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Anti-Mullerian Hormone (AMH) Levels In Patients Before And After Salpingectomy And Hysterectomy

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ABSTRACT

Background: Hysterectomy is the surgical removal of the uterus and, in some circumstances, the ovaries, cervix, fallopian tubes and supporting tissues. Hysterectomy is one of the most performed surgeries in gynecological practice. Hysterectomy is the most common gynecological surgical procedure performed worldwide, with a rate of 2-5 per 1000 women in North America, Europe, Australia, and China. Hysterectomy is used to treat a variety of benign and malignant medical conditions, including fibroids, prolapses, abnormal uterine bleeding, pelvic pain, and cervical, endometrial, and ovarian cancers, pelvic pain associated with endometriosis, pelvic organ prolapse, and adenomyosis.

Objective: Determine serum AMH levels in salpingectomy and hysterectomy patients. Compare serum AMH levels in patients between before and after salpingectomy and hysterectomy. Determine the factors related to changes in serum AMH levels after salpingectomy and hysterectomy.

Methods: The research was conducted at the Educational Network Hospital, Department of Obstetrics and Gynecology, Faculty of Medicine, Hasanuddin University. The research was conducted from April – September 2024. The population of this study is all patients who underwent salpingectomy and hysterectomy at the Education Network Hospital, Department of Obstetrics and Gynecology, Faculty of Medicine, Hasanuddin University.

Results: The subjects of this study were 30-37 years old and had the same proportion related to normal BMI, overweight and obesity. Based on Table 1, it is shown that most of the subjects of this study are more than 9 years of education, not working, primipara, indications of adenomyosis surgery and uterine myoma.

Conclusion: Based on the results of the study and discussion, it can be concluded that serum AMH levels in patients decreased after salpingectomy and hysterectomy. Age and BMI were not associated with changes in serum AMH levels after salpingectomy and hysterectomy. AMH levels can be a biomarker that can help predict the impact of salpingectomy and hysterectomy on women's sexual function after 1 month of undergoing salpingectomy and hysterectomy.

Keywords: *Hysterectomy, Salpingectomy, Serum AMH Levels, Gynecological Surgery*

1. INTRODUCTION

Salpingectomy, which is the removal of all or part of the fallopian tubes, is performed for various indications in current gynecological practice (Kotlyar et al., 2017). According to guidelines issued by The American College of Obstetricians and Gynecologists (ACOG), salpingectomy is routine therapy for cases of ectopic pregnancy (EP) when the patient shows signs of intraperitoneal bleeding or persistent pelvic pain, or when the patient has contraindications to more conservative medical treatment. The American Society for Reproductive Medicine (ASRM) also recommends salpingectomy as a therapy for patients with extensive solid peritual attachments, hydrosalping that cannot be surgically repaired, or fallopian tubes that are damaged by infection or endometriosis (Chen et al., 2020).

Meanwhile, Hysterectomy is the surgical removal of the uterus and, in some circumstances, the ovaries, cervix, fallopian tubes and supporting tissues (Amarin, 2022). Hysterectomy is one of the most performed surgeries in gynecological practice (Kiremitli et al., 2022). Hysterectomy is the most common gynecological surgical procedure performed worldwide, with a

rate of 2-5 per 1000 women in North America, Europe, Australia, and China. Hysterectomy is used to treat a variety of benign and malignant medical conditions, including fibroids, prolapses, abnormal uterine bleeding, pelvic pain, and cervical, endometrial, and ovarian cancers, pelvic pain associated with endometriosis, pelvic organ prolapse, and adenomyosis (Wang and Ying, 2020; Pillarisetty and Mahdy, 2021).

Currently, hysterectomy is performed using one of three surgical approaches: laparoscopy, transabdominal, or transvaginal. Although hysterectomy is generally considered a safe procedure, there are a number of complications including vaginal cuff dehiscence and injury to nerve structures, urinary tract, and gastrointestinal. There is also evidence that hysterectomy can cause changes in sexual function, with different effects depending on whether the underlying condition treated is benign or malignant (Wang and Ying, 2020). Other studies reported that not only hysterectomy, but bilateral salpingoophorectomy performed for benign indications also caused urinary tract disorders in the short term after surgery in sexually active and healthy women, resulting in sexual dysfunction and increased depression. The impact is influenced by age, educational status, and employment factors (Zuitasari et al., 2022).

