VOLUME - 12, ISSUE - 03, MARCH - 2023 • PRINT ISSN No. 2277 - 8160 • DOI : 10.36106/gjra

Original Research Paper | Obstetrics & Gynaecology

EFFECT OF SURGICAL TREATMENT ON SERUM AMH LEVELS IN OVARIAN DISEASES

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ABSTRACT

Introduction The relationship between various ovarian diseases and its treatment on ovarian reserve is a subject of debate. It is difficult to determine the real impact of the ovarian surgery on future fertility of women. This study aimed to assess the effect of conservative ovarian surgeries on ovarian reserve in reproductive age women by correlation of preoperative and post operative S.AMH. **Materials And Methods:** This prospective study included 66 patients of reproductive age with various ovarian diseases. Ethical clearance was obtained from Institutional ethics committee and informed consent from all recruited patients. They were grouped into inflammatory or benign disease, malignant disease and ovarian endometrioma by histology. S. AMH was compared in the three groups pre-operatively, after 4 weeks and after 3-6 months of surgery. The statistical analysis was done with SPSS version 15. **Result:** Mean decline in S> AMH at 4 weeks was 0.16, 0.40 and 0.33 respectively for inflammatory/benign, malignant and endometrioma groups. Similarly, after 3-6months, it was 0.17, 0.75 and 0.37 respectively for the three groups. Statistically, both malignant and endometrioma groups showed significantly higher decline as compared to inflammatory/benign group ($p<0.001$). **Conclusion:** Baseline S.AMH levels are significantly lower in endometrioma and malignant ovarian tumours as compared to benign ovarian tumours. They show a significant decline following surgical treatment in all ovarian diseases but the decline is significantly more endometrioma and malignancy.

KEYWORDS : Anti-Müllerian hormone, ovarian reserve , endometrioma , benign ovarian mass.

INTRODUCTION

Ovarian diseases like endometrioma, benign tumors, and malignant tumors need surgical treatment in reproductive age women. Despite the use of minimal invasive fertility preserving surgery, its effect on ovarian reserve remains a matter of concern. With the easy availability of S.AMH assessment and its established correlation with ovarian reserve, it is now possible to objectively measure the reproductive potential of women with ovarian diseases both before and after surgery[1,2,3].

This study was therefore conducted with an aim to study the effect of fertility preserving ovarian surgery on ovarian reserve by correlation of preoperative and postoperative S.AMH levels.

MATERIALS AND METHODS

This was a prospective cohort study conducted in the department of Obstetrics and Gynaecology of a tertiary care teaching hospital over a duration of one year. The subjects included 70 women aged between 18 to 45 years, with unilateral or bilateral ovarian mass above 5 cm planned for surgical treatment. All women with postmenopausal status and endocrine disorders (PCOS, diabetes mellitus, thyroid dysfunction, hyperprolactinemia, congenital adrenal hyperplasia, Cushing's syndrome, SLE) were excluded.

METHODOLOGY

Institutional ethics committee approval was obtained. After informed written consent, detailed history, general, systemic and gynaecological examination were performed. Along with preoperative investigations, 5ml of venous blood sample was taken for S.AMH analysis done by Ultra-sensitive AMH/MIS ELISA kit. All patients underwent open or minimal invasive surgery as per the surgeon's decision. All tissues were sent for histopathological analysis for confirmatory diagnosis. The cases were subdivided into three groups of benign disease, malignant disease or endometrioma as per histology reports. Out of 70 cases, four were excluded after surgery since two were diagnosed as Granulosa cell tumours and two were lost to follow-up. Out of 66 cases, 48 underwent fertility preserving surgery (42 benign and 6 malignant) and 18 (12 malignant and 6 benign) underwent radical surgery. S.AMH analysis were repeated after 4 weeks in 48 cases and at 3-6 months in 43 cases with fertility preservation surgery.

Statistical Analysis

Details of demographic profile, disease characteristics, surgical findings, procedure and histological reports were recorded. Pre operative and post operative S.AMH levels were compared among the three histological groups. The results are presented in frequencies, percentages and mean±SD. All the analysis were carried out on SPSS Version 15.0 statistical Analysis Software.

OBSERVATIONS AND RESULTS

Majority (84.84%) of patients underwent open surgery. 51.5% cases had ovarian mass of 5-10 cm and rest were above 10 cm size. 71.2% had cystic masses and 30.3% had bilateral involvement. Ascites was seen in 34.8% cases and 10.6% had metastasis.

