanical obstruction, and decreased embryo receptivity and implantation (13).

Among the cases group, most of our cases had primary infertility (64%), with a mean duration of 3.85 years, which was slightly higher than reported by Benaglia et al. (14) of 2.9±1.4 years.

Most endometriomas are unilateral (70%), which is similar to Lima et al. (15), who reported unilateral cases, as 37/60 had unilateral endometriomas (61.6%). In our study, the mean volume of endometrioma was 104.2 cm3, which was higher than the reported figure by Ercan et al. (16) of 69.2±48.4 cm^3.

Total antral follicle count was lower in endometrioma patients (4.42±3.11) compared to the control group (16.14±3.11), a statistically significant difference (P: <0.001).

Research has employed chiefly the antral follicle count (AFC) to estimate the ovarian reserve in women having endometrioma surgery. Two investigations involving unilateral endometrioma have examined the preoperative evaluation of the damaged and healthy ovary. (17) found that the AFC of 43 women with endometrioma was considerably lower in the affected ovary (3.3±3.2 Vs. 8.4±6.0, respectively; P < 0.0001) than in the healthy ovary. These findings are consistent with our findings. Furthermore, women with endometriomas had considerably lower AFC than the controls (P, 0.01), according to (1).

Contrary to our results, [16] analyzed AFC for 36 women with unilateral endometrioma in comparison with the contralateral ovary before surgery. There was a non-statistically significant difference between the site of the endometrioma and the contralateral ovary (4.5±2 vs 5.2±3.5; P: >0.05, NS).

As regards serum anti-müllerian hormone, it was reduced among cases (1.88 ng/ml) than control (2.18 ng/ml), but without statistically significant difference (P: 0.087).

Similarly, a major study published in 2012 showed that endometriomas and endometriosis do not lower AMH levels. Regardless of whether they have endometriomas at the moment, women who have had surgery in the past for endometriotic cysts had lower AMH levels (12).

In addition, research contrasted 102 women with endometriomas with 102 controls with matching body mass indices (BMIs). The serum AMH and the AMH median (AMH-MoM) multiples did not significantly differ between the endometrioma cases and the controls. AMH and AMH-MoM levels in the serum were also lower in women with stage IV endometriosis than in controls (18).

Studies looking at serum antimüllerian hormone in women with endometriomas who haven't had surgery have been conducted to find out how endometriomas affect ovarian reserve. In a retrospective investigation conducted in Taiwan, the control group's mean AMH concentration was significantly higher than the endometrioma group's, based on a comparison of 141 endometrioma-affected women and 1323 infertile patients without endometrioma (19); however, their study included old age (up to 46 years) which limits the results of their research.

The work showed no significant correlation between AMH, total AFC, or endometrioma volume.

AFC and AMH have a high correlation when ovarian disease is absent. That AFC or AMH shows such strong and similar relationships with the size of the primordial follicle pool and follicular recruitment rates is astounding, especially considering the numerous technological constraints (20). The intensity of the connection is similar, indicating that the same 4-6 mm ultrasound-visible follicles are responsible for producing AMH (2). As such, analyses comparing AFC to AMH have repeatedly demonstrated high relationships (21).

The circulating level of AMH will represent the product of all granulosa cells within the follicles; this production is not constant and will depend on factors such as follicle size, potential granulosa cell mass, granulosa cell maturation state, intrafollicular environment, and individual genetics, which may be influenced by a range of single-nucleotide polymorphisms (SNPs) to affect AMH production (22).

In contrast to the lack of correlation considering AMH in our study, there was a moderate negative correlation (r= -0.42) between endometrioma volume and total AFC with a statistically significant difference (P: 0.002). According to our knowledge, there is a lack of studies that evaluated the direct relation between the size of endometrioma and AFC.

These results further support the uncertain reliability of AFC since endometrioma occupying a significant section of the ovary may make it challenging to visualize antral follicles (23). Additionally, the cyst's existence widens the gap between the ultrasonography probe and healthy ovarian tissue, impairing the transvaginal ultrasound scan's resolution (24).

Furthermore, although AFC has been used extensively in studies on ovaries with endometriomas in the past or present, this instrument has never been validated. Notably, according to established guidelines, women who have had prior ovarian surgery or endometriosis should not have their AFC evaluated (14).

Regarding laterality, total AFC, but not AMH, was lower among bilateral cases than unilateral with a statistically significant difference.

