ORIGINAL ARTICLE

OVARIAN RESERVE IN FERTILE WOMEN AS DETERMINED BY ULTRASONOGRAPHY

Ambreen Usmani , Ishrat S. Shokh

ABSTRACT

Objective: To determine ovarian reserve in naturally fertile adult women.

Study design: Cross-sectional, analytical study.

Methods: Healthy fertile females (n = 70) aged 20-39 years with proven natural fertility were recruited between March and December 2006. Of these, 40 met the inclusion criteria. Total ovarian volume was calculated using the transabdominal and transvaginal ultrasound approach and an antral follicle count was performed transvaginally. The height and weight of each individual was taken to calculate the BMI, and the correlation made between ovarian volume (determined transvaginally) and the BMI.

Results: The women were divided into 2 groups of 20 each viz. between 20 – 29 years, and between 30 – 39 years. Total ovarian volume determined by transabdominal scan was 13 ±3.46 ml and 7.92 ±2.0 ml respectively in the two groups, and by transvaginal route was 15.13 ±4.37 ml and 9.97 ±2.99 ml respectively (p-value of both was 0.001).The AFC was 9.40 ± 2.37and 5.3 ± 2.05 in the two groups (p-value 0.001). The BMI of the 2 groups was 23.4 ±3.97 and 24.4 ± 3.8 (p-value 0.421).The correlation between ovarian volume and BMI was -0.40 (p-value 0.05).

Conclusion: Ovarian volume and antral follicle count were reduced significantly in the older age group; there was no difference between the BMI of the two age groups. When BMI of all women was plotted against ovarian volume, a decrease in the ovarian volume was observed with an increase in BMI.

Key words: Ovarian volume, ovarian reserve, antral follicle count, ultrasound.

INTRODUCTION

Ovarian reserve is an estimate of the primordial follicle pool in the ovaries. It is a relatively new concept and is used as a reflection of a woman's reproductive age and her remaining reproductive life span[1]. It can be determined by several methods: directly by an ovarian biopsy[2], by sonographic visualization and measurement of the ovaries and calculation of ovarian volume, antral follicle count, mean follicular volume, or indirectly by biochemical assessment of follicle stimulating hormone, estrogen, anti-mullerian hormone and inhibin-B[3-5].

The human ovary contains a fixed pool of primordial follicles, maximal at five months of intrauterine life, and numbering around 701,000 at the time of birth. This pool reduces to 250,000-300,000 at the time of menarche,[6] and then declines in a bi-exponential fashion with increasing age[7]. At 37-38 years of age, it contains about 25,000 follicles. At this number, the follicular depletion accelerates, and menopause has been estimated to be about 12-14 years away. At a mean age of 50-51 years, only a few hundred or a thousand follicles remain[8]. This age may vary in different populations and countries, and according to a study conducted in Lahore, it was found to be 49 ± 3.6 years in Pakistani women[9].

The follicles in various stages of growth constitute the bulk of ovarian volume. A decline in the number of observable follicles due to atresia (death by apoptosis) occurs concomitant with advancing age[10]. Thus ovarian volume decreases with increasing age. This was demonstrated by Pavlic et al[11] in a population of 13,963 conducted on women between 25 and 91 years of age by annual transvaginal sonography . A statistically significant decrease in ovarian volume was shown with each decade of life from age 30 to 70 years. Mean ovarian volume was 6.6 ml in women <30 years old, 6.1ml in women 30-

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39 years, 4.8 ml in women aged 40 -49 years, 2.6 ml in women 50-59 years old and 2.1ml in women aged 60-69 years. Mean ovarian volume was 4.9 ml in pre-menopausal women and 2.2 ml in post –menopausal women.

The reduction in number of primordial follicles is accompanied by a reduction in fertility[12]. For any given age, the size of the follicle pool can be estimated by a mathematical model of decline[7]. Theoretically, this could help in estimating the reproductive capacity of a woman at a given age; this in turn could assist in predicting a woman's chances of conception during a spontaneous cycle, and a possible outcome in assisted conception. It would also be of value in counseling those considering postponement of child-bearing for any reason[8].

The follicle growth pattern in the menstrual cycles in women of the reproductive age women has been demonstrated by the ultrasonographic technique[10-13]. At each cycle, several follicles are recruited, and grow at a rate of 2 - 6 mm daily in women in mid reproductive life (22-34 years); ovulation occurs at a mean follicular diameter of 16-27 mm[14].