30.30% cases were endometrioma and 27.3% were benign tumors (15.15% serous cystadenoma, 9.09% mucinous cystadenoma and 3.03% dermoid cysts). 25% were malignant (18.18% serous cystadenocarcinoma, 6.06% mucinous cystadenocarcinoma) and 3.03% cases were borderline tumors.

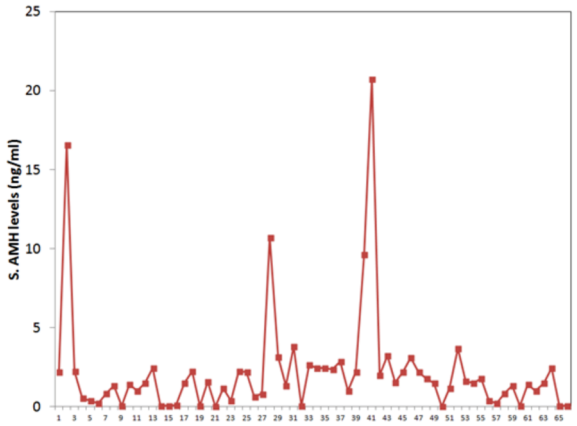

Figure 1 shows preoperative S.AMH levels that ranged from 0.02 to 20.72 ng/ml and majority had S. AMH between 0-4 ng/ml.

Figure 1: Preoperative S.AMH levels (n=66)

Table 1 shows comparison of preoperative and postoperative S. AMH levels in the 3 groups. Statistically significant intergroup difference was observed in mean AMH levels before surgery, at 4 weeks and 3-6 months levels.

Table 1: Comparison of S. AMH levels in the three groups.

SN	HPE type Timing	Benign (n=24)	Malignant (n=6)	Endometrioma (n=18)	ANOVA test
1	Preoperative (n=48)	4.26±5.08	0.78±0.50	1.50±0.66	p=0.026
2.	Postoperative 4 wks (n=48)	3.51±3.80	0.52±0.44	1.05±0.61	p=0.011
3.	Postoperative 3- 6 months (n=43)	3.70±3.76 (n=22)	0.78±0.42 (n=3)	0.99±0.59 (n=18)	p=0.009

Table 2 shows the difference in S. AMH levels after 4 weeks and 3-6 months. There was a statistically significant difference in mean S AMH levels after 4 weeks and at 3-6 months in each group.

Table 2: Change in mean S. AMH levels after 4 weeks and 3-6 months

HPE	N	Mean Preoperative S AMH	Mean Postoperative (4 weeks) S AMH	Chi square P value
Benign	24	4.26	3.51	0.006
Malignant	6	0.78	0.52	0.003
Endometrioma	18	1.50	1.05	<0.001
Total	48	2.79	2.22	<0.001
(b) Preoperative vs 3-6 months Postoperative (n=43)				
Benign	22	4.64	3.70	0.006
Malignant	3	1.08	0.78	-
Endometrioma	18	1.50	0.99	<0.001
Total	43	3.08	2.36	<0.001

Table 3 shows mean decline in postoperative S.AMH for various HPE groups.

A significant reduction in mean S. AMH levels was observed for the whole cohort (p<0.05) as well as individually in all histopathological subgroups. Both malignant and endometrioma groups showed significantly higher decline as compared to benign group (p<0.001).

Table 3: Mean decline in postoperative S.AMH levels.

	Benign (n=28)	Malignant (n=18)	Endometrioma (n=20)	Statistical significance ANOVA
	(n=24)	(n=6)	(n=18)	
Mean decline in 4 weeks	0.16±0.08 b,c	0.40±0.22 a	0.33±0.13 a	<0.001
Mean decline at 3-6 months	0.17±0.07 c	0.27±0.03	0.37±0.14 a	<0.001

- *[a]Statistically significant difference as compared to benign group (p<0.05);*
- *[b]Statistically significant difference as compared to Malignant group (p<0.05);*
- *[c]Statistically significant difference as compared to Endometrioma group (p<0.05);*
- *(Between group differences calculated using Tukey HSD test)*

No significant correlation was seen in S AMH decline with respect to age, cyst size and bilaterality for any of the histopathological group. There was no statistically significant correlation of postoperative S AMH levels at 4 weeks (p=0.618) and 3-6 months (p=0.513) with type of surgical procedure.

