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Original article

Age of women and the number of antral follicles in prediction of ovarian response in intra uterine insemination (IUI)

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Abstract

Background: Fertility specialists assess ovarian responses prior to estimating the prognosis for women who are suffering from anovulation. To diagnose inconsistent between chronological and biological age of ovaries in addition predict ovarian response, transvaginal ultrasound (TVS) ovarian act as an operant method. The aim of the current study was to assess the correlation between the number of antral follicles in both ovaries and the age of women in predicting the ovarian response in intrauterine insemination (IUI).

Methods: The research design of the present study was a cross-sectional. A total of 171 individuals, who were non-smoker patients and had already undergone a standard regimen of ovarian stimulation for IUI, were selected as participants of this study from the Infertility and Reproductive Health Research Center in Babol (Iran). On the third day of the cycle, TVS was conducted to measure the mean of every ovary and also to count the number of antral follicles on the both ovaries.

Results: The mean age of our patients was 27.7. The increased aged of women is significantly associated with lower total number of antral follicles (r= -0.40, P= 0.001) and decreased mean diameter of ovary (r= -0.25, P= 0.001). The mean ovarian diameter was significantly correlated with high number of antral follicles (r= 0.50, p= 0.0001).

Conclusion: The findings of the present study indicated that the age of women and the ovarian diameter are leading factors to help determine ovarian response as well as basal antral follicle counts.

Keywords: Age, Antral follicles, IUI, Ovarian response

Introduction

As the level of education in women has experienced an upward trend over the past few decades, aging is considered to have brought about unwanted infertility in women (1). This is of a particular importance as it is commonly believed that fertility declines with advancing age. It is estimated that this rate of decline in women is exponential until the age of 30 (2). The application of controlled ovarian stimulation in infertility treatment is not recommended in women over the age of 35 with less than five antral follicle count because it can potentially lead to poor response (3). The measurement of antral follicle count has been shown to have the predictive elements of ovarian response and can significantly influence the

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necessary exogenous gonadotropin for ovarian stimulation, the cycle cancellation, pregnancy outcomes, and live birth rates after assisted reproductive technology (ART) in large-scale studies (4, 5, 6). Some researchers even regard it as a superior predictor for ovarian response compared with other expensive and time-consuming endocrine tests (7). Despite its power in predicting ovarian response, there are still many other queries that are not exactly in accordance with that and do not, as a result, back the idea (8, 9). A vivid illustration of that is a research study that has recently shown that the only reliable predictor for achieving a live birth is age, not antral follicle count (10). The aim of the current study, however, was to assess the correlation between the number of antral follicles in both ovaries and the age of women in predicting the ovarian response in intrauterine insemination (IUI).

Materials and Methods

This cross-sectional study was approved by the Ethics Committee of Babol University of Medical Sciences. The researchers selected the sample for this study from among the women who referred to the Infertility and Reproductive Health Research Center. The individuals with mild male infertility, the symptoms of anovulation, and unexplained infertility were regarded as eligible participants for this study. The women over the age of 45 who had basal FSH >4 international units per milliliter, body mass index ≥35 kg/m^2, and polycystic ovarian were not regarded as eligible participants for this study.

Women with >12 antral follicles per ovary, or any ovarian pathology or surgery were also excluded from the study. The study was conducted on 194 women candidates for IUI from June 2012 to December 2013. The age of the participants was recorded. Then, from the beginning of the treatment cycle, the patients were closely evaluated by transvaginal ultrasound (7.5 MHz probe Fokuda, Japan) on the second or third day of their menstrual cycle in order to rule out ovarian cysts.

The researchers followed the basic clinical and technical requirements for the assessment of the antral follicles count in clinical practice (11). All antral follicles in both ovaries were counted carefully and the mean of ovarian diameter measurements in both diameters were calculated. The antral follicles count is defined as the total number of visible round or oval, intraovarian transonic structures with the diameter between 2 and 10 millimeters. Ultrasound examinations were performed by experienced fertility specialists. The relationship between age, antral follicles count, and the ovarian diameter was evaluated. The researchers also made sure that the two ultra-sonographers, operating in the center, had carefully counted the number of all antral follicles of 2 to 10 millimeters in two internal diameters.

Statistical Analysis

Having collected the data, the researchers applied SPSS (version 16) for the analyses. Depending on the normality or non-normality of the data, the researchers used Chi-square, Kruskal–Wallis, Mann-Whitney tests, and Spearman correlation coefficient to analyze the data. Kolmogorov-Smirnov test was also used to determine the normal distribution of variables. Needless to say, the P-value <0.05 was considered significant.