Hysterectomy alters the anatomical, innervation, and pelvic floor blood supply, which could theoretically alter sexual function. Although some previous studies have suggested that sexual function often improves after a hysterectomy for benign uterine disease due to a reduction in symptoms, most patients with benign uterine disorders show worsening sexual function after hysterectomy (Wang and Ying, 2020). Sexual dysfunction increases as a result of the loss of female genital organs, loss of nerve tissue, decreased blood supply, decreased lubrication due to loss of the cervix and the negative effects of scarring in women undergoing hysterectomy. Given that 85% of patients who undergo hysterectomy have an active sexual life, the effects of hysterectomy on sexual life are so important that they cannot be ignored in surgical management (Kiremitli et al., 2022).

In women who undergo salpingectomy, it has the potential to reduce collateral blood flow to the ovaries because the fallopian tubes obtain blood supply from the branches of the uterine artery and ovaries. In addition, lateral thermal spread of electrocoagulation of the tubes as well as surgical manipulation of ovarian tissue can lead to direct ovarian damage (Kotlyar et al., 2017). In addition to causing Ovarian damage, in patients who receive salpingectomy for hydrosalping, can affect disorders in the blood vessels that descend along with the removed fallopian tubes can interfere with ovarian function (Ho et al., 2022). The ovarian blood supply comes from the ovarian artery and the ovarian branch of the uterine artery. The branches of these arteries are anastomosis into a web in the mesosalping. Blood circulation is easily damaged during salpingectomy, and disruption of the ovarian blood supply can lead to ovarian dysfunction (Cheng et al., 2016). The effect of salpingectomy and hysterectomy on ovarian dysfunction, it is necessary to have biomarkers of ovarian dysfunction for postoperative management to maintain women's sexual life. To date, the most recognizable serum biomarkers for ovarian function are Anti-Mullerian hormones (AMH) (Moolhuijsen and Visser, 2020).

Serum AMH is a biomarker of ovarian function, especially in the assessment of quantitative aspects of ovarian reserves. AMH is a glycoprotein dimer that is mainly secreted from granulocytes of preantral follicles and small antral follicles (Tehranian et al., 2017). AMH is produced by granulosa cells from small follicles that grow in the ovaries. The ovarian reserve is formed by the quality and quantity of primordial follicles, both of which decline with age. The number of growing follicles recruited from the primordial follicle pool reflects the number of primordial follicles. Since no serum marker can directly measure the number of primordial follicles, a marker that reflects the number of follicles growing today is the best proxy for the quantitative aspect of ovarian reserve (Moolhuijsen and Visser, 2020). AMH levels are relatively constant throughout the menstrual cycle and have a very strong correlation with the number of follicles and ovarian reserves and are important indicators of fertility (Tehranian et al., 2017).

AMH rates are also expressed as inversely proportional to sexual dysfunction (Gurbuz et al., 2020). Aydin et al. (2013) reported a strong negative correlation between AMH and women's sexual distress scores, suggesting a link between lower serum AMH levels and high total sexual distress scores among infertile women.

Previous studies have reported that women who undergo salpingectomy have reduced AMH levels compared to women without salpingectomy (Chen et al., 2020). However, different results were reported by Vahedpour et al. (2019) in Iran that salpingectomy did not have a significant effect on serum AMH levels and ovarian function. In patients undergoing hysterectomy, serum AMH levels decrease and a greater decrease occurs in total hysterectomy (Tavana et al., 2021). Mean serum AMH levels decreased significantly after surgery in the laparoscopic hysterectomy group, but no significant changes were found in serum AMH levels before and after surgery in the abdominal hysterectomy group (Chun and Ji, 2020a). Different results reported by Findley et al. (2013) that laparoscopic hysterectomy has no short-term damaging effect on ovarian reserve measured by serum AMH levels.

