COMPARISON OF FEMALE REPRODUCTIVE ORGANS MORPHOLOGY BETWEEN FERTILE AND INFERTILE WOMEN WITH POLYCYSTIC OVARIES

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ABSTRACT

Objective: *To compare the morphology of pelvic reproductive organs between fertile and infertile women with polycystic ovaries.*

Methodology: *This cross sectional comparative study was performed at Rahat Hospital, Karsaz Karachi from January 2008 to December 2008. In which 100 women diagnosed with polycystic ovaries identified by ultrasound were inducted for the study; 50 were fertile and 50 were infertile (20-40 years). Transabdominal scan (TAS) was performed to rule out abnormalities other than PCO. Ovarian volume (OV) in cm^3, follicle count (FC) and size (FS) in mm, uterine area (UA) in cm^2, endometrial thickness (Endo) in mm were measured and noted by transvaginal scanning (TVS) ; Basal Metabolic Rate (BMI) was calculated and correlated with endometrial thickness. Unpaired t-test and Pearson correlation were used for analysis.*

Result: *In the total fertile and infertile women with PCO the following result was obtained OV-TAS 7.33 ±3.17 vs. 10.87±2.49(0.001), OV-TVS 8.79±2.19 vs. 12.44±2.36(0.001), FC 14.41±2.18 vs. 14.75±2.80 (0.245), FS 3.26±0.22 vs. 8.99±0.45 (0.001), BMI 25.6±4.7vs. 27.6±5.7(0.04), UA 86.9±25.7 vs. 117.2±29.0(0.001) and Endo 4.5±1.4 vs 5.8±1.9(0.052). BMI and endometrial thickness showed a positive correlation with 'r' value of 0.06(0.05) in the infertile women and a negative correlation with 'r' value of -0.40(0.05) in fertile women.*

Conclusion: *The OV, FS, BMI, UA and Endo show a significant increase in the infertile women who are suffering from PCO. However the FC showed no significant difference between the two groups. The BMI and endometrial thickness has shown a positive correlation with infertility.*

Key Words: *Fertile, Infertile, Polycystic ovaries, Ovarian volume, Follicle count, Follicle size, Endometrial thickness, Uterine area*

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INTRODUCTION

Polycystic ovary was first identified by Stein and Leventhal which was in the year 1935. The authors defined this condition as the presence of 12 or more cystic follicles of diameter between 2-9 mm, the ovaries of such patients show an increase in their volume which results in an increase in their size[1]. These features can be visualized in one or both ovaries by ultrasound. Several studies have linked this condition with signs and symptoms like weight gain, abnormal hair growth especially facial hair growth and infertility (primary and secondary). These signs and symptoms have an effect on the life style of such women leading them to become depressed and socially withdrawn[2]. Usmani et al have shown a relationship of ovarian volume and antral follicle count with fertility. The study showed that the ovarian reserve which is the pool of primordial follicles is responsible for the reproductive capability of women. Any disorder in these follicles may lead to complications in conceiving a child[3]. Other studies have reinforced this concept and strongly suggest that ovarian reserve is a strong parameter for calculating the potential of a

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woman to reproduce[4,5]. Recently researchers have pointed increase in the prevalence of this disease in younger age groups which may be due to identification of PCO by advancement in ultrasonic technology. Due to this many women and young girls are being timely diagnosed and treated before it leads to severe complication. It has been reported that PCO is the most common endocrinopathy during adolescence, the prevalence of which ranges from 4-12%[6]. However another study by Balen et al states that due to this advancement about 20-30% of the female population has been identified as having this disease[7].

An important outcome of PCO is infertility which affects 5-10% of women in their reproductive age. These women suffer from menstrual irregularities and the hormonal profile show increased secretion of luteinizing hormone (LH) leading to hyperandrogenemia[8-10]. This has been predicted to be associated with increased miscarriages. Such patients have also been reported to have high failure rates during assisted reproductive techniques (ART)[11,12]. Although much research on PCO has taken place, it is still undetermined how PCOs are caused i.e. its exact etiology and what the underlying mechanism of its development is. Therefore genetic linkage to PCO has very recently aroused a lot of interest which have lead to several familial aggregation studies[13].