The antral follicular count i.e. the total number of follicles between 2 – 10 mm in diameter the two ovaries is a parameter which has been used as a reflection of reproductive age. Ruess[15] reported a significant reduction in number with age in a group of women 22 - 42 years of age. These differences in follicle counts were independent of the stage of menstrual cycle. Scheffer[16] performed a study on 162 women in the follicular phase and reported a mean yearly decline of antral follicle count of about 5%, which increased to almost 12% after the age of 37 years. Several studies have determined the relation between ovarian volume and BMI and has shown a strong negative relation between the two, thus there is a decrease in ovarian volume with an increase in BMI[17,18]. This may have clinical significance, as obesity has been shown to affect the fertility of a woman.

This study was conducted on healthy fertile women between the ages of 20 – 39 years. Ultrasound was used to visualize the ovaries, calculate their total volume, and to perform an antral follicle count. Its objective was to establish normal values in healthy fertile women, and observe the difference, if any, in two subsets of women viz. between 20 – 29 years and 30 – 39 years.

SUBJECTS AND METHODS

The women were recruited between March 2006 to December 2006 from the outpatient departments of Ziauddin Memorial Hospital, Nazimabad, and Rahat Hospital, Karsaz, Karachi, until the desired number was obtained. A few women were volunteers from Ziauddin University Hospital.

The inclusion criteria were age between 20-39 years, regular menstrual cycles varying from 21-35 days, proven natural fertility with at least one pregnancy carried to term, each pregnancy having arisen spontaneously within 1 year after the start of unprotected intercourse and hormonal contraception, if taken, stopped 2 months before entering study protocol .

Exclusion criteria were evidence of endocrinological disease, secondary sub-fertility, history of ovarian surgery, and a history of hypertension, diabetes mellitus and smoking. In addition, women with ovaries of abnormal morphology on ultrasound examination were excluded.

The subjects were scanned on a complimentary basis at the Ultrasound Clinic, of Karachi. A written informed consent was obtained from all the subjects. Sonography of the ovaries was carried out on a day between the 2nd to 7th day of the menstrual cycle. All sonographic measurements were performed using Toshiba EcoCee and PowerVision 6000.The probes were multi-frequency; the transabdominal probe with a mid frequency of 3.75 MHz and the transvaginal probe with a mid frequency of 7.5 MHz.

The examination was performed transabdominally on an adequately full urinary bladder and transvaginally after emptying the bladder. Each ovary was scanned in 2 planes in which the longest dimension of the ovary was visible was frozen, D1 (depth) and D2 (anteroposterior) measurements were taken. The probe was then rotated through 900 and D3 (height) was measured. The volume of each ovary was calculated from the three dimensions by applying the equation for the volume of an ellipsoid (viz: D1 X D2 X D3 X 0.523 cm^3)[8]. The total ovarian volume was the sum of volume of the two ovaries. On transvaginal scan the volume was assessed, and the antral follicles (measuring between 2-10 mm in diameter) in each ovary were counted. The sum of antral follicles in the two ovaries was taken as the antral follicle count.

The height and weight of all subjects was taken and the body mass index (BMI) calculated from the kg/m^2 formula[19].

The data feeding and analysis was done on computer package SPSS 11.0 for Windows. The results were given in the text as mean, standard deviation of quantitative variables (age, weight, height, BMI, ovarian volume, and antral follicle count). Mean and standard deviation of quantitative variables between groups (20-29 and 30-39 years) were compared by ANOVA test. The correlation coefficient of ovarian volume, antral follicle count vs. age and BMI was determined. In all statistical analysis, p-value <0.05 was considered significant.

This study was approved by the ethical committee of Ziauddin University.

RESULTS

A total of 70 women were recruited. Of these, 30 subjects were excluded: 7 subjects did not come for the scan; in 3, one of the ovaries could not be visualized on ultrasound examination, and 20 had abnormal ovarian morphology (polycystic ovaries in 18 and ovarian enlargement due to the presence of cysts in 2).
Table 1 shows the results of ovarian volume (measured transabdominally and transvaginally), the antral follicular volume (measured transvaginally) and the calculated BMI in the two subsets of women. Significant difference was seen in the total ovarian volume and the AFC in the 2 subsets of women , the volume and count being lower in the older women. There was no difference in the BMI of the two subsets.

