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Research Article

Assessment of Ovarian Reserve After Ovarian Cystectomy by Laparotomy Versus Laparoscopy

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ABSTRACT

The objective of this study was to compare the impact on ovarian reserve between laparoscopic ovarian cystectomy and laparotomic ovarian cystectomy. Sixty-four women with ovarian cysts whether unilateral or bilateral, endometrioma and nonendometrioma were included; 32 of them underwent laparoscopic ovarian cystectomy and the other 32 underwent open ovarian cystectomy (laparotomy). Preoperative blood samples: obtained to measure the level of preoperative of AMH one week before the surgery and one month postoperatively. Histological analysis of the removed specimen for counting the number of follicles that by their removal might affect the ovarian reserve.

The results showed Both laparoscopic and open ovarian cystectomy were found to adversely and significantly affect the ovarian reserve measured by AMH but no statistical significant difference found between the two approaches as regard the neither AMH difference nor number of follicles found in the cyst wall. Meanwhile laparoscopic group found to have significantly lower BMI. In subgroup analysis; endometrioma group found to cause more pronounced decrease in ovarian reserve than nonendometrioma group although not statistically significant while pre and postoperative AMH found to be significantly lower in endometrioma group. Statistically significant positive correlation was detected between AMH change in one hand and number of follicles in cyst wall, rASRM scoring system and preoperative AMH level in the other hand. Moreover, statistically significant positive correlation between number of follicles in cyst wall and cyst dimensions was recorded.

Based on the previous findings, the surgical approach can cause definite harm to the ovarian reserve with no privilege recorded of laparoscopy over laparotomy as regard conservation of ovarian reserve. Other factors rather than type of surgery would determine the extent of this damage.

Key words: ovarian cysts, laparoscopic ovarian cystectomy, laparotomic cystectomy, ovarian reserve.

INTRODUCTION

Ovarian reserve is defined as the existent quantitative and qualitative supply of follicles that are found in the ovaries that can potentially develop into mature follicles that in effect determine a woman's reproductive potential. It is also used as a term to determine the capacity of the ovary to develop oocytes capable of fertilization, resulting in a healthy and successful pregnancy. Follicular exhaustion is a known fact in the fourth decade of reproductive life. With increasing levels of female education, their participation in the labor force, postponement of childbearing has lead to a so-called sexual revolution causing an increasing incidence of subfertility due to ovarian ageing. The evaluations of ovarian reserve have therefore arisen to better counsel couples and guide the assisted reproduction protocols[1].

Benign ovarian cysts develop within the ovarian parenchyma and are often removed either using a minimally invasive procedure such as laparoscopy or an open abdominal procedure called the laparotomy. Both, the cyst in itself and the cystectomy i.e. excision and enucleating of cyst from the ovary can influence the ovarian reserve[1].

Markers of ovarian reserve that can estimate the reserve have evolved such as FSH, inhibin B, 17-estradiol (E2), FSH/LH ratio, antimüllerian hormone) and/or ultrasound variables (ovarian volume, antral Follicle Count, ovarian stromal blood flow) may be of help[2,3].

AMH is a glycoprotein hormone of TGF-β family. AMH also known as Müllerian inhibiting substance is one of the best markers of ovarian reserve[4]. It is considered to be a marker that can estimate the quantity and activity of recruitable follicles in early stages of growth, thus being more reliable for the prediction of ovarian reserve[5].

Studies have shown reduced variability in the levels of AMH as compared to other endocrine markers of ovarian reserve[6]. AMH has also been suggested as an important predictor of response to ovarian stimulation[7] also, has a strong correlation with the number of oocytes retrieved and the total number of antral follicles[8]. AMH thought to relate closely to primordial follicle number, which is considered as an indirect marker of ovarian reserve[9].

