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ORIGINAL ARTICLE

## Anti Müllerian hormone levels before and after uterine artery embolization: A preliminary report

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### Abstract

**Objective:** To determine the effects of uterine artery embolization on Anti-Müllerian hormone levels for women under 40 years of age. **Material and methods:** Non-randomized, observational study of women under 40 years of age and who received UAE. Twenty-seven women under the age of 40 who underwent UAE were included in the study. Hormone levels were measured prior to UAE, and at least six months post UAE. **Results:** Statistical analysis from a paired t-test showed that the AMH levels pre- and post-embolization of these women fell within the normal range. The average AMH level prior to embolization was  $2.54 \pm 3.99$  ng/mL. The mean AMH concentration after embolization was  $2.33 \pm 2.70$  ng/mL. The average change in AMH levels between pre- and post-embolization was  $-0.21 \pm 1.08$  ng/mL. There is no statistically significant difference between the pre- and post- UAE AMH levels (95% CI -0.64 to 0.22,  $p=0.32$ ). **Conclusion:** UAE does not affect ovarian reserve in women under 40 as evidenced by no significant change in AMH levels before and after embolization. Women who are of reproductive age and have fibroids can consider UAE without concern for adverse effects on their fertility.

**Key words:** Anti-Müllerian hormone, fertility, embolization

### Introduction

Some studies suggest that uterine artery embolization (UAE) is a contraindication for women who desire fertility (1–4). The main reason listed is the decrease in ovarian function after UAE (5); however, multiple reports have detailed many successful pregnancies in multiple patients following UAE (6,7).

An indication of ovarian failure, leading to early onset of menopause, is an increase in the levels of the follicle stimulating hormone (FSH) and the luteinizing hormone (LH). Anti-Müllerian hormone (AMH) is another, possibly better, marker for measuring ovarian reserve that is used in fertility counselling (1). Hehenkamp et al. report no change in AMH levels with a rise in FSH preceding selection of the dominant follicle because not all of the follicles will reach dominant growth. Therefore, the remaining follicles maintain AMH production proportionate

to their size (8). Unlike FSH, oral contraceptives have no effect on AMH (9,10).

Our previous study reported normal levels of AMH in a separate group of women following UAE (6). However, that report lacked the control of the patients' pre embolization AMH levels. This paper reports both pre- and post-UAE AMH values in a new group of 27 patients.

The purpose of this report is to present our preliminary data on the effects of uterine artery embolization on a woman's ovarian reserve.

### Material and methods

This observational study was conducted in a private practice. This study shows the preliminary report of an ongoing study with a time frame covering from January 2012 to the present. UAE was performed bilaterally by the same physician. A small incision is

Table I. Normal range for AMH levels for specific age groups.

Age (years old)	Range for AMH (ng/mL)
20-29	0.65-16.40
30-39	0.16-8.43
40-49	<5.20
>49	<2.05

made in the patient's right groin to insert a catheter into the femoral artery. With x-ray guidance, polyvinyl alcohol particles (PVA) of 500 microns or larger were injected into the uterine arteries. Pelvic ultrasound and MRI images were taken between three and six months post-UAE to determine devascularization and shrinkage of fibroids.

Patients were included if they were under 40 years of age and had UAE at least six months prior. Patient inclusion in our study was completely voluntary and women who chose not to participate in the study were offered embolization without measuring AMH levels. All patients in the study gave written consent to have their AMH measurements taken for the purpose of determining their fertility. The patients in the study all had their AMH level measured prior to UAE. The standard protocol for follow-up is MRI at two months and ultrasound and blood testing at six months. The imaging data were not included in the study, as fertility potential was analyzed based on AMH levels. At their standard six-month follow up, patients had a second blood test for AMH along with the normal assays post UAE. All blood samples were analyzed using a lab developed test at Quest Diagnostic. The overall CV of the assay to measure AMH was 15% with an analytical measurement range of 0.030-11.0 ng/mL. Normal ranges for AMH levels in different age groups were determined by numerous validation tests and are listed in Table I. Unlike AMH that can be drawn at any time during the menstrual cycle, basal FSH is only drawn on day 3 following menstrual cycle (11). Since these patients were not able to schedule their appointments around those dates, we chose not to analyze FSH data for these patients.

As part of our procedural follow-up protocol, we measured AMH levels post UAE for patients in the study during their six-month follow up. Pregnancies post UAE in this study group were noted. No IRB approval was necessary because we are observing our patient's ovarian function. In addition, no patients were excluded.

In this study, normality was tested and confirmed with a Shapiro-Wilk W test (Goodness-of-Fit). If the

data were normal, then a paired t test will be tested to compare AMH levels before and after UAE. A p value < 0.05 was considered statistically significant, indicating that there was less than a 5% probability that the difference between pre- and post-AMH levels was caused by random chance alone.

## Results

A total of 27 women were included in this preliminary study. The mean age of these women at the time of embolization was 34.5 years of age (range: 27.2-39.8). The average number of fibroids for these women was  $2.5 \pm 1.26$  and the average diameter of the largest fibroid was  $5.56 \pm 2.24$ . All women experienced shrinkage of their fibroids after pelvic ultrasound and MRI follow-up.

According to the Shapiro-Wilk W test, there was not enough evidence to indicate that the data were not normally distributed. The average value of AMH levels before UAE was  $2.54 \pm 2.99$  ng/mL and post UAE was  $2.33 \pm 2.70$  ng/mL. The mean decrease in AMH level after embolization was  $0.21 \pm 1.08$  ng/mL, which was shown to be not statistically significant (95% CI -0.64 to 0.22,  $p=0.32$ ) based on paired t testing. Figure 1 shows the individual results for each of the 27 patients.