Studies have shown that LHβ and LHR gene mutation have strong relations with anovulatory PCOS. Lui et al showed results that are suggestive of LHG1052A mutation having influence on PCO susceptibility and phenotypes[14]. Several published studies associate PCO with infertility but recently investigators have also pointed out that ovulatory PCOs with normal clinical investigations have also been identified. These patients may or may not suffer from infertility but those who are infertile have a high successful pregnancy rate if treated by ART[15,16].

Zong et al were of the opinion that ovulatory PCO patients might present features of normal ovarian morphology resulting in normal child bearing process. The authors further investigated that the rates of infertility were probably due to abnormal oocyte morphology or changes in cytosolic factors that could affect the quality of the oocytes[17]. This in turn proves that women maybe fertile in spite of the presence of PCO, therefore the objective of this study was to compare the female reproductive organs morphology between fertile and infertile women with polycystic ovaries.

METHODOLOGY

This cross sectional comparative study was performed at Rahat Hospital, Karsaz Karachi from January 2008 to December 2008. In which women diagnosed with PCOs were identified by ultrasound and then inducted for the study. The subjects were informed about the study and permission was sought via a written informed consent.

The inclusion criteria for fertile women with PCOs was married women of ages between 20-40 years, presence of 12 or more cystic follicles in one or both ovaries with regular menstrual cycles. The woman should have had one child in the last one year and should not be using contraceptives for at least 2 months prior to the study.

The exclusion criteria for fertile women with PCOs was birth of her child after ART, any pathology of pelvic reproductive organs other than PCOs, any endocrine disorders and any chronic illness e.g. hypertension, diabetes, cancer etc.

The inclusion criteria for infertile women with PCOs are the same as for fertile women except that the women must be infertile after regular intercourse for one or more years. The exclusion criteria for infertile women with PCOs in addition to the above mentioned were, attempt for ART and husband suffering from infertility. Ultrasound was performed during 2^{nd} to 7^{th} day of the menstrual cycle using Toshiba ultrasound machine, the probes used were transabdominal and transvaginal probes of 3.75 MHz and 7.5 MHz frequency respectively. The transabdominal scan (TAS) was performed to rule out abnormalities other then PCOs e.g. endrometriosis, adhesions, absence of ovaries (one or both), fibroids etc. This was done on a full urinary bladder. Transvaginal scan (TVS) was done if the patient was diagnosed with PCO during TAS; this was performed on an empty urinary bladder.

The ovarian volume, follicle count, uterine size, endometrial thickness were measured and noted by scanning. Both the 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 $D1xD2xD3x0.523cm^3$ and the sum of both ovaries was noted[18].

The follicles between 2-9mm were measured and counted. The uterine area was calculated by measuring the uterine length from the top of the fundus to the cervix and the anteroposterior diameter was taken by TVS, it was calculated by the formula uterine length x anteroposterior diameter in cm^2 [19].

The endometrial thickness was measured in mm by TVS[19].

BMI was calculated by taking the height and weight of each subject recruited and applying the formula Kg/m 2^{20}. The readings were taken twice for all variables and their average considered the final reading, this was done in order to validate the measurements.

During the study a total of 248 women were initially recruited to achieve our desired number. Sampling was done in the radiology department where women were sent for routine ultrasound or sent due to complains of lower abdominal pain. After taking informed consent, the women diagnosed with PCO were recruited as subjects for the study.

From the total number of 248 women, 100 fell into the inclusion criteria for 109 women were excluded due to complains of menstrual irregularities, 14 subjects were suffering from endocrine disorders, 21 had hypertension and 4 had reports showing male infertility. Of the 100 women 50 were fertile and 50 were infertile.

The measurements were fed on SPSS version 12 for windows and analyzed by applying unpaired t-test. Pearson correlation coefficient "r" was used for associating BMI and endometrial thickness with fertile and in-fertile women suffering from PCO. The results were given as mean± standard deviation (SD). P-value of 0.05 or less was considered statistically significant.

