



THE PREVALENCE OF MORPHOLOGICAL CHANGES IN OVARIES IN DIFFERENT AGE GROUPS WITH POLYCYSTIC OVARY SYNDROME

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ABSTRACT

Background: Polycystic ovary syndrome (PCOS) is a common endocrinopathy disorder affecting reproductive aged women and frequently manifest during early reproductive age. It is a heterogeneous disorder, with multiple reproductive, cosmetic and metabolic complexities which is characterized by dysfunction in ovulation and clinical or biochemical hyperandrogenism and the presence of polycystic ovarian morphology. It is the most common endocrine cause of infertility, increased risk of adverse pregnancy outcome, metabolic syndrome, type 2 diabetes mellitus, and some carcinoma. For these reasons a correct and early diagnosis of this syndrome is fundamental, as it allows performing the most appropriate treatments and check-ups thus reducing the risk of developing all the complications related to it. **Objectives:** To measure the ovarian morphology in different age groups of adolescent and adult women with polycystic ovary syndrome. **Methods:** In this observational cross-sectional study 150 married or unmarried adolescent and adult women with PCOS were subdivided into three equal age-based groups of 50 each: 12 – 28 years (group I), 29-36 years (group II) and 37-50 years (group III). The ovarian volume, ovarian area, ovarian stromal area, follicles count and size were determined by trans-abdominal and trans-vaginal scans. All statistical procedures were performed using SPSS 20.0 for Windows (IBM SPSS Statistics, IBM software). Values are expressed as mean \pm standard deviation and compared by one-way Anova $p < 0.05$ is considered significant. Test for normality was done using Kolmogorov-Smirnov test. Bonferroni correction for multiple comparisons was applied. **Conclusion:** In this study, ovarian area showed a positive correlation with age in women with polycystic ovaries. There were no significant changes in ovarian volume, ovarian stromal area, and follicle count during reproductive ages until the perimenopause. It was observed a moderate negative correlation of age with follicle size.

KEYWORDS : Ovarian Volume, Follicle Count, Trans-Abdominal Ultrasound and Trans-Vaginal Ultrasound.

INTRODUCTION

The ovaries are the female pelvic reproductive organs that reside the ova and are also responsible to produce female sex hormones. They are paired organs located on either side of the uterus within the broad ligament below the uterine (fallopian) tubes. The ovaries are responsible for housing and releasing ova, or eggs, necessary for reproduction. The ovaries are small, oval-shaped, and greyish in colour, with an uneven surface. The actual size of an ovary depends on a woman's age and hormonal status; the ovaries, covered by a modified peritoneum, are approximately 3-5 cm in length during childbearing years and become much smaller and then atrophic once menopause occurs. A cross-section of the ovary reveals many cystic structures that vary in size. These structures represent ovarian follicles at different stages of development and degeneration [Katz et al., 2007] [Hentry, 1999] [Kyung et al., 2000].

Every month, the ovaries bear a series of changes, reckoning on stimulation with the resource of the adenohypophysis endocrines the follicle stimulating hormone (FSH) and therefore

the luteinizing hormone (LH). A traditional girl cycle lasts twenty-eight days; but this might vary from 21-35 days. The gonadcycle has two high notch phases: the follicular phase (days 1-14) and therefore the luteal phase (days 14-28). The follicular part is characterized by method of vesicle improvement and growth, the purpose being that one vesicle matures associate degreed releases an egg at the time of organic process, spherical day fourteen of the feminine cycle. The last immature follicles endure levels of degeneration up until day twenty-eight, once the cycle repeats itself. The egg this can be launched is picked up via the fimbriae of the salpinx, and therefore the egg is transported nearer to the womb. If fertilization will not arise, the egg degenerates, and emission happens. Histologically, the ovary has two essential sections: the outer cortex and internal medulla.