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Table 1: Demographic data of the studied populations

Variable	Laparoscopy (n = 32)	Open ovarian cystectomy (n = 32)	P
Age (year)	27.344 ± 5.773	24.938±7.053	0.140
Parity			
Nullipara	4 (12.50%)	2 (6.25%)	0.387
Multipara	28 (87.50%)	30 (93.75%)	
*BMI (Kg/m²)	22.575 ± 2.185	24.189±3.747	0.039*
Length of menstrual cycle (days)	28.406 ± 2.046	27.844±2.157	0.289
Duration of menstruation(days)	4.750 ± 1.414	4.688±1.230	0.851
Menses regularity			
Regular	24 (75.00%)	27 (79.69%)	0.351
Irregular	8 (25.00%)	5 (20.31%)	
Symptoms at time of surgery			
Infertility	17 (53.125%)	11 (34.375%)	0.091
Chronic pelvic pain	10 (31.25%)	19 (59.38%)	
Dysmenorrhea	5 (15.625%)	2 (6.25%)	

*BMI body mass index

Table 2: Comparison between laparoscopic and open ovarian cystectomy as regard histological features of the cyst and ultrasound findings

Variable	Laparoscopy (n = 32)	Open ovarian cystectomy (n = 32)	P
Cyst type			
Endometrioma	20 (62.50%)	20 (62.50%)	0.245
Non- endometrioma	12 (37.5%)	12 (37.5%)	
Hemorrhagic	6 (18.75%)	4 (15.63%)	0.470
Serous	3 (9.38%)	2 (6.25%)	0.122
Dermoid	1 (3.12%)	3 (9.38%)	0.051*
Mucinous	2 (6.25%)	3 (9.38%)	0.122
Laterality			
Unilateral	26(81.25%)	24(75.00%)	0.545
Bilateral	6 (18.75%)	8(25.00%)	
Cyst dimensions (cm)	4.94 ± 0.810	4.911±0.759	0.8830
Ovarian volume (cm³)	22.012±12.331	16.211 ± 5.475	0.018*

Therefore, serum AMH level currently represents the most reliable and easily measurable maker for ovarian reserve[10]. The aim of the present work was to assess ovarian reserve after ovarian cystectomy by laparotomy versus laparoscopy.

Patients and Methods

Sixty-four women with ovarian cysts whether unilateral or bilateral, endometrioma and nonendometrioma (endometrioma; is the formation of a cyst within ovary with ectopic endometrium tissue lining), presented with various symptoms and tend to have ovarian cystectomy were employed in this study, thirty- two underwent laparoscopic ovarian cystectomy while the other thirty-two patients underwent open ovarian cystectomy. Diagnosis of the presence of the cyst was based on vaginal ultrasonography. The study was conducted after the approval of research ethical committee and informed written consents were obtained from patients.

Inclusion criteria

Women in reproductive period (age 18-40 years), with unilateral or bilateral benign ovarian cysts, menstrual cycles (21-35 days), with no evidence of other endocrinal diseases e.g. thyroid dysfunction, hyperprolactinemia or Cushing s disease. Women not receiving oral contraceptives or progestins in the preceding 3 months.

Exclusion criteria

Women with history of previous surgery for benign ovarian cyst or oophorectomy, pregnancy and patients with polycystic ovarian disease or malignancy.

Patients were subjected to:

-Full history taken

-physical examination included; general examination, pelvic examination, transvaginal ultrasound to measure the dimensions of the cyst and ovarian volume.

-Preoperative blood samples: obtained to measure the level of preoperative of AMH one week before the surgery.

-Ovarian cystectomy, either laparoscopically (32 patients) or through Laparotomy (32 patients).

-Histological analysis of the removed specimen for counting the number of follicles that by their removal might affect the ovarian reserve.

Post operative blood samples: obtained to measure the level of post operative of AMH one month after the surgery.

-AMH measurement:

Table 3: Comparison between both groups as regard AMH levels pre and post-operative and histopathology

Variable	Laparoscopy n = 32	Open ovarian cystectomy n = 32	P
Fo follicular number *	5.594 ± 4.055	4.406 ± 2.894	0.182
A AMH preoperative (ng/ml)	2.847 ± 1.319	2.927 ± 1.024	0.787
A AMH postoperative (ng/ml)	1.992 ± 1.295	2.214 ± 0.932	0.433
A AMH change (ng/ml)	0.855 ± 0.680	0.713 ± 0.324	0.289
P	0.000*	0.000*	

AMH= antimüllerian hormone, (*) = number of follicles in cyst wall

Table 4: Comparison between bilateral and unilateral cysts as regard number of follicles in cyst wall