The study was approved by the ethical review committee, Ziauddin University.

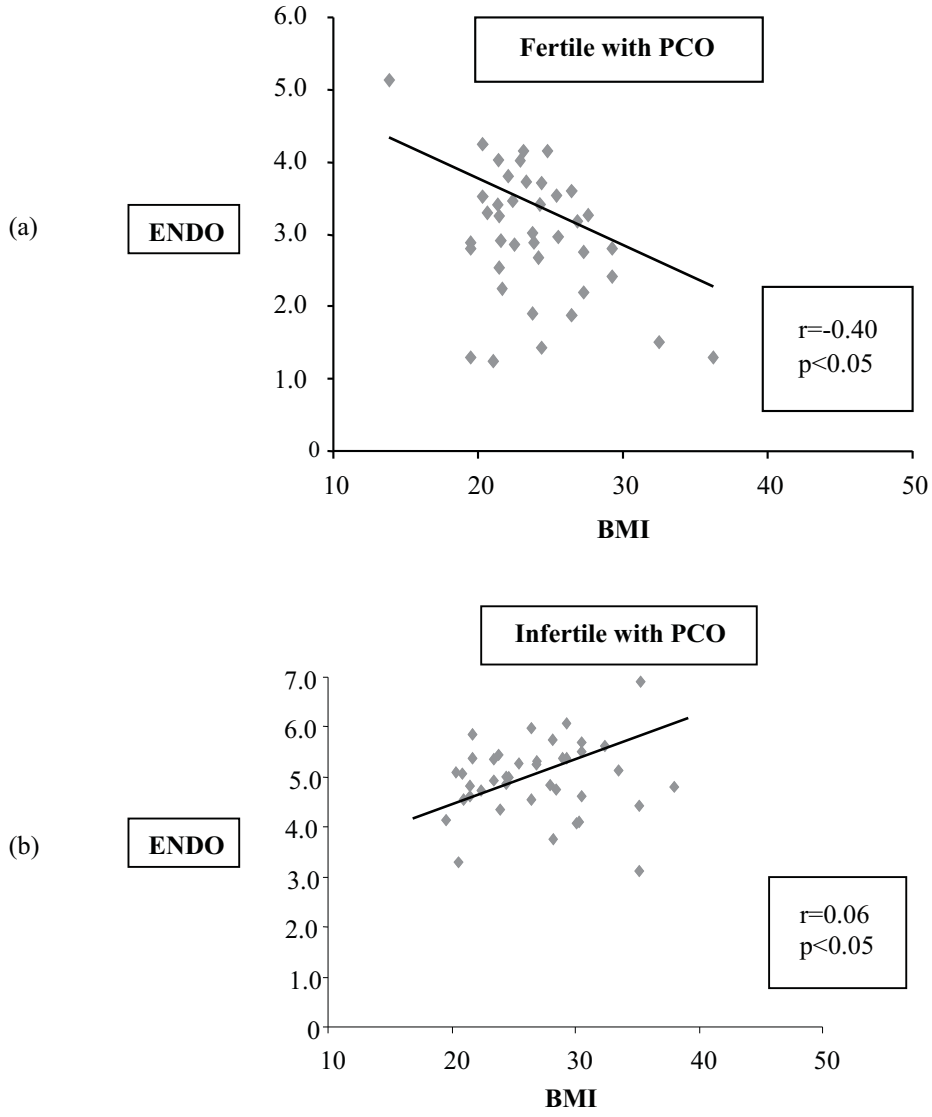
RESULTS

Table 1 shows comparison of pelvic reproductive organs in fertile women with PCOS and infertile women with PCO. Figure 1 shows a correlation of BMI with the two groups of women. The comparison of pelvic reproductive organs is between fertile (n=50) and infertile (n=50) women of ages 20-40 years (mean age was 36±4 years). A significant difference between the two groups of women is present in the ovarian volume (OV) by both methods. The follicles in fertile women were of smaller size as compared to the infertile women though more than 12 in number and show no difference between the two groups. The uterine area is larger in the infertile group of women as compared to the fertile women. The endometrium is significantly thicker in infertile women. BMI was found to be significantly more in infertile women. Some negative co-relation of BMI with endometrial thickness in women who were fertile with PCO could be established but positive significance was observed within the infertile group (Figure 1).

