

The Relationship between Functional Ovarian Cyst and Ovarian Reserve among Infertile Females

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Abstract--- Introduction: Functional ovarian cyst is a common phenomenon in women. Ovarian reserve changes with increasing the age or under the effect of ovarian diseases. This age-related reduction in ovarian reserve, especially in women who have lower ovarian reserve due to ovarian diseases, can have a greater impact on the women's fertility. The present study was conducted to compare the ovarian reserve in the infertile women with and without a functional ovarian cyst by measuring the serum levels of the anti-Müllerian hormone.

Materials and Methods: The present study is an analytical study conducted on 60 infertile women referred to the Infertility Research Center of Ahvaz Jundishapur University of Medical Sciences in 2011. Transvaginal sonography was first performed and based on the sonography, the patients were divided into two groups, including a case group ($n = 30$) with an ovarian cyst and a control group ($n = 30$) without a ovarian cyst. The blood samples were taken from all patients to measure the serum levels of the anti-Müllerian hormone and the samples were sent to a laboratory (Tohidi Laboratory). After 3 months, transvaginal sonography was re-performed on the patients with cysts to diagnose the cases of persistent cysts or other ovarian cysts. The ovarian reserve was compared between the two groups according to the mean serum levels of the anti-Müllerian hormone. The data were analyzed using SPSS version 17 software. The significance level was considered 0.05.

Results: The mean age of the case and control groups was 28.66 and 29.16 years, respectively. Duration of the infertility and the number of people with primary or secondary infertility were not significantly different between the two groups. The mean serum levels of the anti-Müllerian hormone were 2.70 ng / ml in the case group and 2.55 ng / ml in the control group ($P = 0.821$).

Conclusion: Based on the results, the rate of ovarian reserve in the infertile women with and without a physiological ovarian cyst is not different. Further studies with larger sample sizes are recommended to confirm the results of this study.

Keywords--- Ovarian Reserve, Anti-Müllerian Hormone, Ovarian Physiological Cyst.

I. INTRODUCTION

Infertility refers to a couple who has had an unprotected intercourse for one year without a pregnancy (1). The incidence of the infertility is about 10% to 15% in the couples and infertility can be due to masculine, feminine, or a

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combination of both factors (2). The ovary is one of the most important reproductive organs in women for fertility. Ovarian reserve is generally measured by describing the rate of the follicular reserve of the ovarian. Several methods have been described to evaluate the ovarian reserve, including measuring the serum levels of follicular or estradiol stimulating hormones, clomiphene citrate stimulating test, counting antral follicles by the transvaginal sonography, and the anti-Müllerian hormone measurement. The serum levels of the anti-Müllerian hormone (3) can be measured at any time during the menstrual cycle and does not require sampling on a specific day of the menstrual cycle, and its accuracy and efficacy have been reported greater than those of the follicular or estradiol stimulating hormone in previous studies. It also does not require the skills and experience of staffs (4-8). The ovarian reserve changes with increasing the age or under the effect of the ovarian diseases (9). With increasing the age, the follicular number of the ovary is reduced, and this reduction reaches to its peak at the age of 35 to 40 years. This age-related reduction in the ovarian reserve, especially in women who have spontaneously lower ovarian due to ovarian diseases, will have a greater impact on the women's fertility. For this reason, early and timely identification of the people with potentially low ovarian reserve before the onset of the aging effect on it can have a significant impact on the ovarian reserve (2). The ovarian diseases such as polycystic ovary syndrome and endometrioma *can reduce the* ovarian reserve (10 and 11). It has been also reported that surgery and resection of a part of the ovarian tissue is associated with reduced ovarian reserve (12-15).

However, further investigations are needed with regard to the efficacy the physiologic ovarian cysts on the ovarian reserve, since these cysts are very common and can be observed even in the women with an adequate fertility power and their rate increases with increasing the age and approaching to the menopausal stage, which is associated with a reduced ovarian reserve (16). These cysts are among the non-neoplastic ovarian masses that have a variety of follicular cysts, corpus luteum, and theca lutein cysts. Functional ovarian cysts are benign and often do not have symptoms and do not require surgery (17, 18). Statistics on the rate of the ovarian cysts vary, since they are often asymptomatic and can only be diagnosed by sonography. These statistics vary from 5% to 30-50% at different ages. However, its prevalence has been reported 5 to 10% among the reproductive age women in most articles. The prevalence of these cysts has also been reported 14% in women (19–22). The studies conducted in this regard have reported contradictory results on the effect of the physiologic ovarian cysts on response to treatment in the infertile patients (23-26).

The objective of the present study is to reveal whether physiologic ovarian cysts, which are often accidentally detected in the sonography evaluation of the infertile women, can affect the ovarian reserve, and subsequently, the patients' infertility, and whether accidental detection of these cysts in the sonography would necessitate the rapid therapeutic intervention and more decisive methods or not.