Previous studies have reported varying levels of AMH in patients after hysterectomy and salpingectomy, but inconsistent results have been obtained. Therefore, this study is interested in conducting a study of serum AMH levels in salpingectomy and hysterectomy.

2. MATERIALS AND METHODS

The research was conducted at the Educational Network Hospital, Department of Obstetrics and Gynecology, Faculty of Medicine, Hasanuddin University. The research was conducted from April – September 2024. The population of this study is all patients who underwent salpingectomy and hysterectomy at the Education Network Hospital, Department of Obstetrics and Gynecology, Faculty of Medicine, Hasanuddin University. The study sample was patients who underwent salpingectomy and hysterectomy at the Education Network Hospital, Department of Obstetrics and Gynecology, Faculty of Medicine, Hasanuddin University who met the inclusion criteria and sample exclusion criteria. Sampling was carried out by consecutive sampling, where all members of the population at the research site who met the inclusion requirements were taken as samples until the number of samples was met. The subjects are patients who are indicated to have salpingectomy and hysterectomy who are willing to participate in the study and meet the inclusion criteria collected.

Univariate analysis was carried out by calculating the percentage of patient characteristics. Univariate analysis was also carried out by calculating the mean and standard deviation of AMH levels. Previously, Shapiro Wilk's normality test was carried out. Bivariate analysis was carried out to test the relationship between two variables. Bivariate analysis was performed with the Mann Whitney test for the average comparison of the two groups because the data were not normal. The Kruskal Wallis test for comparison averaged more than two groups because the data were abnormal. The average comparison test between before and after treatment was carried out with the Wilcoxon test because the data were not normal. The chi-square test is performed for categorical data testing. The test was conducted at a confidence level of 5%. Before the research was carried out, the researcher asked for information on ethical clearance from the Biomedical Research Ethics Commission in Humans, Faculty of Medicine, Hasanuddin University of Makassar. Research approval has been given in the form of written informed consent. The subject of the sufferer or prospective research subject has been given an explanation of the objectives, benefits, procedures of the research, does not cause harm to the research subject, the identity of the research subject has been kept confidential and not published without the permission of the research subject. Informed consent is carried out before data collection, patients have the right to refuse to be included in the study.

3. RESULTS

This study collected as many patients who underwent salpingectomy and hysterectomy at the Educational Network Hospital, Department of Obstetrics and Gynecology, Faculty of Medicine, Hasanuddin University. The collection of research subjects was carried out from April to September 2024. All the collected research subjects were successfully examined for AMH levels in venous blood samples. The characteristics of the subjects of this study are shown in Table 1.

Table 1. Sociodemographic characteristics

Characteristic	n (%)
Education	
≤ 9 years	14 (30,4)
> 9 years	32 (69,6)
Work	
Work	13 (28,3)
Not working	33 (71,7)
Parity	
Nulipara	16 (34,8)
Primipara	28 (60,9)
Multipara	2 (4,3)
Indications of operation	
Uterine myoma	21 (45,7)
Adenomyosis	22 (47,8)
Cystic ovarian neoplasms	3 (6,5)

In this study, the subjects of this study were 30-37 years old and had the same proportion related to normal BMI, overweight and obesity. Based on Table 1, it is shown that most of the subjects of this study are more than 9 years of education, not

working, primipara, indications of adenomyosis surgery and uterine myoma. The results of the comparison of AMH levels between before and after salpingectomy and hysterectomy were obtained that AMH levels after salpingectomy and hysterectomy were lower (1.94 ± 0.62 ng/mL) than before salpingectomy and hysterectomy (3.19 ± 0.48 ng/mL). The results of the statistical test showed that there was a significant difference in AMH levels between before and after salpingectomy and hysterectomy ($p < 0.001$). Thus, AMH levels decreased significantly after salpingectomy and hysterectomy.

