



# The Difference Between Post-Laparoscopic Cystectomy Anti-Mullerian Hormone Levels In Endometrioma And Non-Endometrioma Cysts Patients



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## ABSTRACT

**Background:** Endometrioma is a complex gynecological disease with increasing global prevalence. Laparoscopic cystectomy remains to be the primary choice of modality. Several studies, however, have revealed that laparoscopic cystectomy in endometriomas can cause ovarian damage and reduction in ovarian reserve. They demonstrated a decrease in serum AMH levels in endometrioma patients following laparoscopic

**Objective:** To identify the difference between the mean post-laparoscopic cystectomy AMH levels in endometrioma and non-endometrioma cysts patients

**Methods:** A prospective cohort study with 40 selected patients undergoing laparoscopic cystectomy in Kariadi General Hospital Semarang. They were divided into 2 groups of endometrioma and non-endometrioma cysts. AMH levels were measured before and after laparoscopic cystectomy surgery in both groups

**Results:** The mean age of endometrioma and non-endometrioma group were  $32.40 \pm 6.26$  and  $30.6 \pm 3.69$  years consecutively. The most common cysts were unilateral cysts with a diameter of  $> 4$  cm which were dominated by endometrioma cysts. The group of subjects with endometrial cysts had lower AMH levels, both before ( $9.47 + 5.26$  ng/mL) and after laparoscopic cystectomy ( $7.80 + 4.27$  ng/mL). AMH levels before and after laparoscopic cystectomy in the endometrioma group showed a significant difference ( $p=0.004$ ). In contrast, there was no significant difference in delta AMH between the non-endometrioma group ( $-1.63 + 4.12$ ;  $p=0.685$ ) and the endometrioma group ( $-1.74 + 2.37$  ng/mL;  $p=0.685$ )

**Conclusion:** Both endometrioma and non-endometrioma groups showed a decrease in AMH levels after laparoscopic cystectomy but they did not show a significant difference.

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## 1. Introduction

Endometrioma is considered as the appearance of normal endometrial glands outside the uterine cavity. Endometrioma usually presents as a pelvic mass in the form of ovarian cysts with an ectopic endometrial lining filled with brown fluid.<sup>1</sup> Based on research conducted by Oral et al, 27.2% cases of benign ovarian mass were endometriomas.<sup>2</sup> Data from the World Health Organization (WHO) states that the global prevalence of endometriomas reaches 10% of reproductive age and the most common location of endometriomas is the ovary.<sup>3,4</sup>

Conservative approach can be administered to patients without prominent complaints and predisposition to ovarian malignancy in ultrasonography examination.<sup>5</sup> However,

endometrioma often does not respond well to medical therapy. Laparoscopic cystectomy in endometrioma preferred as the primary treatment option because the endometrioma recurrence rate after laparoscopic cystectomy is lower than the fenestration method and bipolar cyst wall coagulation.<sup>6, 7, 8, 9</sup>

In addition to removing cyst, the goal of endometrioma treatment is to overcome the problem of infertility. Laparoscopic cystectomy, on the contrary, is reported to have relation to ovarian reserves decreasing. Some studies stated that there was an increase in ovarian damage and resulted in a decrease in ovarian reserves after a cystectomy laparoscopic surgery in women with endometrioma.<sup>6,7</sup>

Anti-Mullerian Hormone (AMH) is expressed by the developing ovarian follicles and can be detected in the blood circulation.<sup>10</sup> AMH levels gradually decrease as the set of primordial follicles decreases.<sup>7,11,12</sup>

Ovarian reserves cannot be measured directly so there are several methods to assess ovarian reserves such as AMH. AMH is very sensitive to changes in ovarian reserves that tend to decrease with age. AMH also has equal sensitivity and specificity to the number of antral follicles (AFC) and has greater sensitivity and specificity than FSH, estradiol, LH, FSH / LH ratio or inhibin-B level.<sup>7, 8, 13, 14</sup>

Given the high incidence of endometrioma while laparoscopic cystectomy is still the main therapeutic choice, it is important to understand the therapeutic output of a decrease in ovarian reserves that is assessed through serum AMH examination, especially in Indonesia.

This study aims to analyse the difference between mean post-cystectomy AMH levels in endometrioma and non-endometrioma cysts patients..

## 2. Methods

This is a prospective cohort study conducted in RSUP Dr Kariadi Semarang during March – May 2022. The subjects of the study were patients who meet the inclusion criteria and didn't satisfy the exclusion criteria. The inclusion criteria for this study was 1) women with endometrioma and not endometrioma with cyst sizes  $\leq 4$ cm and  $> 4$  cm that cause functional impairment, 2) undergo laparoscopic surgery cystectomy, 3) willing to perform anamnesis, physical examination, and examination of serum AMH levels, and 4) willing to be included in the study. Patients undergone previous cystectomy surgery, refuse surgery and are not willing to be examined for serum AMH levels were excluded.

Collectively, there were of 40 research subjects obtained through the consecutive sampling method. All subjects who comply with the criteria were examined to evaluate pre-test AMH levels by the ELISA method before laparoscopic cystectomy. Postoperative AMH levels examination is performed after 3 months post laparoscopic cystectomy.