V Variables	Laterality		P
	bilateral	unilateral	
N Number of follicle	6.643 ± 4.106	4.540 ± 3.271	0.049*
A AMH /pre (ng)	2.856 ± 1.008	2.896 ± 1.223	0.911
A AMH /post (ng)	2.108 ± 0.777	2.102 ± 1.211	0.986
Difference /AMH pre-AMH post (ng)	0.748 ± 0.492	0.794 ± 0.549	0.778

2-3 cm blood samples were collected and centrifuged then serum samples were stored at -20°C until being assayed using commercially available ELISA kits (Glory Science Co., Ltd, USA). The detection range will be 0.5ng/mL - 25ng/mL, All assays were performed in duplicate and mean values were used for data analysis. The intra-assay and inter-assay coefficients of variation (CV) for AMH assay were below 10%. Serum AMH was measured: one week preoperatively and one month post operatively.

Statistical analysis

Analysis of data was done IBM computer using SPSS Version 17; quantitative data were presented using the mean and standard deviation.

Qualitative data were presented using the frequency and percentage. Comparison of quantitative data was done using independent T test (Unpaired Student T-test). Qualitative data were compared using the Chi - square test. Paired Student T-test was used to compare between related samples. Pearson correlation (Linear Correlation Coefficient) was done to estimate the correlation between quantitative data.

RESULTS

Over the study period; 64 patients met all the inclusion criteria whom 32 of them underwent laparoscopic ovarian cystectomy and the other 32 underwent open ovarian cystectomy (laparotomy).

Table 1 shows a significant higher BMI in open ovarian cystectomy group compared with laparoscopy group (P = 0.039). No statistically significant differences were found in age and menses duration and menstrual cycle length, parity, menses regularity and manifestations in form of infertility, chronic pelvic pain and dysmenorrhea between both groups.

Table 2 shows a significant higher ovarian volume in laparoscopy group compared with open ovarian cystectomy group (P=0.018) and higher number of dermoid cysts in open ovarian cystectomy group compared with laparoscopy group (P = 0.051). No statistically significant differences were found (P> 0.05) between both groups in cyst dimensions.

Table 3 shows no statistically significant differences (P >0.05) found between both groups as regard number of follicles found in cyst wall, AMH preoperative and AMH postoperative and AMH change (AMH pre - AMH post) using independent t test While there is highly statistical significant difference between pre and postoperative values of AMH (P =0.000) using paired t test.

Table 4 shows a significant difference between bilateral and unilateral subgroups in number of follicles in cyst wall (P = 0.049) while no statistically significant differences were found in AMH pre and post operative and AMH change using independent t test.

Table 5 shows no statistical significant correlations between number of follicles in cyst wall with different variables except with cyst dimensions (P =0.002), ovarian volume (P =0.001) and change in AMH (P <0.001) there were significant positive correlations.

Table 6 shows no statistical significant correlations could be detected between change of AMH with different variables except with ovarian volume (P = 0.057), number of follicles in cyst wall (P < 0.001) preoperative AMH levels (P = 0.011) and r ASRM (revised American society for reproductive medicine) score (P = 0.002) there were significant positive correlations (Figure 1).

DISCUSSION

There are various markers and imaging criterion for determining ovarian reserve among which antimüllerian hormone is the most reliable parameter to measure the ovarian stock of follicles and hence reflecting the future fertility[11]. Operative laparoscopy compared with laparotomy has been established as the gold standard surgical approach in the treatment of ovarian cysts in terms of reduced postoperative pain, analgesic requirement, hospitalization, and adhesion formation[12]. However the safety of cystectomy for benign ovarian cysts has been questioned with respect to damage to the affected ovary[1].

In the current study no statistical difference was found between laparoscopic and open ovarian cystectomy as regard the effect on ovarian reserve, which is consistent with other investigators[13]. Meanwhile there is decrease

Table 5: Correlations between numbers of follicles found in cyst wall and demographic data, cyst clinical features and AMH levels