Twenty-five out of 27 women (93%) had AMH levels within the normal range with respect to their age prior to embolization. Of the two patients who had pre-AMH levels below normal, one woman's post-

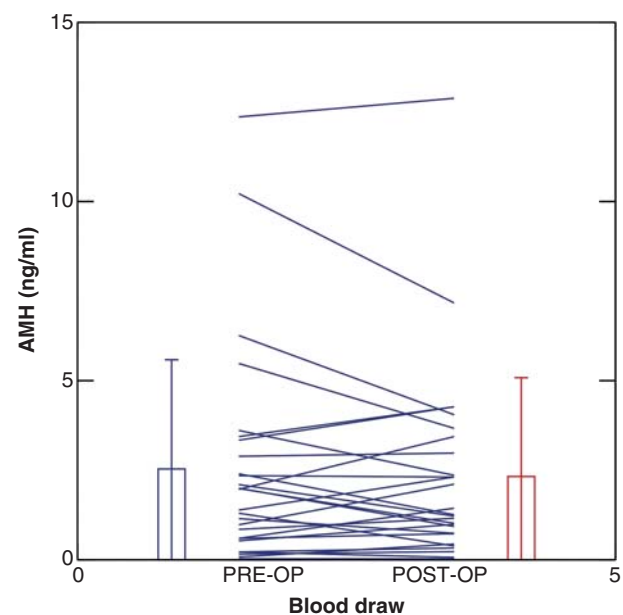


Figure 1. Individual results of AMH levels (pre- and post-UAE).

AMH levels increased and were within normal range and the other woman's post-AMH levels remained the same. Only one patient was pregnant at the time during her blood test post UAE, but her AMH levels were still normal. Two patients became pregnant following UAE. While comparing the AMH levels for pre- and post-UAE, 14 had an increase in AMH concentration post UAE. The other 12 women had a decrease in AMH concentration post embolization and one woman experienced no change in AMH values. However, this decrease in AMH levels was not statistically significant and remained within the normal boundaries. Although there were two women who had AMH levels higher than average, they showed no record of polycystic ovarian syndrome (PCOS) and were normal.

## Discussion

Some authors do not recommended UAE to patients who wish to become pregnant (2,8). However, more recent studies demonstrate that UAE is actually a viable option for women considering pregnancy (6,12).

The main reason for contraindication is a lack of research on UAE in young patients, thus many authors recommend myomectomy over UAE for women with fibroids wishing to conceive (8). A few studies have shown that pregnancy after embolization increases the risk of preterm deliveries and malpresentation as compared to myomectomy (2,8).

Traditionally research measuring ovarian reserve has focused on FSH levels post-UAE (3,6). Kim et al. found an increase in FSH after UAE, which is indicative of earlier menopause. Thus, they suggested that UAE does negatively affect a woman's ovarian reserve (13). However, using FSH levels as a marker may be unreliable due to fluctuations in FSH concentrations (3) that occur during a woman's cycle. Also, our previous study showed FSH levels to remain within the normal ranges after UAE (6).

AMH is associated with the number of developing follicles that decrease with age (9,14). AMH is a reliable marker because it can be drawn at any time during a woman's cycle and does not follow the same endocrine fluctuations as other hormones in the menstrual cycle (15,16). Hehenkamp et al. compared AMH levels in two groups of women: post UAE and post hysterectomy. Although there was a significant decrease in AMH levels, no difference between patients who received UAE and hysterectomy was seen. This study concluded that UAE and hysterectomy both affect the ovarian reserve of women and that UAE should only be offered to those not desiring

future fertility (1). The average age between the UAE group and the hysterectomy group was 45 years. With an older age group, the cohort is associated with increased pregnancy complications and early onset of menopause (17).

Although previous studies have shown that UAE negatively impacts ovarian reserve function, current research has provided evidence that fertility is not affected by UAE. There have been women who achieved successful term pregnancies and had normal vaginal deliveries (18,19).

In this study, the AMH concentrations before and after UAE were not significantly different ( $p=0.32$ ) in women under 40 years of age. This is an important finding because it demonstrates that UAE does not affect AMH concentrations in women. These results are similar to previous studies that used hormones to measure a woman's fertility post embolization (7,11,12,20). In measuring the AMH levels before and after embolization, investigators were able to determine the patient's basal ovarian reserve before UAE, which was a lacking factor in our previously published article (6). AMH levels differ among each patient. Despite the wide variety in AMH concentrations, 93% of our patients had AMH levels within normal range. An explanation for the variation in AMH levels between patients is that no specific value exists for patients that fall in a certain age group. There is a range specifying what is normal for women in different age groups. There was speculation that normal levels for AMH lie within a small range (15). However, this study has shown that there is a wide range of normal. However, when comparing AMH levels within the individual, there was no significant change.

Some articles suggest that there may be a subgroup of women with abnormally low levels of AMH. This subgroup is already at risk for infertility even without undergoing UAE (21,22). This study has its limitations with our small number of subjects. For future studies, more subjects are needed in order to provide generalizability with these results. With a larger subject pool, investigators can make correlations to determine the effects of UAE on fertility levels as well as finding possible patterns in the change in AMH levels and its relation to age. As part of a larger study, AMH values of women under 40 who did not undergo UAE should be compared to another cohort who did have UAE during the same time frame. Therefore, there is a control to also determine the reliability of AMH levels as a marker of the ovarian reserve. After fertility levels are measured using AMH as a marker, determining the number of pregnancies post embolization would further validate the appropriateness of recommending UAE to women desiring fertility.

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