II. MATERIALS AND METHODS

The present study is an epidemiological-analytical study conducted on 60 infertile women referred to the Infertility Research Center of Ahvaz Jundishapur University of Medical Sciences in 2011. The study protocol was approved by the Research Deputy of Ahvaz Jundishapur University of Medical Sciences under the code of FIRC-9012. After determining the sample size, the transvaginal sonography was performed on all patients until the

complete completion of the sample. Based on the sonography, the patients in both groups, including a group with an ovarian cyst (at least one functional ovarian cyst with a size greater than or equal to 30 mm), and a group without an ovarian cyst were included in the study. Blood samples were taken from all patients to measure the serum levels of the anti-Müllerian hormone and the samples were sent to a laboratory (Tohid Laboratory). After 3 months, transvaginal sonography was re-performed on the patients with cysts to identify the cases of persistent cysts or other ovarian cysts to exclude them, if necessary. The ovarian reserve was compared between the two groups according to the mean serum levels of the anti-Müllerian hormone. In the case of large cysts (larger than 50 mm), in which the complication rate of the cysts increases, drug therapy was administrated to protect the patient's safety as possible. The research inclusion criteria included the age range of 18-35 years, no smoking, no history of ovarian disease, ovarian surgery, polycystic ovary syndrome and endometrioma, no use of ovarian stimulating and hormonal drugs and oral contraceptives over the last 3 months, no hormonal disorders such as thyroid disorders and hyperprolactinemia, having a normal menstrual cycle, no ovulation disorders, no history of underlying medical illness, no hirsutism, and no history of premature ovarian insufficiency. The research criteria included ovarian cysts smaller than 30 mm, lack of patient cooperation, and persistent ovarian cyst (more than 3 months). The age, weight, height, duration of infertility, and type of infertility of the patients were obtained. The height and weight of all patients were measured by the researcher using a standard instrument. All study participants completed the informed consent form.

Determining the Sample Size

The sample size was determined 29 people in each group and a total of 60 people were included in the study according to the variance of previous studies (21) and the following formula.

$$n = \frac{(s_1^2 + s_2^2) (z_{1-\frac{\alpha}{2}} + z_{1-\beta})^2}{(\bar{x}_1 - \bar{x}_2)^2} \quad n = (1.96 + 1.28)$$

The Statistical Method and the Data Analysis Method

The quantitative data were presented as mean and standard deviation using the independent t-test and qualitative data were presented as percentage using the chi-square test. The data were analyzed using SPSS version 17 software. The significance level was considered 0.05.

III. RESULTS

In this study, 30 infertile women with a physiologic ovarian cyst in the experimental group and 30 infertile women without a physiologic ovarian cyst in the control group were investigated. The mean age of the experimental group was 28.66 years and the mean age of the control group was 29.16 years. The mean duration of the infertility in the experimental group and control group was 4.03 years and 4.01 years, respectively. The mean serum levels of the anti-Müllerian hormone were 2.70 ng / ml in the experimental group and 2.55 ng / ml in the control group (P = 0.686).

Table 1: Relationship between the Functional Ovarian Cyst and Ovarian Reserve in the Infertile Women

| <i>Variable</i> | <i>Experimental group</i> | <i>Control group</i> | <i>p-value</i> |
|--|---------------------------|----------------------|----------------|
| Age* | 98.66±2.28 | 87.16±2.29 | 512.0 |
| Duration of infertility * | 40.03±2.4 | 44.01±2.4 | 979.0 |
| BMI* | 77.42±3.25 | 14.67±4.25 | 807.0 |
| Primary infertility** | 3).25(%83 | 3).22(%73 | 347.0 |
| Secondary infertility ** | 7).5(%16 | 7).8(%26 | |
| serum levels of the anti-Müllerian hormone * | 42.70±2.2 | 41.55±2.2 | 821.0 |

*Mean and standard deviation - Using the independent t-test

**Frequency and percentage – using the Chi-square test

IV. DISCUSSION

The objective of this study was to compare the ovarian reserve in the infertile women with and without ovarian cysts by measuring the serum levels of the anti-Müllerian hormone in the 30 infertile women with physiologic ovarian cyst in the experimental group and the 30 infertile women without a ovarian cyst in control group referring to the Infertility Center of Jundishapur University of Medical Sciences in Ahvaz. There was no significant difference between two groups in terms of the duration of the infertility and the primary and secondary infertility. The results showed that there was no significant difference between the two groups in the serum levels of the anti-Müllerian hormone, indicating that having a functional cyst in the infertile women did not have an effect on their ovarian reserve (27-29).