V	Variables	r	P
A	Age(years)	-0.055	0.666
L	lenght of cycle (days)	-0.194	0.125
D	Duration of cycle (days)	0.163	0.197
B	BMI (Kg/m²)	-0.123	0.333
C	Cyst dimensions (cm)	0.515	0.000*
O	Ovarian volume (cm³)	0.417	0.001*
A	AMH /pre (ng/ml)	0.216	0.087
A	AMH /post (ng/ml)	-0.140	0.270
D	Difference /AMH pre-AMH post (ng/ml)	0.769	<0.001*

noted in the postoperative values of AMH that agrees with other coworkers[14,15,16].The explanation of such decrease can only be hypothesized, apart from surgical skill, surgery-related local inflammation and electrosurgical coagulation may be due to the damage inflicted to the ovarian cortex and vascularization resulting in loss of healthy ovarian tissue[17]. Alteration of the vascular supply to the ovaries might have occurred during the intervention; however In a prospective nonrandomized study with ovarian endometrioma removed laparoscopically, stromal blood flow, which is recognized as a valid indicator of ovarian reserve did not differ in the operated and in the contralateral intact ovary[18]. Also, two studies[19,20] concerned with the surgical removal of nonendometriotic benign ovarian cysts failed to document significant modifications of serum AMH level which is inconsistent with the results obtained from this study. In the present study the decline in AMH level post operatively found to be more profound in the endometrioma patients than in nonendometrioma patients, this result agrees with the results recorded by Deb[1], although not found to be statistically significant but may be explained by the fact that ovarian tissue adjacent to endometrioma is not normally functioning and even more removing it improves fertility[17,21,22].

Table 6: Correlations between change in AMH (AMH pre- AMH post) and demographic criteria, cyst characteristics, operative characteristics, number of follicle in cyst wall, hormonal profile and rASRM score

V	Variables	r	P
Ag	Age (years)	-0.107	0.402
Le	Length of cycle (days)	-0.073	0.569
Du	Duration of cycle (days)	0.001	0.996
B	BMI (Kg/m²)	-0.065	0.611
Cy	Cyst dimensions (cm)	0.172	0.174
Nu	Number of follicles	0.769	<0.001*
A	AMH /pre (ng/ml)	0.315	0.011*
A	AMH/post (ng/ml)	-0.146	0.249
rA	rASRM score*	0.616	0.000*

* rASRM =revised American society for reproductive medicine

In this study no statistically significant difference was found between laparoscopyic and open ovarian cystectoy groups in preoperative AMH levels, however when comparing the preoperative AMH levels between endometriotic and non endometriotic groups there were statistically significant difference between them suggesting that presence of endometriotic cysts per se and /or the disease itself (endometriosis) may affect the ovarian reserve; this finding agrees with Almong et al.[23] in which an ovary that had nonendometriotic cyst was not statistically significantly different from that of the contralateral ovary that did not contain a cyst as regard AFC, However, an ovary that contained an endometrioma had a statistically significantly lower AFC than the contralateral ovary .This may be explained by the effect of endometriosis on the granulosa cells, follicles, and oocyte and that the damaging effect was actually consequent to the inflammation surrounding the affected ovary, peri-ovarian adhesions or endometrial superficial implants in the ovaries which leads to decreased the number of ovulation.

In the current study no statistical significant difference was found between laparoscopy and open ovarian cystectomy as regard number of follicle found in histopathological examination. This agrees with results from Alborzi et al.[24], meanwhile a statistically significant positive correlation found between number of follicles demonstrated in histopathology and the decline of AMH which agrees with Matsouzaki et al.[25] who found that the volume of ovarian tissue lost may be as high as the post-operative volume of the ovary, which is one of sonographic markers for ovarian reserve, could decrease by 50%, when compared with the controlateral ovary.

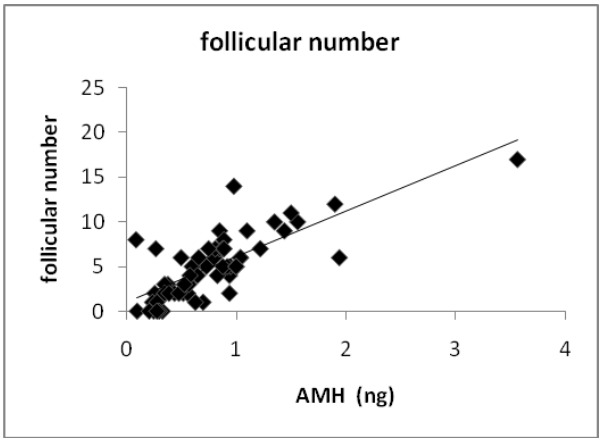

Fig.1: Correlation between number of follicle in histopathology and the decline of AMH