The collected data was carried out statistical analysis using the Saphiro-Wilk normality test. Differences in pre and post intervention AMH levels in each group were tested using paired T-tests if normal distributed data. Meanwhile, to analyse the comparison of serum AMH levels and serum AMH reduction rates between the subject and control groups, data from both groups were examined using an independent T-test or the Mann-Whitney U test for not normally distributed data.

## 3. Results

40 subjects met the inclusion criteria and had no exclusion criteria, divided into 20 non-endometrioma subjects and 20 endometrioma subjects. In the non-endometrioma group, subjects had an average age of  $30.6 + 3.69$  years with an average body mass index of  $24.26 + 2.37$  kg. The average age of subjects in the endometrioma group was older at  $32.40 + 6.26$  years and the average body mass index in this group was also greater ( $25.86 + 3.05$ ). However, there were no significant differences in age ( $p=0.277$ ) and BMI ( $p=0.072$ ) between the two groups. Unilateral cysts and the size of the cyst  $> 4$  cm were found to be dominant in both groups. A total of 13 people of the non-endometrioma group and 15 people of the endometrioma group had unilateral cysts. The number of the study subjects with a cyst size of  $>4$  cm in the control group and endometrioma were 12 people and 17 people consecutively. No significant differences were found in the number of cysts ( $p=0.731$ ) and the size of the cysts ( $p=0.155$ ) between the two groups.

The most common types of cysts in the non-endometrioma group were follicular cysts with a total of 9 people while the least types were corpus luteum cysts and mature teratomas with 2 people.

Research subjects in the non-endometrioma cyst group and the endometrioma cyst group showed a decrease in AMH levels after laparoscopic cystectomy compared to previous AMH levels, but no significant difference was found between AMH levels before and after intervention in the non-endometrioma cyst group ( $p=0.092$ ). In contrast, the endometrioma cyst group showed a significant difference in AMH levels before and after interventional laparoscopy ( $p = 0.004$ ).

As the data shown in table 2 and 3, the highest mean of AMH level was belong to the non-endometrioma group examined before surgery ( $9.47 + 5.26$ ) with the highest AMH level of 17.49 ng/mL. The endometrial cysts group relatively have lower AMH levels, both before laparoscopic cystectomy ( $9.47 + 5.26$ ) and after laparoscopic cystectomy ( $7.80 + 4.27$ ), than the other groups. Regardless, the results of pre- and post-intervention evaluations between the groups demonstrated no significant difference found with p-values of 0.227 and 0.112, respectively.

The difference between AMH levels after and before laparoscopic cystectomy had a mean of  $-1.63 + 4.12$  ng/mL in the non-endometrioma group while in the endometrioma group it was  $-1.74 + 2.37$  ng/mL. There was no significant difference in AMH delta between the non-endometrioma group and the endometrioma group ( $p=0.685$ ).

Table 1. Characteristic of the research subjects

Characteristics	Type of cysts		n	Mean $\pm$ SD; Median (min-max)	p
	Non-endometrioma (n=20)	Endometrioma (n=20)			
Age (years)	-	30,60 $\pm$ 3,69; 29,5 (24-38)	-	32,40 $\pm$ 6,26; 32,5 (24-45)	0,277 <sup>#</sup>
Body Mass Index (kg/m <sup>2</sup> )	-	24,26 $\pm$ 2,37; 23,77 (20,84-27,88)	-	25,86 $\pm$ 3,05; 26,15 (20,58-31,22)	0,072 <sup>#</sup>
The number of cysts					
• Unilateral	13	-	15	-	0,731 <sup>s</sup>
• Bilateral	7		5		
The size of cysts					
• < 4 cm	8	-	3	-	0,155 <sup>s</sup>
• > 4 cm	12		17		
Type of cysts					
• Endometrioma	0		20		
• Follicle	9		0		
• Corpus luteum	4		0		
• Simplex	2	-	0	-	-
• Mucinous Adenoma	3		0		
• Mature teratoma	2		0		

<sup>#</sup>Independent T Test; <sup>s</sup>Pearson Chi Square

Table 2. Type of cysts' effect on AMH levels decrease

Type of cysts	AMH level		p
	Pre-laparoscopic cystectomy	Post-laparoscopic cystectomy	
Non- Endometrioma	9,47 $\pm$ 5,26; 10,36 (2,09-17,49)	7,84 $\pm$ 3,71; 6,83 (2,25-15,40)	0,092
Endometrioma	7,80 $\pm$ 4,27; 7,58 (0,96-13,66)	6,06 $\pm$ 3,19; 5,57 (0,14-13,44)	<b>0,004*</b>

