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A Comparison of Fertility Rates in Women Undergoing IVF with a Tubal Factor with Surgery, Tubal Factor Infertility Without Surgery, and Unexplained Infertility

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ABSTRACT

Background & Objective: Many factors are essential for a pregnancy to be successful. Recognizing the factors caused by surgical trauma may be effective in guiding pregnancies toward success using the assisted reproductive treatment methods. Surgery changes the natural anatomical relation between the ovaries and fallopian tubes. Tubal surgery is hypothesized to reduce ovarian reserve due to the anatomical relationship between the ovarian arteries and nerves and fallopian tubes. There is no consensus on whether or not salpingectomy affects ovarian reserve. Some authors believe that salpingectomy has no effects, while others suggest that it diminishes ovarian reserve. Therefore, comparing fertility rates between women undergoing in vitro fertilization with tubal factor infertility with surgery, tubal factor infertility without surgery, and unexplained infertility can provide valuable data.

Materials & Methods: Eighty patients who met the inclusion criteria were studied. Study groups included people with a history of tubal surgery, individuals who had tubal problems without a history of surgery, and cases with unexplained infertility. Anti-Mullerian hormone (AMH) was measured every day of the cycle and other hormones, including follicle-stimulating hormone (FSH), luteinizing hormone, prolactin, and thyroid-stimulating hormone (TSH) were assessed on days 2-5 of the cycle. On the third day of the menstrual cycle, the uterus, endometrial thickness, ovaries, the size of the ovaries, and antral follicle count were evaluated using transvaginal sonography. Following ovulation induction, treatment-related factors, namely endometrial thickness, gonadotropin (Gn) time and count, E2, viable embryos, and good quality embryos, were examined.

Results: Our findings showed no difference between the study groups in terms of treatment-related factors. No significant correlation was observed between the studied groups and chemical pregnancy (P=0.9514). moreover, the studied groups were not significantly correlated with clinical pregnancy (P=0.5052).

Conclusion: The AMH was correlated with FSH, AFC, E2, and gonadotropin time and count. According to the results of the present study, tubal surgery does not affect the outcome of assisted reproductive cycles.

Keywords: Assisted reproductive cycles, Infertility, Tubal surgery

Introduction

Tubal factors can be mentioned among the major causes of infertility in women with a 30-35% prevalence in infertile women. in vitro fertilization (IVF) was originally developed to treat tubal factor infertility and it is a reasonable alternative for surgery in these patients. Many factors affect IVF outcomes in these groups, including tubal factor infertility **(1)**.

The incidence of miscarriage is 1.5-2% in all pregnancies and the risk of miscarriage is almost doubled in infertile women. This elevation in risk could be attributed to the relationships between infertility and a history of previous pelvic infections, tubal pathology, and ovulation-inducing medications. Conservative surgical treatment methods are not always the best or most appropriate options. Salpingectomy is a better option in some special cases, such as recurrent miscarriages in the same fallopian tube, uncontrolled hemorrhage, or damage to the affected fallopian tube with the opposite side

fallopian tube being normal. The rates of intrauterine pregnancy, recurrent miscarriage, and fallopian tube opening after laparoscopy and laparotomy are the same (1).

Evidence suggests that ovarian surgery affects ovarian reserve (2). Surgical trauma may alter the natural anatomical relation between the ovaries and fallopian tubes. Due to the anatomical relation of the ovarian arteries and nerves and fallopian tubes, it is hypothesized that tubal surgery reduces ovarian reserve. There is no consensus on whether or not salpingectomy affects ovarian reserve. Some authors believe that salpingectomy has no effects (4-7), while others suggest that it diminishes ovarian reserve (8-10).

Ovarian reserve is described as the size and quality of the remaining follicular reserve of the ovaries. Follicle-stimulating hormone (FSH) is the most common test for ovarian reserve. Antral follicle count (AFC) and anti-Mullerian hormone (AMH) predict the response to ovarian stimulation. The AMH is a glycoprotein secreted from the granulocytes of the preantral follicles and small antral follicles (11). Ovarian reserve is better assessed with AMH, which reaches the highest level after puberty (12). The AMH gradually declines in women with normal ovulation (13).

The AMH is not dependent on the day of the menstrual cycle (14, 15) and is known as a reliable marker of ovarian reserve, especially concerning the number of follicles remaining in the ovaries (16, 17). The clinical application of each ovarian reserve test is evaluated by the relationship between test results and the characteristics and results of the IVF cycle (1). We intended to examine ovarian reserve by AMH in people who had undergone tubal surgery. In addition, we evaluated and compared IVF results and pregnancy rate in these cases.