As ladies age, they expertise a decline in fruitful average performance resulting in climacteric. This decline is tied to a decline at intervals the vary of gonad follicles. Even though

regarding one million oocytes are present within the human ovary, only about 500 (about 0.05%) of these ovulate, and the rest are wasted. The decline in gonad reserve seems to arise at an unceasingly growing worth with age and ends in virtually whole exhaustion of the reserve through regarding age fifty. As gonad reserve and fertility decline with age, there is also to boot a parallel growth in being pregnant failure and cell division mistakes succeeding in chromosomally atypical conceptions [Hansen, KR et al., 2008].

It is well known that the uterus and therefore the ovary begin to expand with the onset of puberty. In maturity, female internal reproductive organ and gonad sizes vary individually. Throughout the reproductive period, cyclic modifications in female internal reproductive organs are observed according to the menstrual cycle [Piironen, O. and Kaihola, HR, 1975].

While the proper reason of PCOS is unknown, clinical medical doctors accept as true with that secretion imbalances and biology play a perform. Women are far more probably to expand PCOS if their mother or sister to boot has matters. Over run of the endocrine androgenic hormone is also a couple of totally different tributary bother. Androgen may be a male intercourse hormone that women's bodies additionally turn out. Ladies with PCOS often turn out higher-than-ordinary levels of androgenic hormone. This might have an impression at the development and unharness of eggs throughout organic process. Additional hypoglycaemic agent, insulin might to boot purpose high androgenic hormone ranges. [Jaime Herndon and Steven Kim, 2013].

For those reasons an accurate and early prognosis of this syndrome is crucial, because it permits showing the utmost appropriate remedies and check-ups for that cause lowering the chance of developing all the headaches associated with it. Polycystic ovary syndrome may be a common scenario in younger humans. Physicians wish to require care to touch upon all the associated sequelae of the unwellness, every reproductive and metabolic. With improved recognition of the aptitude cardiometabolic consequences of PCOS, specialists will add conjunction with most wanted care suppliers to reinforce lengthy-time amount fitness consequences for those

patients [Amy, DV, 2013].

PATIENTS AND TECHNIQUES

Study Methodology

In this observational cross-sectional study 150 married or unmarried adolescent and adult women with PCOS were subdivided into three age-based groups of 50 each: 12 – 28 years (group I), 29-36 years (group II) and 37-50 years (group III). This study was conducted from January 2016 to December 2017 in Mediscan Diagnostic Centre, Kunnathurmedu, Palakkad, Kerala.

Ultrasound was performed using Mindray DC-6 Ultrasound machine. The probes used predominantly TAS frequency 3.5 to 5 mhz along with TVS frequency 6 to 8mhz. 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 [Usmani A, 2012]. Physical examination was performed in each person by a physician. All PCOS subjects were examined by a single examiner and patients were evaluated by transabdominal and transvaginal US.

Diagnosis of PCOS turned into primarily based completely at the 2003 metropolis ESHRE/ASRM Sponsored PCOS agreement necessities [Welt, CK et al., 2006], that accommodates at the smallest amount of the subsequent: (i) oligo- and/or organic process (ANO), (ii) organic chemistry hyperandrogenemia and/or hyperandrogenism (scientific signs of excessive androgenic hormone stages) (HA), and (iii) polycystic ovaries on ultrasound (PCO) with twelve or additional follicles of two - nine millimeter diameter in a very single ovary. Scientific variables like age, body weight and high had been assessed altogether topics. Body mass index (BMI) changed into calculated as weight (kg) divided with the help of the square of high (m²). Organic chemistry hyperandrogenemia is represented as serum androgen degrees and/or serum free androgenic hormone Index being on top of 2 in depth deviations higher than the imply stages of an everyday manage population. Medical hyperandrogenism is outlined to the fact the presence of hirsuteness, acne, or sex hormone phalacrois. Hirsuteness is assessed through Ferriman-Gallwey scale [Ferriman, D and Gallwey, JD, 1961]

Married or single adolescent and grown-up ladies, an extended term between 12-50 years, having menstrual irregularity and hyperandrogenism with the presence of multiple follicles in a very single or every ovary and no longer victimization contraceptives for a minimum of five months before the planning at, had been included.