Dependent T-Test

Table 3. AMH levels decrease and AMH delta

AMH level	Type of cysts		p
	Non-Endometrioma	Endometrioma	
Pre-laparoscopic cystectomy	9,47 $\pm$ 5,26; 10,36 (2,09-17,49)	7,80 $\pm$ 4,27; 7,58 (0,96-13,66)	0,277 <sup>s</sup>
Post-laparoscopic cystectomy	7,84 $\pm$ 3,71; 6,83 (2,25-15,40)	6,06 $\pm$ 3,19; 5,57 (0,14-13,44)	0,112 <sup>s</sup>
AMH delta	-1,63 $\pm$ 4,12; -1,40 (-10,37 – 4,33)	-1,74 $\pm$ 2,37; -0,66 (-7,81 – 1,54)	0,685 <sup>^</sup>

<sup>s</sup>Independent T-Test; <sup>^</sup>Mann Whitney U

#### 4. Discussions

In the endometrioma subject group, the average age of the research subjects was 32 years and the non-endometrioma group was 30 years. The majority of

cysts were unilateral cysts with a diameter of >4 cm. The most frequently reported type of non-endometrioma cyst is follicular cyst.

According to Ramachandran A. et al study on the impact of endometrioma cyst diameter and endometrioma severity on ovarian parenchymal

excision during cystectomy laparoscopy, the average patients age was 31.4 years, the average duration of infertility was 4.1 years, and the average cyst diameter was 6.3 cm.<sup>15</sup>

Abduljabbar HS, et al discovered in their study that 79.5% of the 244 cases of ovarian cysts were unilateral cysts, which yielded similar results in terms of the number of cysts.<sup>16</sup> This finding was supported by Zahra F et al, who reported that the majority of subjects (88.9%) had unilateral cysts.<sup>17</sup>

Roman et al. observed an association between endometrioma size and ovarian parenchyma that was accidentally removed during a cystectomy. A study by HK Oh et al. found that moderately sized endometriomas (5-7 cm in diameter) had a greater tendency to lose follicles than smaller endometriomas (5 cm in diameter).<sup>18</sup> A follicular cyst was the most commonly reported type of non-endometrioma cyst in this study. Physiological cysts are large cysts that form in the ovaries during a normal ovarian cycle. The majority of these cysts cause no symptoms. The most common type is a follicular cyst, which occurs when the dominant follicle does not rupture.<sup>19</sup>

In the endometrioma group, there were significant differences in AMH levels before and after laparoscopic cystectomy. Laparoscopic cystectomy is indicated in patients with benign ovarian cysts causing symptoms such as pelvic pain and dysmenorrhea, or in patients at high risk of malignant transformation. Previous study discovered a decrease in ovarian reserve following cystectomy.<sup>20</sup> AMH is a widely preferred ovarian reserve marker. In accordance with these findings, Chang et al demonstrated an early decline in post-operative AMH levels and a return of 65% AMH levels 3 weeks after surgery.<sup>21</sup>

The endometrioma group of this study determined lower AMH levels both before and after laparoscopic cystectomy. The initial average value of AMH levels was significantly lower in the endometrioma group than in the non-endometrioma group. Endometrioma is presumed as the cause of ovarian damage prior to surgery.

The decrease in AMH levels was more noticeable in the endometrioma group. This finding is consistent with previous research by Siresha MU, et al, which found a significant decrease in AMH levels after 1 week (p0.05) and 3 months (p0.05) cystectomy compared to pre-operative AMH levels, and the percentage decrease in AMH values measured on the 7th postoperative day was found to be greater in endometriotic cysts (54%), followed by mucinous cystadenoma (32%).<sup>23</sup> Furthermore, a retrospective study of 32 patients provide a connection between endometriotic cyst removal and obvious loss of ovarian reserve.<sup>24</sup>

Another mechanism for ovarian reserve loss after laparoscopic cystectomy has been proposed. Endometrioma cysts lack a true capsule, leading to mass cortex ovarium loss and most ovarian follicle loss. This explains why postoperative AMH levels in endometriotic cysts are lower.

Inflammation and oedema following surgery similarly cause initial ovarian reserve to decline.<sup>25</sup>

This study has several limitations, including the inability to measure the definite diameter of the cyst due to the limitations of measuring instruments used during laparoscopic procedures. Second, it did not include kappa values, which could indicate differences in laparoscopic cystectomy operators and techniques. The number of samples and study time were also limited in comparison to previous studies, and the stage of disease during surgery was not investigated.

## 5. Conclusion

Endometrioma patients had a lower average post-laparoscopic AMH level of 6.06 ng/mL, whereas non-endometrioma patients had a higher average post-laparoscopic AMH level of 7.84 ng/mL. There was no statistically significant difference between the delta AMH endometrioma and non-endometrioma groups (P=0.685).

## Ethical Approval

Ethical approval was given by the Research and Development Ethics Committee of Medicine Faculty of Diponegoro University with the number No. 1149/EC/KEPK-RSDK/2022.

## Conflicts of Interest

The authors declare that there was no conflict of interest.

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## Author Contributions

Conceptualization, CDK, STH, IM; methodology, CDK, STH; software, CDK; validation, CDK, IM, EA, and RDC; formal analysis, CDK and STH; investigation, CDK; resources, CDK; data curation, CDK; writing—original draft preparation, CDK and STH; writing—review and editing CDK, STH, IM, EA, RDC, and YT; visualization, CDK, IM, EA, RDC; supervision, YT; project administration, CDK”

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