In the current study, positive correlation was found between the preoperative serum AMH level and the number of follicles removed. This may explains the significantly positive correlation between the preoperative serum AMH and the rate of decline of AMH, hypothetically the more reserve of the ovary detected pre surgically, the more follicle offered to be removed during surgery and the more the decline in AMH will be. This is consistent with findings in Hirokawa et al[26] study that found positive correlation between the number of follicles removed in the specimens and the preoperative serum

AMH level suggesting that patients who have more follicles tend to lose more follicles during the removal of ovarian endometriotic tissue but they fail to correlate between the no of follicle and the decline in AMH level

In the current study no statistically significant difference was found between the two groups as regard laterality and further more bilateral cysts did not show further decline in AMH than unilateral cysts in contrast to the study done by Hirokawa et al[26] who found that the rate of decline of the serum AMH level was significantly higher in the bilateral group than the unilateral group. This could be explained by lesser percent of bilateral cases (21.875%) in our study in relation to higher percent of unilateral cases (78.1%) while in the other study there were 47.4% bilateral cases and 52.6% unilateral cases.

In this study, no positive correlation has been found as should be expected between the cyst size and the decline in AMH. This agrees with Hirokawa et al.[26] that found that the decline of the serum AMH level did not show a significant correlation with cyst diameter that is not useful for predicting the severity of the decrease of ovarian reserve. Also, positive correlation was found between rate of AMH decline and the severity of endometriosis assessed by r ASRM scoring system, this finding was consistent with Iwase et al[10] and Hirokawa et al[26], which supports the previous finding, However, no definitive data support that reducing r ASRM scores before surgery using preoperative medical treatment result in a better surgical outcome[25].

CONCLUSION

Based on the previous findings, the surgical approach can cause definite harm to the ovarian reserve with no privilege recorded of laparoscopy over laparotomy as regard conservation of ovarian reserve. Other factors rather than type of surgery would determine the extent of this damage.

REFERENCES

1. Deb S, (2012): assessment of ovarian reserve in women undergoing cystectomy for benign ovarian disease. PhD thesis, University of Nottingham.
2. Broekmans FJ, Soules MR, & Fauser BC (2009): Ovarian Aging: Mechanisms and Clinical Consequences. Endocrine Reviews; 30:465-93.
3. Maheshwari A, Gibreel A, Bhattacharya S & Johnson NP (2009): Dynamic tests of ovarian reserve: a systematic review of diagnostic accuracy. Reprod BioMed Online; 18: 717-34.
4. Nelson SM, Yates RW, Lyall H, Jamieson M, Traynor I, Gaudoin M, Mitchell P, Ambrose P & Fleming R (2009): Anti-Mullerian hormone-based approach to controlled ovarian stimulation for assisted conception. Hum Reprod; 24:867-75.
5. Kwee J, Schats R, McDonnell J, Schoemaker J& Lambalk C B (2006): The clomiphene citrate challenge test versus the exogenous follicle-stimulating hormone ovarian reserve test as a single test for identification of low responders and hyperresponders to in vitro fertilization. Fertil Steril; 85: 1714-22.
6. Elgindy E A, El-Haieg DO & EL sebaey A (2008). "Anti- Mullerian hormone: correlation of early follicular, ovulatory and midluteal levels with ovarian response and cycle outcome in intracytoplasmic sperm injection patients." Fertil Steril; 89:1670-6.
7. Ficicioglu C, Kutlu T , Baglam E & Bakacak Z (2006): Early follicular antimullerian hormone as an indicator of ovarian reserve." Fertil Steril ;85: 592-6.
8. Dehghani-Firouzabadi R , Tayebi N & Asgharnia M (2008): "Serum level of anti-mullerian hormone in early follicular phase as a predictor of ovarian reserve and pregnancy outcome in assisted reproductive technology cycles." Arch Iran Med 11: 371-6.
9. Kevenaar M E, Meerasahib M F, Kramer P, De long Born BMNV, De Jong fh, Groome NP Themmen APN & Visser JA (2006). "Serum anti-mullerian hormone levels reflect the size of the primordial follicle pool in mice." Endocrinology; 147: 3228-34.
10. Iwase A, Hirokawa W, Goto M, Takikawa S, Nagatomo Y& Nakahara T (2010): Serum anti-M€ullerian hormone level is a useful marker for evaluating the impact of laparoscopic cystectomy on ovarian reserve. Fertil Steril; 94: 2846-9.
11. Raymond Li HW, Wongb CYG, Yeunga WSB, Hoab PC & Nga EHY (2010): Serum anti-Müllerian hormone level is not altered in women using hormonal contraceptives. Contraception; 83: 582-5.
12. Tsolakidis D, Pados G, Vavilis D, Athanatos D, Tsalikis T & Giannakou A (2010): The impact on ovarian reserve after laparoscopic ovarian cystectomy versus three-stage management in patients with endometriomas : a prospective randomized study. Fertil Steril; 94:71-7.
13. Palmaraa V, Sturlesea E, Romeoa C, Arenaa F, De Dominicia R, Villarib D, Impellizzeria P & Santoro G (2012): Morphological study of the residual ovarian tissue removed by laparoscopy or laparotomy in adolescents with benign ovarian cysts. J Ped Sur; 47:577-80.
14. Chang HJ, Han SH, Lee JR, Jee BC, Lee BI & Suh CS (2010): Impact of laparoscopic Cystectomy on ovarian reserve: serial changes of serum anti-M€ullerian hormone levels. Fertil Steril; 94:343-9.
15. Hwu YM, Wu FS, Li SH, Sun FJ, Lin MH& Lee RK (2011): The impact of endometrioma and laparoscopic cystectomy on serum anti-Mullerian hormone levels. Reprod Biol Endocrinol; 9:80.
16. Celik HG, Dogan E, Okyay E, Ulukus C, Saatli B, Uysal S, Koyuncuoglu M. (2012): Effect of laparoscopic excision of endometriomas on ovarian