Women with records of abortion, PCOS-associated remedy sooner than this analysis, patients with massive general illness, with any pathology of pelvic reproductive organs apart from PCOS and with any continual contamination e.g. high blood strain, diabetes, most cancers and girls tried to conceive via ART, smokers, those taking sex hormones or capsules effecting hypoglycaemic agent secretion, Clomid, intense physical activity, an ovarian mass or cyst (more than 10 mm in diameter) detected by ultrasound examination in this study were excluded.

All statistical procedures had been meted out the usage of SPSS 20.0 for windows (IBM SPSS records, IBM software system program). Values are expressed as mean \pm standard deviation and compared through one manner ANOVA $p < 0.05$ is considered significant 95% confidence interval. Test for normality was done using Kolmogorov-Smirnov test. Bonferroni correction for multiple comparisons turned into applied. Values are statistically appreciable at $p < 0.05$

The ovarian volume, ovarian area, ovarian stromal area, follicles count and size, were determined by trans-abdominal and trans-vaginal scans. The two ovaries were scanned within

the longitudinal (D1), antero-posterior (D2) and transverse diameter (D3); the whole volume calculated by applying the prolate ellipsoid equation that is $D1 \times D2 \times D3 \times 0.523\text{cm}^3$ and the mean gonad volume was calculated by adding the sizes of every ovary and so dividing by two. Whereas these criteria guarantee a specificity of ninety eight percent, it does not provide the most effective sensitivity [Jonard, S, Robert, Y and Dewailly, D, 2005]. According to the metropolis agreement criteria, associate degree gonad volume $> 10\text{cm}^3$ is diagnostic of PCO.

In line with trendy studies, it is miles larger applicable to decrease the limit to 7cm^3 in order to have a greater sensitivity of the test. In fact, the limit of 10cm^3 incorporates a specificity of near to 100%, however sensitivity decrease five percent [Scheffer GJ et al., 2002]. For each ovary, the complete wide selection of seen antral follicles measure two-to-nine-millimeter in diameter changed into counted with the help of manner of non-stop scanning of the entire ovary, from the inner margin to the outer margin in longitudinal pass-segment.

Ovarian Area: In 2-D US ovarian area (OA) is calculated by using the formula $\pi/4 \times \text{length} \times \text{width}$ (area of an ellipse), by adapting an ellipse to the ovary, whose area is calculated from ultrasound or by hand drawing the ovarian outline, automatically calculating the area below the line. Although OA is less frequently used in research protocols, it has better diagnostic power than those OV. The limit for this parameter is 5cm^2 [Balen, AH et al., 2003].

Ovarian stromal area: evaluated by outlining with the caliper the peripheral profile of the stroma, identified by a central area slightly hyperechoic with respect to the other ovarian area. Ovarian volume correlates well with ovarian function and is both more easily and reliably measured in routine practice than ovarian stroma. In order to define the polycystic ovary, either qualitative or quantitative assessment of the ovarian stroma is required [Jonard, S, Robert, Y and Dewailly, D, 2005].

Number of follicles: To evaluate the number of follicles, each ovary was scanned in cross section by the interior edges to the external ones in order to achieve to the total number of cysts/follicles. The number of follicles estimated on two levels of the ovary so as to calculate its dimension and position. According to the Rotterdam Consensus criteria polycystic ovary should contain 12 or more follicles of 2-9 mm in diameter. This is a useful parameter to distinguish PCO cases from multi ovarian follicular (MFOs), a transitory condition generally associated to delayed puberty, hyperprolactinemia, hypothalamic anovulation, amenorrhea related to weight [The Rotterdam.]. The multifollicular ovary is morphologically characterized by a number of follicles, lower than PCO (between 6 and 10), distributed throughout the ovary and by the absence of hypertrophy of the stroma. The presence of multiple follicles is due to an incomplete stimulation of the Gonadotropin-releasing hormone (GnRH) follicular development. Moreover, unlike what occurs in PCOS, patients suffering from ovarian multifollicular show normal levels of LH and T, but reduced levels of FSH. Generally, the ovary resumes its normal aspect after therapy and/or change of body weight [Porter, MB, 2008]