Table1: Comparison of variables between fertile and infertile young women

Ages 20-40 years	Fertile with PCO Mean ± S.D (n=50)	Infertile with PCO Mean ± S.D (n=50)	P-value
OV(TAS)	7.33 ± 3.17	10.87 ± 2.49	0.001
OV(TVS)	8.79 ± 2.19	12.44 ± 2.36	0.001
FC	14.41 ± 2.18	14.75 ± 2.80	0.245
FS	3.26±0.22	8.99±0.45	0.001
BMI	25.6 ± 4.7	27.6 ± 5.7	0.04
UA	86.9 ± 25.7	117.2 ± 29.0	0.001
ENDO	4.5 ± 1.4	5.8 ± 1.9	0.052

Figure 1: Correlation between body mass index and endometrial thickness in fertile and infertile women with PCO



BMI= body mass index, ENDO= endometrial thickness in mm, PCO= polycystic ovary

DISCUSSION

In our study we have made an attempt to compare the pelvic reproductive organs between fertile and infertile women of ages between 20-40 years. It was conducted on women with PCOs in which it was observed that the ovarian volume is significantly more in the infertile group of women whereas the follicle count is approximately the same in both the fertile and infertile groups. However the increased ovarian volume can be attributed to the large average follicle size in the infertile women. Several studies have shown PCOs with ovarian volume of ⩾ 10ml and have also correlated this condition with ovulatory and anovulatory PCOS. Their findings also show an increase in follicle count with large size ranging from 2-9mm. [21, 22.] Conversely most of the studies are limited in their power due to their small sample size. The Rotterdam consensus criteria show the prevalence of PCOS in age groups 18-22 years as 83-84%, in 23-27 years as 66-84%, in 28-32 years as 42-79%, 33-37 years as 19-33% and 38-40 years as 0-33%. It is also mentioned that these women had ovulatory cycles[23].

Although the ovarian volume and follicle number decreased with increasing age, they showed a positive correlation between follicle number and ovulation day. Therefore PCOS prevalence reduces with increased age but it is also related to decreased fertility. BMI is shown to be more in the infertile group with PCO in this study. There is an established association of obesity with PCOS. Some investigators have also shown a significant correlation of BMI with uterine size and ovarian volume. Dandolu et al have reported that the uterine weight shows an increase of 7.56 g for every point of increase in BMI[24]; in our research we have found no significant correlation between BMI and uterine size or ovarian volume. It has also been observed that incidence of miscarriages is increased if the woman is obese; it also lowers the success rate of assisted reproduction technique (ART) cycles[20, 24].

In our study the uterine area and endometrial thickness is shown to be significantly more in the infertile women with PCO. The normal anatomical change in the size of the uterus depends on the age and hormonal condition of the women. The uterine area of a woman in her reproductive age measures 8cmx6cmx4cm. The capacity of non pregnant uterine cavity varies between 75cc to 200cc; its weight is about 100-200grams. The uterine size however may be adversely affected due to abnormalities of associated organs; it may enlarge due to increase in hormonal secretions[19,24]. PCOS can also be responsible for causing an enlarged uterus, the associated symptoms are pressure and pain in lower abdomen and back[25].