Materials and Methods

This prospective cohort study was performed on IVF candidates, who referred to Yas Hospital, affiliated to Tehran University of Medical Sciences during 2016-2018 and met the inclusion criteria. The inclusion criteria were age < 40 years old, regular menstrual cycles (21-35 days), no history of ovarian surgery, being non-smoker, and having normal euthyroid and prolactin. Exclusion criteria entailed women with polycystic ovary syndrome, ovarian dysfunction, and endometriosis. Study groups consisted of people with a history of tubal surgery, individuals who had tubal problems without a history of surgery, and cases with unexplained infertility. Written consent forms and demographic information were obtained from all the patients.

In the group with unexplained infertility, FSH, luteinizing hormone (LH), prolactin, and thyroid-stimulating hormone (TSH) were normal on days 2-5 of the cycle. Moreover, the hysterosalpingography was normal and the patients' husbands had normal semen samples. The AMH was measured daily for each cycle and other hormones, including FSH, LH, prolactin, TSH, and estradiol were assessed on days 2-5 of the cycle. On the third day of the menstrual cycle, the uterus, endometrial thickness, ovaries, the size of ovaries, and AFC were assessed using transvaginal ultrasonography.

All the patients selected for IVF/intracytoplasmic sperm injection (ICSI) in our center underwent clinical evaluation and basic transvaginal sonography. According to the guideline of the IVF ward at Yas Hospital, IVF started with the administration of ovulation-inducing medicines. Suitable sperms were selected for IVF/ICSI. In this regard, the oocyte was monitored for the formation of pronucleus 18 h after fertilization and was graded microscopically three days following embryo culture. In embryo quality assessment, embryos of classes I to III were considered viable.

Serum human chorionic gonadotropin (hCG) levels were measured for the biochemical confirmation of pregnancy on days 14-16 after administration. If positive, the women underwent transvaginal ultrasonography three weeks later. Clinical pregnancy was defined as the presence of a pregnancy sac with a visible fetus who had a heartbeat.

All the collected data were entered into SPSS creating a database. Next, data cleaning and exploration were performed and the outliers and missing data were examined. Quantitative variables were described by mean, standard deviation, and other measures of dispersion. Furthermore, frequency tables and related graphs were used for the qualitative variables. The one-way analysis of variance (ANOVA), Kruskal-Wallis test, as well as Pearson and Spearman correlation coefficients were utilized.

Results

A total of 80 patients were studied. Reasons for having a surgery in the tubal factor group with surgery included salpingectomy following the treatment of ectopic pregnancy or hydrosalpinx, salpingectomy after ectopic pregnancy treatment, fallopian tube catheterization, and tubal ligation (TL).

Table 1. Profiles of patients

Variable	Tubal Factor Without Surgery (n=25)	Tubal Factor With Surgery (n=20)	Unexplained infertility (n=35)	P-value
Age (yrs)	33.76±5.30	33.8±3.27	31.48±4.19	0.07
Husband's age	36.41±4.51	35.95±5.58	35.22±6.21	0.34
BMI	25.67±3.85	25.09±4.23	25.21±3.87	0.86
Duration of infertility	6.92±5.36	4.45±3.64	5.21±3.44	0.124
AFC	9.39±5.49	12.36±5.24	10.75±5.02	0.141
Serum LH (IU/L)	4.94±2.58	4.49±3.89	7.10±6.93	0.0297
Serum FSH (IU/L)	7.21±2.39	6.85±3.18	6.89±2.74	0.632
Serum AMH (ng/ml)	1.96±1.41	2.87±2.65	2.81±2.02	0.24
Protocol				0.079
Long	10(40)	10(50)	24 (68.6)	
Antagonist	15(60)	10(50)	11(31.4)	

There was no difference between the studied groups in terms of demographic characteristics, such as the age of patients and their husbands, body mass index, AMH, FSH, AFC, oocyte, gonadotropin time, gonadotropin count, E2, viable embryos, and good embryos. However, LH in the unexplained infertility group had a significant difference with the tubal factor group with surgery (P=0.0048) and without surgery (P=0.0674).

Table 2. Treatment-related factors of patients

Variable	Tubal Factor Without Surgery (n=25)	Tubal Factor With Surgery (n=20)	Unexplained infertility (n=35)	P-value
E2 on the hCG injection day (Pg/ml)	1478.22±1619	1992.66±1661.80	1756.77±1058.38	0.254
Endometrial thickness (mm)	7.21±1.99	8.54±2.12	8.6±1.8	0.0553
Gn time	10.56±2.66	9.55±2.06	9.97±2.3	0.3637
Gn count	38.64±16.48	30.55±10.95	30.74±16.18	0.1
Oocyte retrieved	6.08±3	7.75±4.74	6.77±3.68	0.5068
Viable embryos	3.08±2.15	4.4±2.7	3.28±1.87	0.1992
Good embryos	2.84±1.84	4±2.86	2.51±1.26	0.1634

The study groups were not significantly different in terms of treatment-related factors, including ET, oocyte removed, gonadotropin time, gonadotropin count, E2, viable embryos, and good embryos. Results showed that 33 patients had a chemical pregnancy and 25 patients had clinical pregnancies. There were two pregnancies in the FET cycle.