Based on the previous studies, removal of the ovarian cysts by laparoscopy clearly reduces the ovarian reserve, but the effect of these cysts on the ovarian reserve before treatment is controversial. Based on a research conducted by Somigliana et al in three groups of women with an ovarian endometrial cyst, non-endometrial ovarian cyst, and women without an ovarian cyst, serum levels of the anti-Müllerian hormone did not show a significant difference ($p = 0.60$) and in the people with bilateral cysts, compared to unilateral and no-cyst, serum levels of the anti-Müllerian hormone were significantly lower (30, 31).

In previous studies, the researchers investigated mainly the effect of the endometrioma on the ovarian reserve. In a prospective cohort study conducted by Csokmay et al on 84 infertile women who were ovulated with clomiphene citrate, the effect of the ovarian cysts before the onset of the clomiphene on the ovarian response was investigated. Results revealed that patients with ovarian cysts had significantly fewer ovulations than those without the cyst, but pregnancy rates were not significantly different between the two groups (32-36). In the study conducted by Hirokawa et al, the serum levels of the anti-Müllerian hormone were measured in 38 patients who underwent unilateral endometrial cystectomy and bilateral endometrial cystectomy. The results showed a significant reduction in the serum levels of the anti-Müllerian hormone in the group with a bilateral endometrioma compared to that of the patients with a unilateral endometrioma ($p < 0.001$) (37-40). In their study on the patients with benign ovarian masses (endometrioma, adult teratoma, and mucinous adenoma cysts), Chang et al performed laparoscopic cystectomy and measured the serum levels of the anti-Müllerian hormone serially before the surgery, one week, one month, and three months after the surgery and total ovarian volume was measured by 3-D sonography before and

after the surgery (41-45). The mean serum levels of the anti-Müllerian hormone decreased by 2.23 ng / ml and then increased by 1.14 ng / ml in the first month after the surgery and 1.5 ng / ml three months after the surgery (46). The serum levels of the anti-Müllerian hormone reached 65% three months after the surgery and reached its maximum level in the first week after the surgery (endometrioma was lower than non-endometrioma cases) (33.9% versus 69.2%). The serum levels of the anti-Müllerian hormone in the bilateral mass group were lower than those of the unilateral mass group (16.9% versus 62.9% before the surgery), and the researchers concluded that laparoscopic cystectomy can reduce the ovarian reserve, although this reduction was greatly improved three months after the surgery (47-50). The study conducted by Yuming et al investigated the effect of the endometrioma and laparoscopic cystectomy on the serum levels of the anti-Müllerian hormone (25). The mean serum levels of the anti-Müllerian hormone in the control group (women without endometrioma) were significantly higher in the endometrioma group or those with a previous history of the cystectomy in each age subgroup, while the mean serum levels of the anti-Müllerian hormone in the endometrioma group were significantly higher than those in the group with a previous history of cystectomy (51-53). The mean serum levels of the anti-Müllerian hormone were lower in the group with a history of the bilateral cystectomy than those in the group with a history of unilateral cystectomy and were lower in the patients with a bilateral endometrioma than those with a unilateral endometrioma (54, 55). These researchers concluded that both cases of ovarian endometrioma and cystectomy were associated with a significant reduction in the ovarian reserve. The bilateral endometrioma has a more negative effect on the ovarian reserve than unilateral endometrioma, whether treated surgically or conservatively (56-58). To evaluate the ovarian reserve following the laparoscopic cystectomy, Iwase et al measured the serum levels of the anti-Müllerian hormone and the follicular stimulating hormone. The serum levels of the anti-Müllerian hormone in the endometrioma group before and after the surgery were 2.98 ng/ml and 3.29 ng / ml, respectively. However, the follicular stimulating hormone serum levels did not change significantly before and after the surgery. The researchers concluded that measurement of the serum levels of the anti-Müllerian hormone was a useful marker to evaluate the effect of laparoscopic cystectomy on the ovarian reserve (26, 59). Investigating the women who underwent the ovarian cystectomy of single-hole and unilateral benign cysts, Keita Jima et al observed a reduction in serum levels of the anti-Müllerian hormone in the women with endometrioma who underwent cystectomy (27, 60). Lee et al examined the effect of electrocoagulation after the removal of the laparoscopic ovarian cyst on the ovarian reserve. The ovarian reserve was evaluated by measuring the serum levels of the follicular stimulating hormone and the serum levels of the anti-Müllerian hormone and transvaginal sonography for counting the antral follicles and determining the mean ovarian diameter and blood flow rate of stroma of the ovary on the first, third, sixth, twelfth days after the surgery. Finally, they concluded that there was a statistically significant reduction in the ovarian reserve in the use of electrocautery after the laparoscopic cystectomy. A possible mechanism was the damage to the ovarian vascular system using the electrocautery (28).

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VI. CONCLUSION

According to the results of our study and comparing them with the results of previous studies, it seems that the rate of the ovarian reserve in infertile women with and without the ovarian physiological cysts is not different. Further studies with larger sample sizes are recommended to confirm the results of this study.

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