Table 2. Results of analysis of factors related to changes in AMH levels after salpingectomy and hysterectomy

Parameters	AMH level (ng/mL)	p-value
	Mean ± SD	
Age		
≤ 35 years	1.21 ± 0.52	0.056A
> 35 years	1.45 ± 0.58	
IMT		
Underweight	1.36 ± 0.00	
Usual	1.26 ± 0.67	0.862c
Overweight	1.19 ± 0.38	
Obesity	1.30 ± 0.56	

aIndependent sample t test, bMann Whitney test, cKruskal Wallis test

The results of the analysis in Table 2. Showed Age effects AMH levels while BMI were not related to changes in AMH levels after salpingectomy and hysterectomy ($p > 0.05$). Thus, BMI are not confounding factors in the effect of salpingectomy and hysterectomy on AMH levels.

4. DISCUSSION

This study was conducted on women who underwent salpingectomy and hysterectomy aged 30-37 years, most of the subjects of this study were educated for more than 9 years, not working, primiparous, indications for surgery for adenomyosis and uterine myoma. Adenomyosis and uterine myoma are benign gynecological conditions. This result is as explained in previous studies that salpingectomy with hysterectomy is recommended for benign gynecological conditions to prevent the development of cancer (van Lieshout et al., 2019). If there is no desire for further fertility and no desire for uterine preservation, hysterectomy with bilateral salpingectomy is the gold standard treatment for symptomatic adenomyosis (Bischiniotis, Mikos and Grimbizis, 2024).

Hysterectomy with salpingectomy is stated to be a safe treatment and has no adverse effects on ovarian reserve. Hysterectomy maintains the ovaries and tubes through a salpingectomy close to the uterus to maintain the blood supply to the ovarian mesosalping. Hysterectomy performed in conjunction with salpingectomy prevents the development of cancer (Tehranian et al., 2017). Prophylactic salpingectomy is stated to prevent high-grade serosa cancer and can be performed during any type of hysterectomy without affecting ovarian function or surgical outcomes (Carugno and Fatehi., 2023). Simultaneous bilateral salpingectomy during hysterectomy can reduce the incidence of ovarian serosa carcinoma and some benign pelvic diseases, thereby reducing the risk of reoperation after hysterectomy (Hello et al., 2019). Ovarian blood flow and steroid hormone production after hysterectomy with opportunistic salpingectomy for uterine fibroids are close to reference values up to 36 months postoperatively (Proshchenko and Ventskivska, 2022).

The results of this study showed that AMH levels decreased significantly after 1 month of salpingectomy and hysterectomy. These results are in line with research Tehranian et al., (2017) that serum AMH levels decreased at 3 months after salpingectomy with abdominal hysterectomy. Similar results in the study Song et al. (2017) that postoperative AMH levels were significantly lower than those of preoperative LAPAROSCOPIC hysterectomy with opportunistic salpingectomy. The AMH decline rate was 12.5%. Similar results were reported by Tavana et al. (2021) that serum AMH levels decreased significantly after total abdominal hysterectomy and bilateral salpingectomy.

These results can be explained that the initial decline in AMH levels indicates that an abnormal decrease in ovarian reserve can lead to a decrease in fertility (Lin et al., 2021). AMH is consistently correlated with the clinical rate of follicle pool thinning in young women who experience elevated FSH levels (Meena et al., 2014). AMH is a glycoprotein dimer that is mainly secreted from granulocytes of preantral follicles and small antrals. AMH levels are relatively constant throughout the menstrual cycle and have a very strong correlation with the number of follicles and ovarian reserve and are an important

indicator of fertility (Tehranian et al., 2017).

