

Effect of Polycystic Ovaries on the Morphology of Uterus and Ovaries

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ABSTRACT

Background: The presence of around 12 or more follicles in one or both ovaries with diameter ranging from 2-9mm is known as polycystic ovaries (PCO). This condition is associated with hyperandrogenemia and is one of the most common causes of infertility. Due to increase in use of ultrasonography as a diagnostic tool, more cases of PCOs are being timely reported. This has also lead to diagnosis of PCO in younger age group.

Objective: To measure the effect of age on ovarian and uterine morphology in infertile women with polycystic ovaries (PCO).

Methods: The cross sectional study was conducted in Karsaz Hospital, Karachi from January 2010 to March 2011. One hundred infertile women with PCOs were subdivided into age groups (years) 20-30 (group I) and 31- 40 (group II). The ovarian volume (OV), follicles count (FC) and size (FS), uterine area (UA) and endometrial thickness (Endo) were determined by ultrasonography. Unpaired t-test was applied to analyze the result.

Results: The ovarian morphology showed a significant decrease in group II; the OV transabdominally was 14.26 ± 2.42 vs 10.56 ± 1.0 (0.00) and transvaginally 14.93 ± 2.55 vs 11.75 ± 1.06 (0.00). The FC was 14.00 ± 1.60 vs 12.3 ± 0.78 (0.023) and FS was 8.23 ± 8.9 vs 3.29 ± 6.9 (0.00). The uterine morphology however showed a significant increase in group II. The UA was 87.79 ± 5.83 vs 118.71 ± 22.83 (0.00) and endo was 0.46 ± 0.10 vs 0.57 ± 0.12 (0.00).

Conclusion: Ovarian morphology variables include OV, FC and FS decrease in the older infertile group of women with PCOs but the uterine morphology variables showed an increase in area with thickening of endometrium in the older group. The association of endometrium and PCOs has not been reported in this part of the world and the study is an attempt to fill this gap and prevent misdiagnosis of endometrial cancer.

KEY WORDS: *Polycystic Ovaries, Infertile, Ovarian Volume, Follicle Count, Follicle Size, Uterine Area, Endometrial Thickness.*

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INTRODUCTION

The presence of around 12 or more follicles in one or both ovaries with diameter ranging from 2-9mm is known as polycystic ovaries (PCO). This condition is associated with hyperandrogenemia and is one of the most common causes of infertility. Due to increase in use of ultrasonography as a diagnostic tool, more cases of PCOs are being timely reported. This has also lead to diagnosis of PCO in younger age group of girls.¹¹

Infertility is defined as the inability to conceive a child for 2 or more years. In a normal fertile woman the ovarian reserve which is present in the ovaries in the form of primordial follicles decrease with increasing age, indicating that the average reproductive age of a woman ends by 45±5 years.^{2,3} However, in case of PCOs due to hormonal imbalance of the luteinizing hormone the follicle reserve increases in size and becomes cystic. This in turn causes the ovarian volume to increase and become greater than 10ml.^{4,5,6} In this condition insulin resistance also develops and the ovaries produce oocyte with abnormal morphology. Due to the distorted quality of the oocyte there is reduction in the fertilization capability of the ovum that results in infertility.⁷ The exact cause of PCO is still unknown but investigators have identified potential genetic associations. It has been reported that LHβ and LHR gene mutation are linked to anovulatory PCOs. Research results by Lui Nana et al suggest 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 age. Most of these causes suffer from menstrual irregularities with an increase in luteinizing hormone. Such women have repeated failure during assisted reproductive techniques (ART) and report miscarriages after this procedure.⁹ Several studies have also associated PCO with cardiovascular diseases. Strong association of PCO with insulin resistance and obesity has also been reported. Balen et al have shown in their study that 20-30% of female population suffers

from this disease with more cases being diagnosed in adolescence.¹⁰ PCO results in weight gain and abnormal hair growth in areas like the face, chest and abdomen. The prevalence of PCOs by the Rotterdam consensus criteria shows a decrease of the condition with increasing age group. Although the volume of the ovaries and the number of polycystic follicles decrease with increase in age the infertility status enhances. The reason behind this is that there is depletion of primordial follicle pool with increasing age.¹¹

The objective of the study is to measure the effect of age on ovarian and uterine morphology in infertile women with poly cystic ovaries.

METHODOLOGY

The patients were recruited from Karsaz Hospital Karachi from January 2010 to March 2011. This was an observational cross sectional study in which women diagnosed with PCOs were inducted for the study. The included women were diagnosed clinically and by ultrasound prior to inclusion. The subjects were informed about the study and permission was sought via a written informed consent.