Studies have shown a normal endometrium in women with regular menstrual cycle but the thickness changes with the phase of the cycle ranging from 3mm after mensus to 15 mm in the luteal phase but a normal range in postmenopausal women is from 5.4mm to 10.8mm[19,25,26]. Abnormal increase in endometrial thickness is associated with obesity, PCOS and diabetes mellitus but in accordance with a study by Goldstein it is suggested that if the increased endometrial thickness is asymptomatic and not associated with any disease then further investigation and treatment is not required[27]. Shah et al demonstrated in their study on PCOS in adolescent girls that the endometrium was enlarged (>7mm) in 31.4% , the uterine length identified was less than the normal size in 15.7% and was of normal size in 41.2% girls. The association of endometrial hyperplasia with PCOS is well recognized; thick cystic appearing endometrium with PCOS has been reported. It has also been shown that endometrial cancer tends to develop in such patients and that too at a young age of less than 35 years. [28] Therefore it is critical to recognize this association. Women with PCOS have a higher chance of developing endometrial cancer and if it is associated with irregular cycles the risks increase. The underlying mechanism for this phenomenon is that after exposure to estrogen during normal menstrual cycles the endometrial lining undergoes the phases of proliferation, thickening and shedding but in cases of PCOS when ovulation does not take place the lining is not shed leading to great exposure to estrogen causing endometrium to thicken more than its normal ranges. This is when increase risks for endometrial cancer develop[29,30]. Therefore it is important to examine the endometrial thickness, uterine area, ovarian volume, follicular morphology in PCO cases which may be used as a fertility predictor and can contribute for prevention of many associated diseases if diagnosed and treated timely.

CONCLUSION

The OV, FS, BMI, UA and Endo have shown a significant increase in the infertile women as compared to the fertile women who are suffering from PCO. However the FC showed no significant difference between the two groups. BMI is shown to be positively correlated to the endometrial thickness in women suffering from PCO with infertility but negative correlation is seen with the fertile women.

REFERENCES

1. Stein IF, Leventhal ML. Amenorrhea associated with bilateral polycystic ovaries. Am J Obstet Gynecol 1935;29:181-91.
2. Usmani A, Shokh IS. Ovarian reserve in fertile women as determined by ultrasonography. J Dow Uni Health Sci 2007;1:69-73.
3. Zaidi S, Usmani A, Shokh IS, Alam SE. Ovarian reserve and BMI between fertile and subfertile women. J Coll Physicians Surg Pak 2009;19:21-4.
4. Zaidi S, Usmani A, Shokh IS. Ovarian reserve and reproductive age. Pak J Med Sci 2007; 23:449-53.
5. Wallace WH, Kelsev TW. Ovarian reserve and reproductive age may be determined from measurement of ovarian volume by transvaginal sonography. Hum Reprod 2004; 19:1612-7.
6. Broekmans FJ, Knauff EA, Valkenburg O, Laven JS, Eijkemans MJ, Fauser BC. PCOS according to the Rotterdam consensus criteria: change in prevalence among WHO-II anovulation and association with metabolic

factors. BJOG 2006;113:1210-7.