In this study. AMH levels after salpingectomy and hysterectomy by 1.94 ± 0.62 ng/mL, which is lower than the AMH level before salpingectomy and hysterectomy of 3.19 ± 0.48 ng/mL. In previous studies it was reported that in the general population, serum AMH levels above 3 ng/mL are considered high, between 1.0–3.0 are considered normal, between 0.4-0.9 are considered low and below 0.4 are considered very low. According to different age groups, the lower limit of serum AMH levels is 3.0 ng/mL between 25-29 years, 2.5 ng/mL between 30-34 years, 1.5 ng/mL between 35-39 years and 0.5 ng/mL between 40 and 45 years (Singh et al., 2023). Meanwhile, another study reported that normal serum AMH levels in healthy women under the age of 38 years old 2–6.8 ng/ml (Meena et al., 2014). In the meta-analysis study, it was reported that the AMH cut off differed in predicting a decrease in fertility in women, which was 0.75–2 ng/ml. In this study, it was carried out at the age of 30-37 years so that before salpingectomy and hysterectomy, AMH levels were normal and after salpingectomy and hysterectomy, AMH levels decreased to low. These results indicate that salpingectomy and hysterectomy can lower abnormal ovarian reserves, which can lead to a decrease in fertility.

The impact of salpingectomy and hysterectomy on decreased ovarian reserve can be caused by decreased blood flow. Hysterectomy can impair ovarian function due to decreased ovarian blood flow which accelerates follicle thinning (Tavana et al., 2021). Decreased AMH levels after hysterectomy may be caused by the effects of Ovarian perfusion compensation is given directly from the aorta after hysterectomy. Decreased ovarian reserve after hysterectomy can also be caused due to acute hypoxia of the ovaries after perfusion disruption given from the arteries of the uterina during hysterectomy (Atabekoğlu et al., 2012). At

Salpingectomy, the blood flow of the ovarian stroma from the operated side is relatively disturbed compared to the non-operated side so less blood supply can result in decreased ovarian function. The most important blood supply to the fallopian tubes is the medial tubal artery, which originates at the same point as the median ovaric artery. The ovarian blood supply is very closely related to the fallopian tubes. During salpingectomy due to cutting, binding or cauterization, it can interfere with normal blood flow to the ovaries (Begum et al., 2021). Salpingectomy decreases ovarian vascularization and consequently ovarian function because the medial tubal artery originates from the same point as the median ovarian artery. The close anatomical link of the vascular supply to the fallopian tubes and ovaries is a rational risk of ovarian damage (Mizusawa et al., 2020).

The measurement of AMH levels in this study was carried out at 1 month after hysterectomy and salpingectomy. In protocol, AMH measurements are carried out at 1 month, in various studies many are carried out at 4 to 6 weeks postoperatively (van Lieshout et al., 2019). In the research Yuan et al. (2019) which compared AMH levels in patients undergoing hysterectomy for uterine fibroids with the results that AMH levels decreased significantly 1 and 4 months after surgery, compared to preoperative levels. In a prospective longitudinal study, short-term measurements of serum AMH levels after ovarian surgery showed that AMH levels decreased at 1 week and 1 month postoperatively but were restored at 3 months postoperatively (Song et al., 2017).

In previous studies it was reported that serum AMH levels were after the first month after total abdominal hysterectomy, which improved after three months (Tavana et al., 2021). There is a tendency that AMH levels recover at 3 months after surgery compared to 1 month after surgery (Iwase et al., 2014). Thus the effect of reducing total abdominal hysterectomy on ovarian function is temporary (Tavana et al., 2021). AMH is produced by primary, preantral, and antral follicles but not primordial follicles. If a rearrangement of the follicle group from a healthy pool of primordial follicles occurs, then the decreased serum AMH levels due to surgery can be recovered (Iwase et al., 2014). This study only measured AMH levels after 1 month after hysterectomy and salpingectomy which showed that this study only measured the effect of hysterectomy and salpingectomy on ovarian function.

In this study, age was not related to changes in AMH levels after salpingectomy and hysterectomy. In previous studies it was reported that AMH describes a continuous decline in follicle collection with age and AMH being the best marker of a gradual decrease in follicle count and ovarian volume. AMH provides the most reliable reflection of reproductive aging (Meena et al., 2014). In the research Kozlowski et al. (2022) stated that with age, AMH levels, the number of oocytes taken, and the number of mature oocytes decreased significantly. However, no significant difference in the number of mature oocytes was observed when patients were 36-39 and ≥40 years old. This study was conducted at the age of 30-37 years which supports these results.