The patients that were included fell into the following criteria, a) Primary infertility b) Married women of ages between 20-40 years c) Presence of 12 or more cystic follicles in one or both ovaries d) The woman should have had no child in the last two years after regular intercourse e) Not using contraceptives for at least 2 months prior to the study

The exclusion criteria was a) Tried to conceive via ART b) Abortion c) Any pathology of pelvic reproductive organs other than PCOs d) Husband suffering from infertility e) Any chronic illness e.g. hypertension, diabetes, cancer etc

During 2nd to 7th day of the menstrual cycle ultrasound was performed using Toshiba ultrasound machine. Transabdominal and transvaginal probes were used; these were of 3.75 MHz and 7.5 MHz frequency respectively.

To exclude abnormalities other than PCOs e.g. cancers, adhesion, endometriosis, tubal ligation, absence of ovaries (one or both), fibroids etc the transabdominal scan (TAS) was performed on a full urinary bladder. If the patient was diagnosed with PCO only during TAS then transvaginal scan (TVS) was done on an empty urinary bladder.

By scanning, the following were measured and noted a) ovarian volume b) follicle count and size (2-9mm) c) uterine area d) endometrial thickness. The two ovaries were scanned in the longitudinal (D1), anteroposterior (D2) and transverse diameter (D3); the total volume was calculated by applying the ellipsoid equation which is $D1 \times D2 \times D3 \times 0.523 \text{ cm}^3$ and the sum of the two ovaries was noted.

The uterine area was calculated by the formula uterine length X anteroposterior diameter in cm^2 . This was performed by measuring the uterine length from the top of the fundus to the cervix and the anteroposterior diameter by TVS. The endometrial thickness was measured in mm by TVS.

To validate the measurements the readings were taken twice for all variables and their average was calculated which was considered as the final reading. A total of 153 women clinically diagnosed with signs and symptoms of PCO visited the ultrasound clinic to confirm the diagnosis. Out of the total women 12 had normal ovaries on ultrasound, 13 were suffering from endometriosis, 8 were fertile, 7 had undergone ART, 5 had other associated problems and 5 refused to be a part of the study. Thus 53 women were excluded. In this way 100 women of which 50 belonged to the age group of 20-30 years and 50 of 31-40 years. The recruiting of the subjects was done till our desired number was attained. Females were divided into two study groups; age range 20-30 (Group I) and females with age range 31-40 were included in Group II.

SPSS version 12 for windows was used to enter and analyze the measurements; the application used was unpaired t-test. The results were given as mean \pm standard deviation (SD). P-value of 0.05 or less was considered statistically significant.

Figure 1 shows comparison of ovarian morphology with PCOs, assessed by ovarian

volume (OV), follicle count and follicle size. Table 1 shows effect of age on uterine area and endometrial thickness

RESULTS

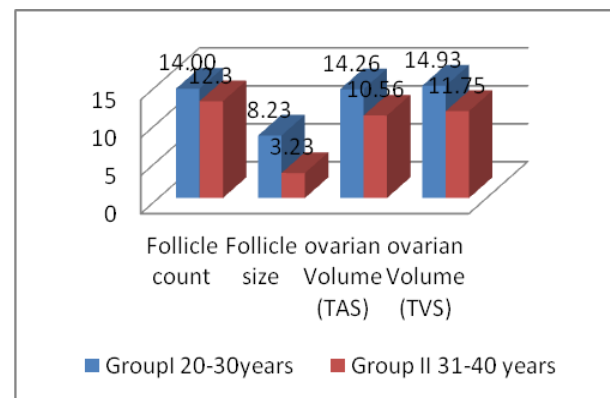
The mean age of females in group I (50) was 26.14 ± 3.65 and in group II (50) was 36.70 ± 3.17 (Mean \pm SD). Trans abdominal and Trans vaginal scan declared a significant decrease in OV with the advancement of age ($p=0.00$, $p=0.00$ at 95% CI: Table 1). There was a reduction in follicle count as well as follicle size in group II; $p=0.00$ and $p=0.00$ at 95% CI respectively. The effect of age on uterine area between group I and group II was 87.79 ± 5.83 vs 118.7 ± 22.83 . The endometrial lining of PCO (Table 1) showed significant rise in group II: 0.46 ± 0.10 vs 0.57 ± 0.12 ($p=0.00$ in both variables at 95CI).