DISCUSSION

AMH is the ideal marker for ovarian reserve[4] and its depletion after ovarian surgery.[1-3] Ovarian cystectomy is currently the first option for treating large ovarian endometrioma but it remains controversial whether the surgery adversely affects the ovarian reserve [5]. The reduced number of retrieved oocytes in operated endometrioma cases and premature ovarian failure reported in some articles have raised these concerns.[6,7] The present study showed that postoperative mean S.AMH levels at 4 weeks in all ovarian diseases including endometrioma, benign and malignant cases was significantly lower than the preoperative levels (p=0.01). Above results are similar to **Chen Y et al** [8] who found that S.AMH were decreased in endometrioma cases and benign ovarian cyst (p<0.001) after 1 month of laparoscopic ovarian cystectomy.

Mean postoperative S.AMH at 3-6 months was 3.70 in benign, 0.78 in malignant and 0.99 in endometrioma cases. Though the S.AMH in malignant and endometrioma cases are low but not in the range of ovarian failure. This confirms that positive prospects of fertility persist in in both the groups. The equivalent decline of S.AMH in endometrioma and malignant cases in our study indicates that extent of depletion in ovarian reserve is comparable in both diseases. **Won kyu Jang et al** [9] also found significantly lower S.AMH in endometrioma cases at 3 months post cystectomy (p<0.05) as compared to non-endometrioma group.

Mean decline in S.AMH at 4 weeks surgery was 0.33 in endometrioma, 0.16 in benign and 0.40 in malignant cases. It is similar to the findings of **Chen Y et al** [8] who reported that the mean decline in the endometrioma group (0.62) was significantly more (p=0.001) than the decline in benign group (0.32) after 1 month after cystectomy. **Gurkan Uncu et al**[10] also showed significant (p=0.02) decline in S.AMH level in endometrioma cases after 6 month of cystectomy. The decline in S.AMH in endometrioma and malignant cases was significantly more than in the benign cases (p<0.001) at 3-6 months in our study, **Won kyu Jang et al** [9] similarly found that S.AMH levels were significantly (p=0.02) lower in endometrioma as compared with non-endometriotic cyst at 3 months post cystectomy. **Celik et al**[11] also found decline in S.AMH 6 months post cystectomy.

Tsolakidis et al[12] and **Biacchiardi et al**[13] reported significantly lower S.AMH levels (p<0.05) in endometrioma cases 6 month post surgery. **Muzii et al**[14] proposed that this difference is due to presence of pseudocapsule in an endometrioma versus true capsule in non endometriotic cyst which had separate tissue plane making dissection from tissue easy and complete. **Chang et al**[6] in contrast reported decline in S.AMH

immediately after cystectomy which then gradually increased after one month and there was 65% recovery of preoperative level after 3 months.

There was no statistically significant correlation of decline of S.AMH with age, cyst size and bilaterality for any of the histopathological groups in our study. **Gurkan Uncu et al** [10] and **Celik et al**[11] similarly stated that rate of decline in S.AMH was not correlated with age, laterality of endometrioma, cyst diameter or the number of primordial follicles on the surgical specimens. **Chen Y et al**[13] in contrast showed that mean decline in S.AMH levels in endometrioma with cysts above 7cm was significantly higher than cysts below 7 cm in diameter (p=0.001). They also found that the decline was greater in bilateral (0.85±0.19) endometrioma as compared to unilateral (0.46±0.34) endometrioma. **Iwase A et al** [15] also reported that bilateral endometrioma excision caused a greater decline in S.AMH levels than unilateral endometrioma excision.

Correlation of postoperative S.AMH and different conservative surgical approaches in our study showed a decline in mean S. AMH levels at both 4 weeks and 3-6 months for all the procedures. There was no statistically significant difference in mean post-operative S. AMH levels of different surgical procedures at 4 week and at 3-6 months. The review of literature did not show any other study comparing the effect of different conservative surgical procedures on S.AMH levels.

The limitation of this study is the lack of longterm follow-up. A long term study with continued follow-up AMH is suggested . There is also need to further investigate whether endometrioma related decline in ovarian reserve is disease or surgery related .

CONCLUSION

S AMH levels are significantly lower in endometrioma and malignant ovarian tumours as compared to benign ovarian tumours. They show a significant decline following surgical treatment but the maximum decline is seen in endometrioma and malignant tumours. Hence It may be prudent to measure AMH levels preoperatively and use tailored surgical techniques for future fertility.

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