Similarly, Uncu et al. (25) found no relationship between bilaterality and AMH, but that total AFC was significantly lower in bilateral instances (7.73±4.22) compared to unilateral cases (11.73±4.56)

Endometrioma size had no discernible effects on the AMH decline following surgery, consistent with our findings (26). However, in contrast to individuals with unilateral endometrioma, those with bilateral endometrioma had a considerably reduced average concentration of AMH in the serum (27).

Conclusion

Antral follicle count is inversely correlated with bilateral endometriomas compared to unilateral ones, supporting the previously reported underestimate. AMH appears to be a more precise method of ovarian reserve estimation.

Author contribution

In the study, all authors contributed equally.

Conflict of interest

Regarding this study's implementation, authorship, or publishing, the authors state that they have no potential conflicts of interest.

Data sharing plans

Data are available from the corresponding author upon reasonable request

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References

1. Yılmaz Hanege B, Güler Çekıç S, Ata B. Endometrioma and ovarian reserve: effects of endometriomata per se and its surgical treatment on the ovarian reserve. Facts Views Vis Obgyn. 2019 Jun;11(2):151-157. PMID: 31824636
2. Almeida FR, Costermans NG, Soede NM, Bunschoten A, Keijer J, Kemp B, et al. Presence of anti-Müllerian hormone (AMH) during follicular development in the porcine ovary. PLoS One. 2018 Jul 31;13(7):e0197894. doi: 10.1371/journal.pone.0197894.
3. Moolhuijsen LM, Visser JA. Anti-Müllerian Hormone and Ovarian Reserve: Update on Assessing Ovarian Function. J Clin Endocrinol Metab. 2020 Nov 1;105(11):3361–73. doi: 10.1210/clinem/dgaa513.
4. Zhang Y, Xu Y, Xue Q, Shang J, Yang X, Shan X, et al. Discordance between antral follicle counts and anti-Müllerian hormone levels in women undergoing in vitro fertilization. Reprod Biol Endocrinol. 2019 Jul 4;17(1):51. doi: 10.1186/s12958-019-0497-4.
5. Biniasch M, Laubender R, Hund M, Buck K, De Geyter C. Intra- and inter-cycle variability of anti-Müllerian hormone (AMH) levels in healthy women during non-consecutive menstrual cycles: the BICYCLE study. Clinical Chemistry and Laboratory Medicine (CCLM). 2022;60(4): 597-605. doi: 10.1515/cclm-2021-0698.
6. Bessow C, Donato R, de Souza T, Chapon R, Genro V, Cunha-Filho JS. Antral follicle responsiveness assessed by follicular output RaTe(FORT) correlates with follicles diameter. J Ovarian Res. 2019 May 25;12(1):48-49. doi: 10.1186/s13048-019-0522-4.
7. Shahrokh TE, Mehrabi F, Taati R, Kalantar V, Aziminekoo E, Tarafdari A. Analysis of ovarian reserve markers (AMH, FSH, AFC) in different age strata in IVF/ICSI patients. Int J Reprod Biomed. 2016 Aug;14(8):501-6. PMID: 27679824
8. Ulrich ND, Marsh EE. Ovarian Reserve Testing: A Review of the Options, Their Applications, and Their Limitations. Clin Obstet Gynecol. 2019 Jun;62(2):228-237. doi: 10.1097/GRF.0000000000000445.
9. Chung MS, Han SJ. Endometriosis-Associated Angiogenesis and Anti-angiogenic Therapy for Endometriosis. Front Glob Womens Health. 2022 Apr 5;3:856316. doi: 10.3389/fgwh.2022.856316.
10. Gałczyński K, Jóźwik M, Lewkowicz D, Semczuk-Sikora A, Semczuk A. Ovarian endometrioma - a possible finding in adolescent girls and young women: a mini-review. J Ovarian Res. 2019 Nov 7;12(1):104. doi: 10.1186/s13048-019-0582-5.
11. Pais AS, Flagothier C, Tebache L, Almeida Santos T, Nisolle M. Impact of Surgical Management of Endometrioma on AMH Levels and Pregnancy Rates: A Review of Recent Literature. J Clin Med. 2021 Jan 22;10(3):414. doi: 10.3390/jcm10030414.
12. Streuli I, de Ziegler D, Gayet V, Santulli P, Bijaoui G, de Mouzon J, et al. In women with endometriosis anti-Müllerian hormone levels are decreased only in those with previous endometrioma surgery. Hum Reprod. 2012;27:3294–3303. doi: 10.1093/humrep/des274.