Research on the effect of age on AMH also varies depending on many factors, one of which is race/ethnicity factors. Decline in ovarian reserve is a phenomenon that affects women in the middle to end of the third decade of life and there is a sharp decrease in follicle reserve by the age of 37–38 years (Hosseinzadeh et al., 2022). Another study reported that the association between AMH levels and maternal age showed a positive correlation trend before age 25 and gradually declined with age from about 30 years to menopause (Money et al., 2013). However, it is reported that there is a relationship between age and AMH levels based on race or ethnicity. When compared to age-appropriate Caucasian women, AMH levels tend to be lower in black and Hispanic women. Chinese women tend to have significantly higher AMH levels before the age of 25 than Caucasian women. AMH levels increase with age until age 25 and experience a consistent decline after age 34 until

menopause. Research in China reported that AMH peaks at age 18 with a consistent decline until age 50 (Kotlyar and Seifer, 2021). Although this study was conducted in the same race that was only conducted in patients in Makassar, these results reported that there was no association between age and changes in AMH levels after salpingectomy and hysterectomy. These results show that age is not a confounding factor in this study.

The results of this study showed that BMI was not associated with changes in AMH levels after salpingectomy and hysterectomy. In the research Yuan et al. (2019) also stated that there was no correlation between BMI and preoperative serum AMH and FSH levels. Meanwhile, in the research Lim et al. (2021) states that Obesity can interfere with ovarian function.

The mechanisms that cause obesity affect the microenvironment of the ovarian follicles. Aromatase activity and estrogen-androgen ratio in obese women interfere with AMH production. Adiponectin inhibits ovarian aromatase activity and obese women secrete comparatively less adiponectin than normal-weight women. In addition, insulin resistance in obese women affects ovarian granulosa cells to induce changes in AMH levels (Lim et al., 2021).

In this study, BMI was not associated with changes in AMH levels after hysterectomy and salpingectomy. This is because the relationship between BMI and AMH levels is influenced by race and it has been reported that high BMI is negatively correlated with AMH in Caucasian women but not in African-American, THispanic or Asian women. However, there is no mechanism to explain this (Moy et al., 2015). In addition, there is no relationship between BMI and AMH levels also because BMI cannot provide information about body fat distribution. AMH was also reported independently and negatively associated with central obesity but did not show a link to general obesity.

This result explains that there are two patterns of obesity including general obesity (peripheral) and central obesity (abdomen). The association between AMH and central or abdominal obesity is related to greater insulin (IR) resistance that is likely mediated by free fatty acids and paracrine action from the stomach depot than general or peripheral obesity. In addition, central obesity also worsens insulin-related metabolic and reproductive features. Insulin resistance exerts its negative effect on AMH directly or indirectly to reduce the inhibitory effect of AMH on follicle development, thereby increasing the sensitivity of granulosa cells to follicle-stimulating hormones (Zeng et al., 2022). The absence of a relationship between BMI and changes in AMH levels in this study shows that BMI is not a confounding factor in this study.

5. LIMITATIONS

Research on the comparison of AMH levels before and after salpingectomy and hysterectomy has never been done before in Indonesia, which is the advantage of this study. This is because the trend of AMH levels is related to race. This study only measured AMH levels at one time and did not follow up continuously and did not evaluate other outcomes such as sexual function.

6. CONCLUSION

Based on the results of the study and discussion, it can be concluded that serum AMH levels in patients decreased after salpingectomy and hysterectomy. Age and BMI were not associated with changes in serum AMH levels after salpingectomy and hysterectomy. AMH levels can be a biomarker that can help predict the impact of salpingectomy and hysterectomy on women's sexual function after 1 month of undergoing salpingectomy and hysterectomy.

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Conflict of Interest

The authors declare that there is no conflict of interest related to this study. The research was conducted independently, without any influence from pharmaceutical companies, funding bodies, or other external organizations that could affect the objectivity of the results and conclusions.

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