Table 1: Effect of age on uterine morphology in infertile patients with PCO

Variable	Group I: (n=50) Age: 20-30	Group II: (n=50) Age: 31-40	P-value
UA	87.79 ± 5.83	118.7 ± 22.83	0.00
Endo	0.46 ± 0.10	0.57 ± 0.12	0.00

UA=uterine area in cm^2 , ENDO = endometrial thickness in mm. Values expressed are mean \pm SD; p-value ≤ 0.05 are considered to be significant

Figure 1: Effect of age on ovarian morphology in infertile females with PCO



Effect of age on ovarian morphology in infertile females with PCO

DISCUSSION

The study shows a comparison between younger and older infertile women suffering from PCOs. An enormous increase in the incidence of PCO has been observed which can be attributed to the technological enhancement of the study through ultrasonography. With increasing age the ovarian reserve which is the pool of primordial follicles decrease and eventually results in menopause.^{12, 2, 3} Due to the depletion of the primordial follicles at the age of 45± 5 years the female is unable to conceive. However during normal ovarian functioning certain diseases like PCOs can develop. This condition can be associated with endocrinopathies and now evidence is available that it is also due to genetic mutations.^{13, 8}

In the present study the morphology of pelvic reproductive organs of ages between 20-30 years (I) and 31-40 years (II) has been done. Women with PCOs and primary fertility underwent ultrasound and it was observed that ovarian volume, follicle count and follicular size was significantly raised in the younger infertile group. Several studies have shown PCOs with an ovarian volume greater 10ml but as shown by our report that the large ovarian size is more in the younger age group of women and as these women start to age, the volume decreases but the ovaries still remains in the cystic state.¹⁴ The depletion of the primordial pool, present at the time of birth is a physiological process which continues from menarche till menopause (Rehana 2012). The process continues in PCO, as a result although follicle count decreases yet uterine size persists to be increased.¹⁵

The prevalence of PCO as shown by the Rotterdam criteria in different age groups is 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 age group. Therefore the prevalence of PCOs reduces with increase in age but studies have shown that patients with PCO show ovarian size and follicle number reduction, their fertility does not improve. This is attributed to aging of the ovaries.¹⁶

In our study the uterine area and endometrial thickness is significantly increased in the older age group of infertile women. Due to the morphological distortion of the associated pelvic reproductive organs the uterine size may be

affected.^{17, 18, 19} One of the causes of enlarged uterus could be PCOS. The endometrium of the uterus shows variations in thickness due to the different phases of the menstrual cycle. The ranges in thickness are from 3mm which is usually seen after menses to 15 mm during the luteal phase but this range reduces after menopause.¹⁹ This study shows that the endometrial thickness is more in the older group of infertile women which is in contradiction with some studies showing that in normal women with advancing age the endometrium becomes thin. However other studies show no such correlations. It has been proven that abnormal endometrial thickness has been associated with obesity, PCOS and diabetes mellitus.^{20, 21} A study by Shah B et al reported that in 31.4% of adolescent girls suffering from PCOs had endometrial thickness of > 7 mm. Therefore there is a strong association of PCO with thickness in the endometrium.²² In such patients the incidence of endometrial cancer development is more. Thus this association must be recognized as early as possible to avoid cancerous changes, since women with PCOs have a higher chance of developing endometrial cancer especially if associated with irregular menstrual cycles. The underlying physiological changes in case of PCOs is that due to this condition when ovulation does not take place the endometrial lining is not shed which in turn is exposed excessively to estrogen resulting in endometrial thickening and hence more risk of developing endometrial cancer.^{23, 24}

Other factors are known to be associated with uterine area and endometrial thickness of which the most common factor in infertile women is hormonal replacement therapy. It has also been reported that the endometrial thickness of ≤6mm will rarely be able to conceive naturally.²⁵ Several observations state that PCOs are being diagnosed at an early age which is critical since early diagnosis leads to prompt treatment which can prevent infertility due to this condition and other associated problems.⁷ Histopathological examination is still not a routine practice in many parts of Pakistan. Carcinoid tumors of appendix, regardless of rarity, need to be investigated properly to ensure their treatment and management is appropriately approached. It is recommended that routine histopathological examination should be made a necessity post appendectomies.

CONCLUSION

PCOs are a major cause of infertility; this study measures the ovarian and uterine morphology in infertile women with this disease by using ultrasonography. It was reported that the ovarian volume, follicle count and follicle size are found to be raised in the younger infertile women however the uterine area and endometrial thickness are found to be significantly increased in the older infertile women with PCOs.

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