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Comparison between AMH level in Multipara and Nullipara in Women More than 40 Years Old

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Abstract

Decreased ovarian reserve is considered as one of the main causes of infertility. It is about the availability of preovulatory oocytes in the ovaries. With increase age, ovarian reserve decreases. Nowadays, "ovarian reserve" assessment became a strategy to assess female infertility.

Objective: The current study aims to find the relationship between age and infertility type with measures of ovarian reserve (FSH, AMH and AFC) in infertile patients.

Material and Method: The cross-sectional study design was used for this study and a survey was conducted among 100 infertile women.

Result: Results revealed that Relationships between age and ovarian reserve indicators show a highly significant negative correlation with AFC ($p= 0.001$) and AMH ($p= 0.007$) level while positive correlation is found with FSH level ($p= 0.001$). The relation between age and FSH was moderate ($rs=0.38$, $p<0.0001$) and revealed that AMH and AFC level decreases while FSH level increases with age.

Conclusion Study of AMH level is the most reliable source to measure age-specific changes.

Key words: *Female infertility, ovarian reserve, anti-mullerian hormone.*

Introduction

In the modern world, the determination of the strategy to manage female infertility by assessing ovarian reserve has become necessary. Traditionally, ovarian reserve used to be evaluated by age and ultrasound investigation of Follicle stimulating hormone, Antral follicle count, and estradiol levels at the early follicular phase [1]. AMH (Anti-Mullerian Hormone) or Mullerian inhibiting substance is promising marker for ovarian reserves. It is a dimeric glycoprotein and involved in growth and differentiation. It is gonadal factor causes Mullerian duct regression and precursor of female reproductive tract. Plasma level of AMH is detectable at birth, gradually increases till puberty and then decreases until undetectable at menopause[1]. For evaluation of low ovarian reserve, FSH and E2 levels were considered to be determining biochemical markers for several years. However, it has been recently found that high level of FSH is associated with decreased functioning of ovary. Moreover, evaluation of AFC at later stages are considered to be more reliable in the assessment of ovarian reserve. High-resolution sonographic systems help obtain follicle count quickly, but there are certain difficulties in assessing correct AFC such as anatomical variations and high inter-observer differences [2] . AFC is considered the first choice to determine ovarian reserve by several health care professionals because it predicts poor response effectively when compared to basal FSH. Recently, it has been suggested that Anti-mullerian hormone are essential in the evaluation of ovarian response. It is a Mullerian inhibiting hormone which is a dimeric glycoprotein. This hormone belongs to the family of transforming growth factor – β. In women of reproductive age, AMH is produced in the ovary by granulosa cells and is secreted by small antral follicles [3] . The primary function of AMH in the ovary is resisting the accumulation of primordial follicle and reducing pre-antral and small antral follicles sensitivity to FSH in the ovary. There are certain advantages of AMH when compared with other tests in the assessment of ovarian reserve. One of the significant advantages is AMH levels can be evaluated at any day of the menstrual cycle as they are stable throughout the cycle [4] . Moreover, they are not affected by variations in any other hormone as well as the use of oral contraceptives. Bentzen et al. have suggested in a recent study that makers of ovarian reserve are lower in women who use contraceptive methods involving steroids.

On the other hand, AMH cannot be detected in women until they reach puberty and reaches its highest level at the age of 24-25 years, while it cannot be detected after menopause. With increasing age, AMH level, as well as the quality of oocytes, reduces [5]. According to recent studies, depletion of follicles doubles when the amount of primordial follicle reaches approximately to the value of 25,000. Women reach at this critical stage at about 37-38 years, after which ovarian reserves sharply reduced. The normal AMH level value with female age is 5.4, 3.5, 2.3, 1.3 and 0.7ng/ml in 25, 30, 35, 40 and >43 years respectively (fertility, 2019). These changes in ovarian reserves are not only associated with age; hence, a woman's age alone is not sufficient to evaluate ovarian reproductive potential. This enables the need for implementation of individual biological age-specific ovarian reserve determining tests. These tests can be highly reliable in determining ovarian reserves and reproductive potential of a woman at the early stages of infertility [6]. According to recent studies, AMH can be a good predictor of ovarian reserves and the success rates of in vitro fertilization.

On the other hand, some other studies have shown that pregnancy can also be achieved even at low levels of AMH. Evaluation of ovarian reserves by identifying AMH levels is a modern method, and the data obtained are contrasting, implementation of further studies and collecting more data in the field are seemed to be reasonable [7] . Hence, this study aimed to explore the relationship between different age groups and type of infertility with measures of ovarian reserve (FSH, AMH, and AFC) in infertile women.

Material and Method

This was a cross-sectional study which consisted of the study population of 100 infertile women. Patients were recruited from outpatient's private clinics during the period from June 2017- March 2019. These women were divided into two groups by age above and below 45-years old and by type of infertility into primary and secondary infertile groups. All patients underwent detailed fertility assessment including history, physical examination, laboratory and radiological (transvaginal ultrasound) investigations. AFC and serum FSH and AMH were measures and compared between groups. The study was approved by the Ethics Committee of University of Babylon.All patients consented to participate in the study. Statistical analysis was performed using SPSS v.24 (IBM, USA).

