ORIGINAL ARTICLE

Effect of age on uterine and ovarian morphology with Polycystic Ovaries

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Abstract

Objective: To measure the outcome of age on ovarian and uterine morphology in primary infertile women with polycystic ovaries.

Methods: The observational cross-sectional study was conducted from January 2009 to March 2010, and the subjects were recruited from Ziauddin Hospital, Nazimabad, Karachi. The primary infertile subjects with polycystic ovaries were subdivided into two age groups:20-30 years (group I), and 31-40 years (group II). Both groups had equal number of subjects. The ovarian volume, follicles count and size, uterine area and endometrial thickness were determined by transabdominal and transvaginal scans. Shapiro-Wilk's test and Mann-Whitney test were applied, with $p<0.05$ being significant.

Results: There were 200 female subjects in the study who were divided into two equal age-based groups of 100(50%) each. The mean age of group I was 26.46±3.55 years and that of group II was 36.73±3.19. An increase in uterine area from 89.99±5.83 to 119.0±23.33 ($p<0.03$) and endometrial thickness from 0.48±0.11 to0.59±0.13 ($p=0.01$) was observed in group II. A decline in follicular count and size was also noticed in group II ($p<0.02$, $p=0.001$).Ovarian volume declined from 15.36±2.56 to 10.57±1.29 ($p=0.001$)in group II. A positive correlation of age with uterine area ($r=0.202$; $p<0.003$) and endometrial thickness ($r=0153$; $p<0.025$) was noticed.

Conclusion: Ovarian morphology decreased in the elder infertile group of women with polycystic ovaries, but the uterine morphology variables showed an increase in area with thickening of the endometrium in the elder group.

Keywords: Polycystic ovaries, Infertile, Ovarian volume, Follicle count, Follicle size, Uterine area, and Endometrial thickness. (JPMA 64: 1119; 2014)

Introduction

Twelve or more small follicles less than 1cm in diameter should be seen in an ovary on ultrasound examination. The follicles may be oriented in the periphery, giving the appearance of a 'string of pearls'. The numerous follicles contribute to the increased size of the ovaries, that is, 1.5 to 3 times larger than normal, this definition is in accordance with the Rotterdam criteria.[1] Androgen Excess and Polycystic Ovaries Syndrome Society[2] proposed a tightening of the diagnostic criteria to the definition of PCOs. This included excess androgen activity, oligoovulation/anovulation and/or polycystic ovaries. Other entities that would cause excess androgen activity are excluded as due to enhancement in the use of ultrasonography, more cases of PCOs are being aptly reported. This has also guided diagnosis of PCO in younger age group of girls.[1]

Infertility is "a disease of the reproductive system defined by the failure to achieve a clinical pregnancy after 12 months or more of regular unprotected sexual intercourse."[2,3] Fertile women have an ovarian reserve which is available in the ovaries in the appearance of primordial follicles. Due to hormonal imbalance in PCO patients, the luteinising hormone (LH) causes the follicle reserve to increase in size and becomes cystic, the result of which is increase in the ovarian volume (OV) which becomes $\geq$10ml.[4-6] In this situation, insulin resistance (IR) also develops and the ovaries create oocyte with anomalous morphology. Due to the unclear value of the oocyte, there is a deficiency of fertilisation capability of the ovum causing infertility.[7] The precise cause of PCO is still under investigation, but researchers have shown genetic association to this condition. Hβ and luteinising hormone receptor (LHR) gene mutation have been reported to be connected to anovulatory PCOs. Research has shown results that recommend linkage of PCO susceptibility and phenotype with LHG1052A mutation.[8]

Infertility due to PCO affects around 5-10% of women who are in their reproductive period. Most of these cases suffer from menstrual irregularities with an increase in LH. Such women have recurring failure during assisted reproductive techniques (ART) and show miscarriages after this method.[9] Several studies have also associated PCO with cardiovascular diseases. Strong connection of PCO with IR and obesity has also been reported since long. Studies revealed that 20-30% of female population suffers from this disease and more cases are being

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diagnosed in adolescence.[10] PCO results in weight increase and abnormal hair growth in areas like the face, chest and abdomen. The Rotterdam consensus criteria show that prevalence of PCOs decline with increasing age group. Although the volume of the ovaries and the number of polycystic follicles diminish with advancement in age, the infertility condition increases due to exhaustion of primordial follicle pool with growing age.[11]

The current study was planned to measure the outcome of age on ovarian and uterine morphology in infertile women with PCOs.

Patients and Methods

The observational cross-sectional study was conducted from January 2009 to March 2010, and the subjects were recruited from Ziauddin Hospital, Nazimabad, Karachi. The subjects were from middle and low socioeconomic status. The sample size was calculated by Number Cruncher Statistical System (NCSS) software. Non-probability simple random sampling technique was adopted. After approval by the institutional ethics committee, the study enrolled women with PCOs. Those included were diagnosed clinically and by ultrasound.[12] Informed consent was obtained from all participants.