reserve: serial changes in the serum antimullerian hormone levels. Fertil Steril; 97: 1472-8.
17. Busacca M and Vignali M (2009): Endometrioma Excision and Ovarian Reserve: A Dangerous Relation. J Minim Invasive Gynecol;16, 142–8.
18. Candiani M, Barbieri M, Bottani B, Bertulessi C, Vignali M & Agnoli B (2005): Ovarian recovery after laparoscopic enucleation of ovarian cysts: insights from echographic short-term postsurgical follow-up. J Minim Invasive Gynecol; 12:409-14.
19. Ercan CM, Sakinci M, Duru NK, Alanbay I, Karasahin KE&Baser I (2010): Antimullerian hormonel evels after laparoscopic endometrioma stripping surgery. Gynecol Endocrinol; 26:468-72.
20. Ercan CM, Duru NK, Karasahin KE, Coksuer H, Dede M& Baser I (2011): Ultrasonographic evaluation and anti-mullerian hormone levels after laparoscopic stripping of unilateral endometriomas. Eur J Obstet Gynecol Reprod Biol; 158:280-4.
21. Kennedy S, Bergqvist A, Chapron C, D`hooghe T, Dunselman G ,Greb R, Hummelshoj L,Prentice A, Saridogan E and on behalf of the ESHRE Special Interest Group for Endometriosis and Endometrium Guideline Development Group.(2005): guideline for the diagnosis and treatment of endometriosis. Hum Reprod; 20:2698-704.
22. Muzzi L, Bellati F, Bianchi A, Palaia I, Manci N & Zullo MA (2005): Laparoscopic strippingof endometriomas: a randomized trial on different surgical techniques. Part II: pathological results. Hum Reprod; 20:1987-92.
23. Almog B, Shehata F, Sheizaf B & Tulandi T (2010): Effect of different types of ovarian cyst on antral follicle count. Fertil Steril; 94:2338-9.
24. Alborzi S, Foroughinia AL, Kumar PV, Asad N, & Alborzi S (2009): 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; 92:2004-7.
25. Matsuzaki S, Houlle CL, Darcha C, Pouly JL, Mage G, & Canis M (2009): Analysis of risk factors for the removal of normal ovarian tissue during laparoscopic cystectomy for ovarian endometriosis Hum Reprod; 24, 1402–6.
26. Hirokawa W, Iwase A, Goto M, Takikawa S, Nagatomo Y& Nakahara T (2011): The post-operative decline in serum anti-Mullerian hormone correlates with the bilaterality and severity of endometriosis. Hum Reprod; 26:904-10.