Results

A total number of 23 women out of 194 patients who were candidates for IUI were excluded from the study due to their vaginal bleeding (three cases), overstimulation of the ovary (two cases), lack of the dominant follicle growth (seventeen cases), and cyst

Table 1. Chracteristics of infertile women undergone intrauterine insemination

variables	Mean	Range (min, max)
Age (years)	27.7	16, 44
Age of husband(years)	31.8	20, 70
Infertility duration(years)	4.9	1, 27
Mean diameter of ovary(millimeter)	25.5	13.8, 40.8
Number of antral follicles	2.2	1, 8
Used fertility drugs injections	4.9	1, 27

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Table 2. Relationship of age and follicles in women undergone intrauterine insemination

	Number of antral follicles		Mean diameter of ovary	
	r	P-value	r	P-value
Age (years)	-0.40	0.001	-0.25	0.001
Infertility duration (years)	-0.01	0.85	0.03	0.68

(one case). Therefore, the current study was performed on 171 women, with the mean age of 27.7, ranging between 16 and 44 (table 1). The mean number of antral follicles showed a significant negative relationship with age ((r= -0.40, P= 0.001). In addition, the mean ovarian diameter showed a significant negative relationship with age (r= -0.25, P= 0.001). The mean diameter of ovary was 25.5 (13.8- 40.8). The mean ovarian diameter was significantly associated with high number of antral follicles (p=0.0001) (table 2).

Discussion

The mean number of antral follicles and the mean number of ovarian diameter were found to be significantly in negative relationship with age. Scheffer et al. and Frattarelli et al. conducted a research study based on which they concluded that the number of antral follicles had a close association with age in normal women with infertility (12, 13). This conclusion is congruent with the result of this study. Antral follicles, 4–6 millimeters in diameter during the early follicular phase, may be the best manifestation of the age-dependent pattern of the antral follicle pool. Counting these follicles only would not only prevent the use of atretic follicles but also the overestimation of the antral follicles count (14). Kwee et al. also reported that antral follicle counts can also act as a test for ovarian response (7). Unfortunately, antral follicles count is not often used clinically. Basal FSH concentration or the mean ovarian volume is pronounced more than antral follicles counts (15). Antral follicles counts are currently regarded as a valuable predictor of ovarian response to stimulation, and it can also be applied in counseling prior to clinical treatments (16, 17).

The women with enough oocytes in middle age and with abate reserve in young age need to be properly consulted around the outset of infertility treatment. A treatment scheme adjustments need to be designed and developed for such women, which can be implemented through stimulation instruction, early initiation of treatment, other replacement options. Tartalzis et al. concluding based on the results of their study, asserted that such groups of women need to be identified and should be managed and treated individually. This can help them have a higher chance of becoming pregnant before experiencing any diminish in ovarian reserve of female reproductive mechanism due to aging (18). Some studies have reported that the follicular phase of the menstrual cycle in older women becomes shorter (19, 20). It is also estimated that hormonal variation, which are age-dependent, become evident late and that these variations occur only when follicle numbers are clearly diminished (21).

In this study, however, we found that ovarian volume is inversely associated with age. This result was reported by some studies conducted on women above the age of 30 (22). It is evident that clear changes in reproductive life occur at the extreme of it; therefore, no clinical assessment of ovarian volume can be conducted then. As a result, the use of ovarian volume to predict ovarian responsiveness has been a grey area so far (23). Antral follicles count is regarded more as a useful clinical marker of ovarian responsiveness than ovarian volume because it declines over time (annual losses of 0.35–0.95 antral follicles/year) (24). The quality of follicles cannot be accessed through ultrasound, either. The antral follicles in ultrasound may be atresetic and can poorly respond to stimulation (25).

In the current study, we closely followed the standardization of the assessment of antral follicles count, i.e. the simple and practical recommendations to improve the prediction of ART outcomes. Through fulfilling these basic clinical and technical requirements for the evaluation of the antral follicles count, the difficulties in the Ultrasound assessment of antral follicles count and the possibilities of any errors in sonography or any other misinterpretations would be minimized (11). Our results also suggest an urgent need for further investigations to study the histological

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assessment of antral follicles in order to invest the various stages of atresia in middle-aged women.

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Conflict of interest

The authors declare that there are no conflicts of interest.

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