According to the Spearman correlation coefficient, there was a strong negative correlation between age and AMH (P<0.001). Furthermore, significant correlations were revealed between AMH and FSH (P=0.02), AMH and AFC (P=0.0013), AMH and gonadotropin time (P=0.0016), AMH and gonadotropin count (P<0.001), AMH and E2 (P=0.0257), LH and FSH (P=0.0092), LH and oocyte (P=0.0108), AFC and oocyte (P=0.0431), AFC and gonadotropin count (P<0.001), E2 and oocyte (P<0.001), viable embryos and oocyte (P<0.001), good embryos and oocyte (P<0.001), gonadotropin time and gonadotropin count (P<0.001), gonadotropin time and E2 (P<0.001), viable embryos and good embryos (P<0.001), gonadotropin time and gonadotropin count (P<0.001), gonadotropin time and gonadotropin count (P<0.001), and viable embryos and E2 (P=0.0047). The results of Pearson correlation demonstrated that the studied groups were not significantly correlated with chemical pregnancy (P=0.9514) and clinical pregnancy (P=0.5052).

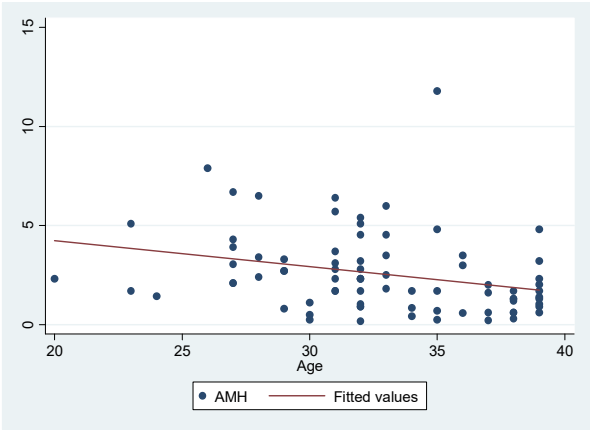

Figure 1. Correlation between AMH and the age of patients in the three groups

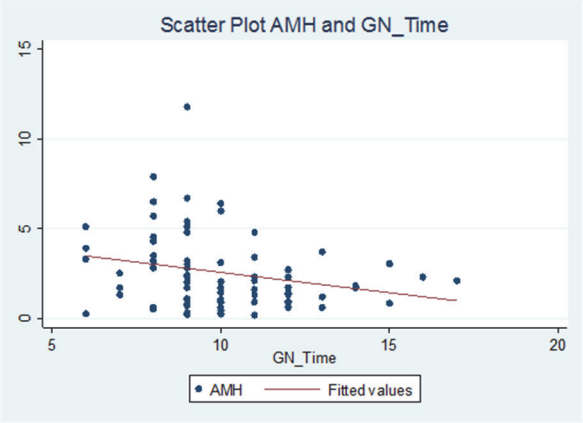

Figure 2. Correlation between AMH and gonadotropin time of the patients in the three groups