RESULTS

Data Analysis And Interpretation

The areas of research mainly focused on adolescent and adult women of ages between 12-50 years, having menstrual irregularity and hyperandrogenism with multiple follicles in one or both ovaries and not using contraceptives for at least 5 months prior to the study. In this observational cross-sectional study hundred and fifty married or single adolescent and adult women with PCOS were subdivided into three age-

based groups of 50 each: 12 – 28 years (group 1), 29-36 years (group II) and 37-50 years (group III). The study is limited prospective approach.

In this study the mean age in group I was 22.74 ± 3.14 years, group II was 31.78 ± 2.42 years and 39.86 ± 2.98 years in group III. The present study examined that ovarian morphology, ovarian area increased from 8.93 ± 1.13 to 9.43 ± 1.13 ($p < 0.048$) in group III. The researcher found that the mean value of antral follicle size is larger in the younger age, group I (age 22.74 ± 3.14) (follicle size $5.94 \pm .66$) when compared with that of age group II (age 31.78 ± 2.42) (follicle size $5.64 \pm .48$) and group III (age 39.86 ± 2.98) (follicle size $5.88 \pm .53$) in patients with PCOS.

The current study noticed a positive correlation of age with ovarian area ($p < 0.048$) (Figure:1) There were no significant changes observed in ovarian volume (Figure:4), ovarian stromal area (Figure:5) and antral follicle count (Figure:3) during reproductive ages until the perimenopause. It was found that there is a moderate negative correlation of age with Follicle size (Fig-2).

Table: 3 : Morphological Changes In Ovary And Uterus In Different Age Groups With Polycystic Ovary Syndrome

	GROUP1	GROUP2	GROUP3	P VALUE
NUMBER	50	50	50	
PATIENTS AGE	22.74 ± 3.14	31.78 ± 2.42	39.86 ± 2.98	NS
OVARIAN VOLUME	16.79 ± 3.21	16.37 ± 2.86	17.08 ± 2.62	.470
OVARIAN AREA	8.93 ± 1.13	8.97 ± 1.06	9.43 ± 1.13	.048
OVARIAN STROMAL AREA	2.70 ± 0.48	2.71 ± 0.54	2.62 ± 0.37	.576
FOLLICLE SIZE	5.94 ± 0.66	5.64 ± 0.48	5.88 ± 0.53	.022
OVARY FOLLICLES COUNT	12.44 ± 1.75	12.31 ± 1.68	12.13 ± 1.40	.632

Values are expressed as mean \pm SD: compared by One Way Anova $p < 0.05$ is considered significant 95% confidence interval, ovarian volume in cm^3 , ovarian area in cm^2 , ovarian stromal area in cm^2 , follicle size in mm, follicle counts in number

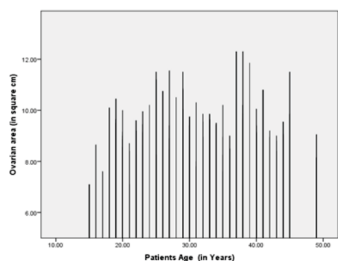


Figure:1 Association Of Age With Ovarian Area Measured In Cm^2

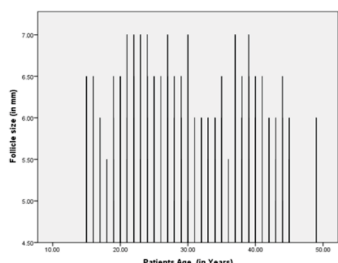


Figure:2 A Moderate Negative Correlation Of Age With Follicle Size.