The inclusion criteria for the patients comprised primary infertility, females of ages between 20-40 years, existence of 12 or more follicles less than 1cm in one or both ovaries, regular intercourse, and no use of contraceptives.[4]

The exclusion criteria was ART, history of abortion, any pathology of pelvic reproductive organs other than PCOs, report showing that the husband was infertile, hypertension, diabetes, cancer etc. or any other chronic illness.

Ultrasound was performed on any day between the 2nd and the 7th day of the menstrual cycle using Toshiba ultrasound machine. The instruments used were transabdominalscan (TAS) and transvaginalscan (TVS) which were respectively of 3.75MHz and 7.5MHz frequency. To eliminate abnormalities other than PCOs, e.g. absence of ovaries (one or both), adhesions, tubal ligation, endrometriosis, fibroids, cancers etc., TAS was conducted on a full urinary bladder. TVS was done on an empty urinary bladder only if the patient was diagnosed with PCO during TAS.[5,6]

Measurements taken and noted included those of OV, follicle count (FC) and follicle size (FS) (2-9mm), uterine area (UA), and endometrial thickness (ET). Scanning of the two ovaries was done in the longitudinal (D1), anteroposterior (D2) and transverse diameter (D3). The total volume was analysed by applying the ellipsoid equation which is D1XD2XD3X0.523cm3 and the sum of the two ovaries was considered.[6]

By applying the formula, uterine length X anteroposterior diameter in cm^2, the UA was calculated as reported in other studies. The uterine length from the top of the fundus to the cervix and the anteroposterior diameter was measured by TAS.[5,13] The endometrial thickness was measured in mm by TVS.[5,13]

The measurements of the readings were taken in double of all variables and their average was calculated which was considered the final reading. This was done for validation of the result. The women selected were divided into two equal groups: those in the 20-30 age bracket were designated as group I, and those in the 31-40 age range were called group II. In order to meet this sample size criterion, we kept on recruiting women till the desired number was achieved.

Data were entered into MS Excel 2007 and analysed using SPSS 12. Shapiro-Wilk's test detected that data was non-parametric, so Mann-Whitney test was applied, and $p<0.05$ was considered statistically significant.

Results

A total of 254 women were initially approached. On scanning, 14(5.5%) had normal morphology of the ovaries; 10(4%) had adhesion bands and endometriosis; 11(4.3%) were not suffering from primary infertility; 8(3%) had undergone some assisted procedure, 4(1.6%) were suffering from other associated problems, and 7(2.7%) did not give their consent. All these 54(21%) women were excluded and the final study sample stood at 200(79%), which was divided into two age-based groups of

Table: Association of age with uterine and ovarian morphology in primary infertile patients with PCO.

Variable	Group I	Group II	P-value
Number	100	100	
Age in years	26.46 ±3.55	36.73±3.19	NS
Uterine area	89.99 ± 5.83	119.0 ± 23.33	0.03
Endometrial thickness	0.48 ± 0.11	0.59 ± 0.13	0.01
Follicle Count	14. 41 ±2.18	12.75 ± 2.80	0.02
Follicle Size	8.23 ± 0.41	3.29 ± 0.25	0.001
Ovarian Volume by TAS	15.36 ±2.56	10.57±1.29	0.001
Ovarian Volume by TVS	15.74 ±2.23	10.37± 1.08	0.001

PCO:
TAS: Trans abdominal scan
TVS: Transvaginal scan
Values expressed are mean±SD; compared by Mann Whitney test $p<0.05$ is considered significantat 95% confidence interval.Uterine area in cm^2, endometrial thickness in mm. Follicle count in numbers, follicle size in mm, ovarian volume in cm^3.

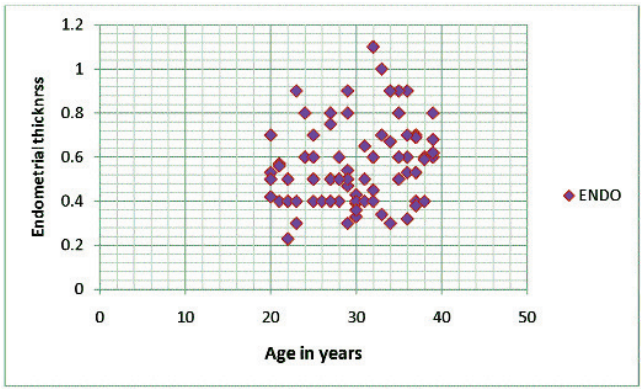

Figure-1: Association of Endometrial thickness with age.

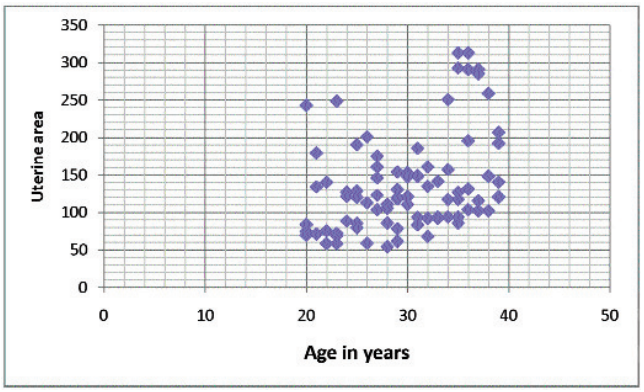

Figure-2: Association of age with uterine are measured in cm^2.