13. Bonavina G, Taylor HS. Endometriosis-associated infertility: From pathophysiology to tailored treatment. Front Endocrinol (Lausanne). 2022 Oct 26;13:1020827. doi: 10.3389/fendo.2022.1020827.
14. Benaglia L, Candotti G, Busnelli A, Paffoni A, Vercellini P, Somigliana E. Antral follicle count as a predictor of ovarian responsiveness in women with endometriomas or with a history of surgery for endometriomas. Fertil Steril. 2015;103(6):1544-1550.e1-3. doi: 10.1016/j.fertnstert.2015.03.013.
15. Lima R, Abdalla-Ribeiro H, Nicola AL, Eras A, Lobao A, Ribeiro PA. Endometriosis on the uterosacral ligament: a marker of ureteral involvement. Fertil Steril. 2017 Jun;107(6):1348-1354. doi: 10.1016/j.fertnstert.2017.04.013.
16. Ercan CM, Duru NK, Karasahin KE, Coksuer H, Dede M, Baser I. Ultrasonographic evaluation and anti-mullerian hormone levels after laparoscopic stripping of unilateral endometriomas. Eur J Obstet Gynecol Reprod Biol. 2011 Oct;158(2):280-4. doi: 10.1016/j.ejogrb.2011.04.043.
17. Biacchiardi CP, Piane LD, Camanni M, Deltetto F, Delpiano EM, Marchino GL, et al. Laparoscopic stripping of endometriomas negatively affects ovarian follicular reserve even if performed by experienced surgeons. Reprod Biomed. 2011;23(6):740–746. doi: 10.1016/j.rbmo.2011.07.014.
18. Suardi D, Permadi W, Djuwantono T, Hidayat YM, Bayuaji H, Edo Gautama GP. Correlation of Serum Anti-Mullerian Hormone (AMH) Level on Ovarian Volume in Women with Endometrioma. Int J Gen Med. 2021 Jan 6;14:1-8. doi: 10.2147/IJGM.S272071.
19. Lee J, Kim JM, Chong GO, Hong DG, Lee YH. Comparison of serum anti-Müllerian hormone between unilateral and bilateral ovarian endometriomas during follicular, luteal, and random menstrual phases: a retrospective study. J Yeungnam Med Sci. 2023;40(l):65-72. doi: 10.12701/jyms.2023.00661
20. Nelson SM. Biomarkers of ovarian response: current and future applications. Fertil Steril. 2013;99(4):963-969. doi: 10.1016/j.fertnstert.2012.11.051.
21. Van Disseldorp J, Lambalk CB, Kwee J, Looman CW, Eijkemans MJ, Fauser BC, et al. Comparison of inter- and intra-cycle variability of anti-Mullerian hormone and antral follicle counts. Hum Reprod. 2010;25:221–227. doi: 10.1093/humrep/dep366.
22. Silva MS, Giacobini P. New insights into anti-Müllerian hormone role in the hypothalamic-pituitary-gonadal axis and neuroendocrine development. Cell Mol Life Sci. 2021 Jan;78(1):1-16. doi: 10.1007/s00018-020-03576-x.
23. Asgari Z, Rouholamin S, Hosseini R, Sepidarkish M, Hafizi L, Javaheri A. Comparing ovarian reserve after laparoscopic excision of endometriotic cysts and hemostasis achieved either by bipolar coagulation or suturing: a randomized clinical trial. Arch Gynecol Obstet. 2016;293(5):1015-22. doi: 10.1007/s00404-015-3918-4
24. Ata B, Urman B. Endometrioma excision and ovarian reserve; do assessments by antral follicle count and anti-Mullerian hormone yield contradictory results. Hum Reprod. 2014;29:2852–2854. doi: 10.1093/humrep/deu269.
25. Uncu G, Kasapoglu I, Ozerkan K, Seyhan A, Oral Yilmaztepe A, Ata B. Prospective assessment of the impact of endometriomas and their removal on ovarian reserve and determinants of the rate of decline in ovarian reserve. Hum Reprod. 2013 Aug;28(8):2140-5. doi: 10.1093/humrep/det123.
26. Celik HG, Dogan E, Okyay E, Ulukus C, Saatli B, Uysal S, et al. Effect of laparoscopic excision of endometriomas on ovarian reserve: serial changes in the serum antimüllerian hormone levels. Fertil Steril. 2012;97(6):1472-1478. doi: 10.1016/j.fertnstert.2012.03.027.
27. Hwu YM, Wu FS, Li SH, Sun FJ, Lin MH, Lee RK. The impact of endometrioma and laparoscopic cystectomy on serum anti-Müllerian hormone levels. Reprod Biol Endocrinol. 2011 Jun 9;9:80. doi: 10.1186/1477-7827-9-80.