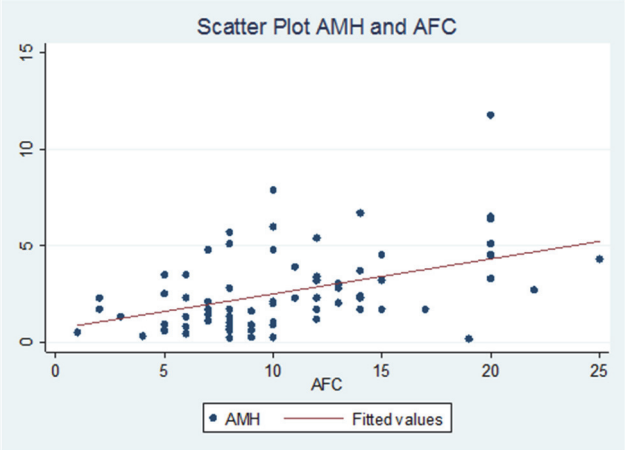

Figure 3. Correlation between AMH and AFC of the patients in the three groups

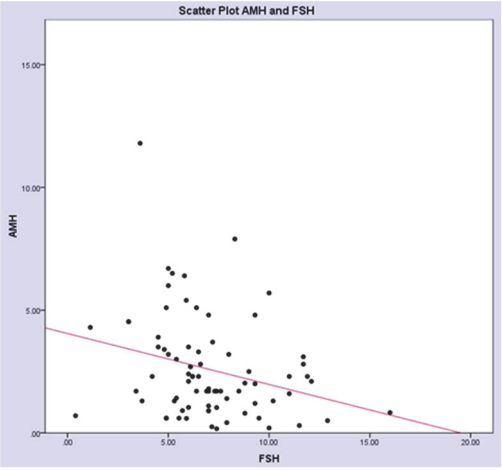

Figure 4. Correlation between AMH and FSH of the patients in the three groups

Discussion

Surgical trauma may alter the natural anatomical relation between ovaries and fallopian tubes. Tubal surgery is hypothesized to reduce ovarian reserve due to the anatomical relationship between the ovarian arteries and nerves and fallopian tubes. There is no consensus on whether or not salpingectomy affects ovarian reserve. Some authors believe that salpingectomy has no effects **(4-7)**, while others suggest that it diminishes ovarian reserve **(8-10)**.

The results of the current study showed that the fertility rate in the three groups, in terms of both chemical pregnancy and clinical pregnancy, was not statistically significant. These rates in people who had a tubal factor with surgery were similar to those of the unexplained infertility group and the group who had a tubal factor without surgery. In this study, the treatment-related factors, including gonadotropin time, gonadotropin count, E2 on the hCG injection day, endometrial thickness, the number of oocytes obtained, the number of viable embryos, and the number of good quality embryos were not significantly different between the three studied groups.

We observed a statistically significant correlation between AMH and FSH. Moreover, AMH, AFC, AMH, gonadotropin time and count, AMH, and E2 were significantly correlated. However, no significant correlation was found between AMH and some other factors, such as endometrial thickness and the number of obtained oocytes. Another study results like present study indicated that there were no significant correlation in the gonadotropin time and count and E2 on the injection day, endometrial thickness, the number of oocytes removed, viable embryos, and good quality embryos **(9)**.

Lin *et al.* **(6)** examined 251 women in 288 cycles in the two groups of laparoscopic salpingectomy and non-salpingectomy, which included primary bilateral TL, primary tuboplasty, or proximal ovarian tube obstruction. They did not find any difference in replacement rate, clinical pregnancy, and live birth. The results of the current study were in line with the mentioned study **(6)**. However, the present study, TL and tuboplasty were considered as tubal manipulations.

Some authors reported that salpingectomy does not affect ovarian reserve or ovarian response to gonadotropin stimulation, while some have acknowledged the effect of this parameter. Lass *et al.* **(28)** revealed that in IVF patients who underwent a salpingectomy, the follicles grew less on the operated side than on the other side resulting in significantly fewer oocytes. However, a comparison of the total number of follicles and oocytes obtained from both ovaries indicated no difference in pregnancy rates between the patients who had primary surgery and those who had unexplained or male factor infertility.

Ye *et al.* **(9)** conducted a study on 198 patients in three groups of unilateral salpingectomy, bilateral salpingectomy, and no tubal surgery. The mean AMH level was significantly higher in the patients without tubal surgery, compared to those with bilateral salpingectomy. Furthermore, FSH was significantly lower in the patients without tubal surgery than in the cases with bilateral salpingectomy. No significant differences were found in the duration of gonadotropin therapy, the amount of gonadotropin used, estradiol level on the hCG injection day, endometrial thickness, the number of oocytes retrieved, viable embryos, and good quality embryos between the three groups. The AMH concentration was not correlated with the number of oocytes.

In a study by Grynnerup *et al.* **(10)**, 71 infertile and 21 fertile patients were compared. The AMH level was lower in the infertile group who underwent a salpingectomy than the infertile group with no tubal surgery. In all these groups, AMH was positively correlated with the number of oocytes removed. These controversial results in the literature may be attributed to the differences in the sample sizes, variable factors during IVF treatment, and various salpingectomy procedures.

Due to the limited number of samples, we did not separate the surgical cases based on the type of surgery and whether the surgery was unilateral or bilateral. Comparisons of AMH and AFC showed that AMH was correlated with AFC and the removed oocytes. However, in the present study, AMH was not correlated with the removed oocytes, the reason for which is unclear. In the current investigation, the evaluated AMH was not follicular-fluid AMH and different kits were used to evaluate AMH. According to the meta-analyses conducted by Qin *et al.* **(37)** and Yoon *et al.* **(38)**, further studies are required for confirming these findings.

Conclusion

Our findings demonstrated that the AMH concentration correlates with FSH, AFC, E2, and gonadotropin time and count. Moreover, tubal surgery does not affect ovarian reserve and the outcome of assisted reproductive cycles.

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Conflict of Interest

Authors declared no conflict of interests.

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