7. Balen AH, Conway GS, Kaltsas G, Techatrasak K, Manning PJ, West C, et al. Polycystic ovary syndrome: the spectrum of the disorder in 1741 patients. Hum Reprod 1995;10:2107-1.
8. Iftikhar S, Collazo-Clavell ML, Roger VL, St Sauver J, Brown RD, Cha S, et al. Risk of cardiovascular events in patients with polycystic ovary syndrome. Neth J Med 2012; 70:74-80.
9. Mortensen M, Rosenfield RL, Littlejohn E. Functional significance of polycystic-size ovaries in healthy adolescents. J Clin Endocrinol Metab 2006;91:3786-90.
10. Kuivadaari-Pirinen P, Raatikainen K, Hippelainen M, Heinonen S. Adverse outcomes of IVF/ICSI pregnancies vary depending on aethiology of infertility. ISRN Obstet Gynecol 2012;2012:451915.
11. Kim CH, Moon JW, Kang HJ, Ahn JW, Kim SH, Chae HD, et al. Effectiveness of GnRH antagonist multiple dose protocol applied during early and late follicular phase compared with GnRH agonist long protocol in non-obese and obese patients with polycystic ovary syndrome undergoing IVF/ICSI. Clin Exp Reprod Med 2012;39:22-7.
12. Lam PM, Raine Fenning N. The role of three dimensional ultrasonography in polycystic ovary syndrome. Hum Reprod 2006;21:2209-15.
13. Pigny P, Jonard S, Robert Y, Dewailly D. Serum anti-Mullerian hormone as a surrogate for antral follicle count for definition of the polycystic ovary syndrome. J Clin Endocrinol Metab 2006;91:941-5.
14. Liu N, Ma Y, Wang S, Zhang X, Zhang Q, Zhang X, et al. Association of genetic variants of luteinizing hormone, Luteinizing hormone receptor and polycystic ovary syndrome. Reprod Biol Endocrinol 2012;10:36.
15. Bu Z, Kuok K, Meng Jie, Wang Rui, Xu B, Zang H. The relationship between polycystic ovary syndrome, glucose tolerance status and serum preptin level. Reprod Biol Endocrinol 2012;10:10.
16. Wang Y, Shannon M. Polycystic ovary syndrome: a common but often unrecognized condition. J Midwifery Women Health 2012;57:221-30.
17. Zhong YP, Ying Y, Wu HT, Zhou CQ, Xu YW, Wang Q, et al. Comparison of endocrine profile and in vitro fertilization outcome in patients with PCOS, ovulatory PCO or normal ovaries. Int J Endocrinol 2012;2012:429803.
18. Erdem M, Erdem A, Biberoglu K. Age related changes in ovarian volume, antral follicle counts and basal stimulating hormones levels: comparison between fertile and infertile women. Gynecol Endocrinol 2003;17:199-205.
19. Kenneth MN, John SP, Eran BL. Imaging the endometrium: disease and normal variants. Radiographics 2001;21:1409-24.
20. Su HI, Sammel MD, Freeman EW, Lin H, DeBlasis T, Gracia CR. Body size affects measures of ovarian reserve in late reproductive age women. Menopause 2008;15:857-61.
21. Nazir F, Tasleem H, Tasleem S, Sher Z, Waheed K. Polycystic ovaries in adolescent girls from Rawalpindi. J Pak Med Assoc 2011;61:961-3.
22. Dewailly D, Gronier H, Poncelet E, Robin G, Leroy M, Pigny P. Diagnosis of polycystic ovary syndrome (PCOS): revisiting the threshold values of follicle count on ultrasound and of serum AMH level for the definition of polycystic ovaries. Hum Reprod 2011;26:3123-9.
23. Johnstone EB, Rosen MP, Neril R, Trevithick D, Sternfeld B, Murphy R, et al. The polycystic ovary post-Rotterdam: a common age dependant finding in ovulatory women without metabolic significance. J Clin Endocrinol Metab 2010;95:4965-72.
24. Dandolu V, Singh R, Lidicker J, Harmanli O. BMI and uterine size: is there any relationship? Int J Gynecol Pathol 2010;29: 568-71.
25. Zohav E, Orvieto R, Anteby EY, Segal O, Melter S, Tur-Kaspa I. Low endometrial volume may predict early pregnancy loss in women undergoing in-vitro-fertilization. J Assist Reprod Genet 2007;24:259-61.
26. Park JC, Lim SY, Jang TK, Bae JG, Kim JI, Rhee JH. Endometrial histology and predictable clinical factors for endometrial disease in women with polycystic ovarian syndrome. Clin Exp Reprod Med 2011;38:42-6.
27. Goldstein SR. Modern evaluation of the endometrium. Obstet Gynaecol 2010;116:168-76.
28. Shah B, Parnell L, Milla S, Kressler M, David R. Endometrial thickness, uterine and ovarian ultrasonographic features in adolescents with polycystic ovarian syndrome. J Pediatr Adolesc Gynaecol 2010;23:146-52.

29. Mahajan NN, Singh R, Mahajan KN, Levine D. Sonographic evaluation of the endometrium in patients with a history on an appearance of polycystic ovarian syndrome. J Ultrasound Med 2007;26:862.

30. Gao JS, Shen K, Lang JH, Huang HF, Pan LY, Wu M, et al. Clinical analysis of endometrial carcinoma in patients aged 45 years or younger. Zhonghua Fu Chan Ke Za Zhi 2004;39:159-61.

CONTRIBUTORS

AU designed research proposal, conducted reseach, compiled data, wrote and reviewed the article. ZUI and ZA helped in writing and reviewing the manuscript. All the authors contributed significantly to the research that resulted in the submitted manuscript.