100(50%) each.

The mean age in group I was 26.46±3.55 years and 36.73±3.19 years in group II (Table) An increase in UA from 89.99±5.83 to 119.0±23.33 ($p<0.03$) and ET from 0.48±0.11 to 0.59±0.13 ($p=0.01$) was observed in group II. A decline in FC and FS was also noticed in group II ($p=0.02$, $p<0.001$). OV declined from 15.36±2.56 to 10.57±1.29 ($p<0.001$) in group II, and from 15.74 ±2.23 to 10.37± 1.08 ($p<0.001$) when measured by TAS and TVS respectively.

A positive correlation of age with endometrial thickness ($r=0153$; $p<0.025$) (Figure-1) and uterine area ($r=0.202$; $p<0.003$) (Figure-2) was noticed.

Discussion

The study compared young and relatively older primary infertile women with PCOs. An enormous increase in the incidence of PCO has been reported which can be credited to the technological development of ultrasonography. With rising age, the ovarian reserve (collection of primordial follicles) declines and ultimately results in menopause.[2,3,12] This depletion of primordial follicles at the age of 45±5 years results in the female being unable to conceive. PCOs and other pelvic disorders can, however, develop during regular ovarian functioning. Association of PCOs with endocrinopathies and certain genetic mutations is now evident and has been proved often.[8,13]

The morphology of pelvic reproductive organs of ages between 20-30 years (group I) and 31-40 years (group II) has been shown by this study. Women with PCOs and primary fertility went through ultrasound scanning and it was reported that OV, FC and FS was significantly raised in the younger primary infertile group. Numerous studies have revealed PCOs with an ovarian volume of $\geq$10ml. However, as shown by our study, the large ovarian size is more common in the younger age group and as these women progressively age, the volume decreases, but the ovaries still remain in the cystic condition.[14] The exhaustion of the primordial pool which is available at the time of birth is a physiological course which is present from menarche till menopause. The development continues in PCO, as an effect the FC decreases yet the uterine size continues to increase.[15]

Studies based on the Rotterdam criteria showed the prevalence of PCO in different age groups as 83-84% between ages 18-22 years, 66-84% in 23-27 years, 42-79% in 28-32 years, 19-33% in 33-37 years and 0-33% in 38-40 years. Hence, the prevalence of PCOs declines with enhancing age. Though patients with PCO show ovarian size and follicle number reduction, their fertility does not improve. The reason for this is the aging of the ovaries.[16]

The present study reports that UA and ET were considerably increased in the elder age group. It is known that due to the morphological alteration of the related pelvic reproductive organs, the uterine size may be affected.[17-19] Enlarged uterus could be due to the presence of PCOs. Due to the different phases of the menstrual cycle the endometrium of the uterus shows variations in thickness. These variations in thickness range from 3mm, which is usually seen after menses, to 15mm during the luteal phase. However, this thickness normally reduces after menopause.[19] It has been reported by this study that ET was more in the elder group which is in contradiction with other studies. Other studies showed no such correlations.[13,19,20] Abnormal endometrial thickness has been associated with obesity, PCOs and diabetes mellitus.[20,21] A study reported that 31.4% of adolescent girls suffering from PCOs had endometrial thickness of>7mm.[13] Therefore, there is a strong link of PCO with ET in the younger age group.[13] The incidence and danger of endometrial cancer development is more in such individuals. Thus, this connection must be

acknowledged as early as possible to avoid cancerous changes, for these women have a greater chance of developing endometrial cancer, particularly if accompanied with irregular menstrual cycles.[20] Physiological changes that occur in such cases of PCOs are because when this condition occurs, the process of ovulation is affected and stopped,[22,23] which in turn leads to the endometrial lining not being shed, since it is exposed greatly to oestrogen, resulting in the thickening of the endometrium and, hence, bigger threat of endometrial cancer.[23,24]

Endometrial thickness of ≤6mm will rarely be able to conceive naturally and it is important to note that hormonal replacement therapy (HRT) is one of the most common factors in infertile women which is known to be connected with increased UA and ET.[25]

A number of studies state that PCOs are now being diagnosed at an early age[1-3] which is significant since early diagnosis leads to timely treatment which can avoid infertility due to this state and other associated problems. There is limited research of the association of uterine morphology with PCOs and none in this region. We made an effort to fill this gap. It is important to understand this relationship to avoid misdiagnosis of endometrial cancer, especially in the older age group.

In terms of limitations, the study did not opt for external validity of the sampled subjects.

Conclusion

The study measured the ovarian and uterine morphology in women with PCOs by using ultrasonography. It was found that OV, FC and FS levels were raised in the younger primary infertile women. However, UA and ET were found to be significantly increased in the older primary infertile women with PCOs.

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