Results

The study population was distributed based on age as follows: group I comprises on female of age less than 45 years (83%) and group II comprises on female of age more than 45 years (17%). There were 48% (n=48) primary infertile patients and 52% (n=52) secondary infertile patients. Table 1 and 2 show the values for AMH, FSH and AFC, respectively, according to the study groups. All of the three indicators of ovarian reserves in both age groups differed significantly from each other (AMH: p=0.007; FSH: p=0.001; AFC: $\chi 2$= 15.45,p= 0.001). These indicators varied according to age. Results are expressed as mean± SD.

Table 1. AMH and FSH levels in women with age below and above 45 years

	Age (<45 years) (n=83)	**Age (>45 years) (n=17)**	**P value**
AMH (ng/ml)	1.94±2.65	0.17±0.34	0.007
FSH (IU/ml)	10.48± 6.06	26.3±23.84	0.001

AMH (ng/ml) level was higher in women < 45years (1.94±2.65, p value: 0.007) while the level of FSH (IU/ml) was higher in women >45 years (26.3±23.84, p value: 0.001).

Table 2. Antral follicles count in women with age below and above 45 years

	Age (<45 years) (n=83)	**Age (>45 years) (n=17)**	
Normal AFC	43(51.8%)	0(0%)	**X2=15.45,1 P=0.001**
Decreased AFC	40(48.2%)	17(100%)	

Antral follicle number was normal and decreased in women of >45years age 0% and 100% respectively, with p-value 0.001.

Table 3. Parity in women with age below and above 45 years

	Secondary infertility (n=52)	Primary infertility (n=48)	P value
AMH (ng/ml)	2.16±3.2	1.07±1.20	0.02
FSH (IU/ml)	13.12± 13.7	13.84± 11.19	0.77

AMH (ng/ml) has high parity effect on secondary infertility (2.16±3.2, p value: 0.02) while FSH (IU/ml) has high effect on primary infertility (13.84± 11.19, p value: 0.77)

Table 4. AMH and FSH levels in nulliparous and multiparous women

	Age (<45 years)	Age (>45 years)	
Secondary infertility	45 (54.2%)	7 (41.2%)	X2= 0.96,1 P= 0.23
Primary infertility	38 (45.8%)	10 (58.8%)	

Secondary and primary infertility in nulliparous and multiparous women associated with AMH and FSH level was higher in women of <45years as 54.2% and 45.8% respectively with p-value: 0.23

Table 5. Antral follicles count in nulliparous and multiparous women

	Secondary infertility (n=52)	Primary infertility (n=48)	
Normal AFC	27 (51.9%)	16 (33.3%)	X^2=3.51,1 P=0.07
Decreased AFC	25 (48.1%)	32 (66.7%)	

Normal AFC count was observed in secondary infertility in nulliparous and multiparous women (51.9%) while decreased AFC count was observed in primary infertility in nulliparous and multiparous women (66.7 %) with p-value: 0.07

Discussion

Results from the current study revealed that assessment tests of ovarian reserve reflected age-specific changes in both age groups. As an ovarian reserve marker, AMH is useful to estimate the reproductive lifespan of healthy young women and to predict the ovarian response to stimulation for in vitro fertilization (IVF), namely poor and hyperresponses [8]. Reduction in AMH and increased in FSH level is associated with age increase while there is no significant association among age and AFC level. No clear link between infertile women age and AMH, FSH values with infertility type and there is no association between primary and secondary infertilities and AFC values is evident from current study. AFC and AMH serum level decreases with age. MH levels vary in both age groups, AFC levels significantly higher in women below 45years, while FSH levels were higher in women above 45years. AMH value is more reliable in assessing age-specific changes when compared to other indicators. Relationships between age and ovarian reserve indicators show difference between indicator levels. The relation between age and FSH was moderate and revealed that AMH and AFC level decreases while FSH level increases with age. Above mentioned trends are also confirmed by other researchers [9,10,11] . Similar results were found by different studies [12]. We found a significant difference existed in the mean FSH of fertile and infertile women. There is a significant difference in AMH between fertile and infertile women. There was a negative correlation between FSH and AMH in both fertile and infertile [13], stated that the plasma AMH levels were significantly higher in women with the polycystic ovarian syndrome. The significant association was seen between FSH and AFC with AMH. However, no significant association was observed between AMH levels with age, BMI, ovarian volume and type of treatment protocols.

It is cleared from current and previous studies that observed AMH value was significant in all age groups, while AFC value was significant in women above 45years. Hence, we conclude that age-specific changes are better reflected by considering AMH values [14,15]. Study of AMH level is the most reliable source to measure age-specific changes. This correlation is also confirmed by other researchers [16,17] .

Conclusion

Among ovarian reserve evaluation tests that are used in modern practice, the serum levels of AMH should be considered more authentic. Measuring serum AMH levels along with AFC levels may enhance the evaluation of ovarian reserve for assessing fertility potential and examining infertility treatment. Study of AMH level is the most reliable source to measure age-specific changes.

Ethical Clearance- Taken from University of Babylon committee

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Conflict of Interest - None

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