Table 1: Analysis of ovarian volume on transvaginal and transabdominal ultrasound compared to antral follicle count and body mass index.

	FERTILE GROUP		
	Age 20-29	Age 30-39	P-Value
	Mean ± S.D (n=20)	Mean ± S.D (n=20)	
OV(TAS)	13.00 ± 3.46	7.92 ± 2.00	0.001*
OV(TVS)	15.13 ± 4.37	9.97 ± 2.99	0.001*
AFC	9.40 ± 2.37	5.30 ± 2.05	0.001*
BMI	23.4 ± 3.97	24.4 ± 3.8	0.421

* p-value < 0.05 are significant
OV –ovarian volume
TAS – transabdominal scan TVS - transvaginal scan.
AFC – antral follicle count.
BMI- body mass index

The results of correlation between BMI and ovarian volume showed a negative value (-0.399) as shown in Fig. 1.

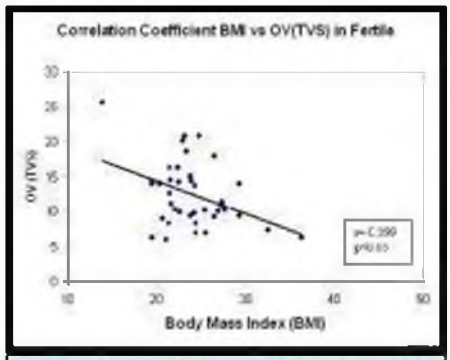

Figure 1: Correlation between ovarian volume (ov) and body mass index.

DISCUSSION

We estimated ovarian reserve by calculating ovarian volume and carrying out an antral follicle count (AFC) by an ultrasound examination in healthy fertile women not using hormonal contraception.

We compared the results in two subsets of women: i) between ages 20-29 years, and ii) between ages 30-39 years, and showed a significant reduction in total ovarian volume and AFC in the second group. This negative correlation of ovarian volume[11] and of AFC with age is in keeping with the concept of reproductive ageing , and has been shown in several studies conducted during the past few years[1,6].

Scheffer et al[1] compared the mean values and ranges of several sonographic parameters for 3 age groups: young (25 – 34 years), middle-aged (35- 40 years) and the old (41 – 46 years). The total ovarian volume in the third older group differed significantly from that in the two younger groups, measuring 11.8, 11.4 and 8.3 ml respectively. The number of antral follicles differed significantly in all three groups (the count being 15, 9 and 4 respectively). The total follicular volume showed a decrease with increasing age (0.71, 0.58 and 0.39 ml), the decrease in volume being less steep than the drop in follicular count. They concluded that the antral follicle count was valuable in assessing ovarian reserve, and its use as a single test to predict response to controlled ovarian stimulation and the probability of pregnancy in assisted reproduction seemed rational.

We rehashed the data to make the age groups comparable to those of Scheffer et al. Ovarian volume calculated for groups 25-34 years and 35-39 years was 10.49±2.72 and 7.47±3.8 ml respectively; these values were a little less than those of Scheffer et al's, but the difference was not statistically significant.

A comparison of ultrasound with other tests for detecting ovarian reserve shows ultrasound to be of great value as it is non-invasive, easily performed and reproducible, readily available, and inexpensive[20,21]. Biochemical tests such as FSH, estrogen, anti-mullerian hormone and inhibin –B,[22] are relatively expensive and not all are freely available in the laboratories of our country. Ovarian biopsy as a test of ovarian reserve is no longer practised, as it is invasive, carries the risk of adhesions, and the distribution of follicles in the ovarian tissue could be irregular and not representative of the total reserve [23-24].

The limitations of this study include the exclusion of age group above 40 years, and the failure to record the waist hip ratio (WHR); thus the relation between ovarian reserve and WHR could not be estimated. Although BMI and ovarian volume showed a negative value of 0.40, it is possible that WHR and ovarian reserve may have demonstrated a better correlation.

CONCLUSION

The ovarian reserve in the menstrual phase determined by sonographic measurements of ovarian volume and antral follicle count was significantly decreased with age. The ovarian volume also showed a decrease with an increase in the BMI, indicating the possible decrease in fertility with an increase in the woman's weight.

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