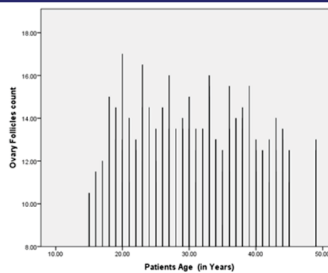


Figure:3 Picture Represents The Age-related Antral Follicles Count (in Numbers) In Pcos

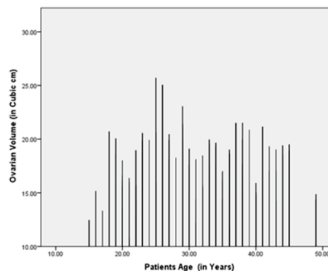


Figure :4 Picture Showing The Effect Of Age On Ovarian Volume

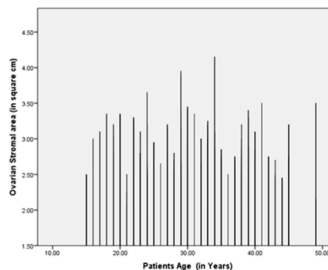


Figure:5 Association Of Ovarian Stromal Area With Age.

DISCUSSION

The objective of the study was to determine the morphological changes in ovary in different age groups of adolescent and adult women with polycystic ovary syndrome. The researcher observed an increase in ovarian area from 8.93 ± 1.13 to 9.43 ± 1.13 ($p < 0.048$) in group III. This study showed a positive correlation of age with ovarian area ($p < 0.048$). Increased gonad space might be due to the presence of higher antral follicle count in PCOS. There were no significant changes observed in ovarian volume ($P < 0.470$), ovarian stromal area ($p < 0.576$) as the PCOS women progressively age. The ovarian size and volume are affected by diseases, drugs, ovulation, and age [Pavlik EJ et al.,2000] [Lass A et al., 1997]. In normal ovulatory women, ovarian volume decreases with age, with measurable decreases across each decade of reproductive life starting at age 40 years [Pavlik, EJ et al., 2000]. Women with PCOS are likely to have a higher antral follicle count and the excess number of follicles keep the ovarian volume unchanged in PCOS patients. Hyperinsulinemia stimulates the development of antral follicles, increasing the sensitivity of granulosa cells to FSH, thus increasing the numbers of follicles and ovarian volume [Lobo RA and Carmina E, 2000].

In normal women, with rising age, the ovarian reserve (collection of primordial follicles) declines and ultimately results in menopause. This depletion of primordial follicles at the age of 45 ± 5 years results in the female being unable to conceive. The present study examined that there was no significant age-related decline in the AFC among women with PCOS ($p < 0.632$). This result confirms previous reports of reduced loss of follicles by atresia (i.e., increased survival during folliculogenesis) in PCOS [Webber et al., 2003] [Senthil

K A et al., 2016] [Wiser A et al., 2013]. The age-related decline in AFC was constant in PCOS patients, while in non-PCOS women, it was accelerated up to 30 years of age; afterwards, the rates became similar in both groups of women. The rate of follicle loss per year was slower in PCOS women compared with that in non-PCOS women. However, in both groups the highest rate of follicle loss was between the ages of 18 and 30. These results confirm previous reports of age-related decrease in AFC among women with or without PCOS [Al-Sunaidi et al., 2007] [Almog et al., 2011]. The results of the present study were supported by earlier studies conducted by Young SH et al. (2017) and Ng EH et al. (2003). In their study, Young SH et al. (2017) could not identify any relationship between age and OV in the PCOS group, this result was due to the inclusion of young nulliparous women. Ng EH et al. (2003) experienced a moderate negative correlation of age with OV, suggesting that there are no major changes in OV during reproductive ages until the perimenopause.

The current study found that the mean value of antral follicle size is larger in the younger age, group I (age 22.74 ± 3.14) (follicle size $5.94 \pm .66$) when compared with that of age group II (age 31.78 ± 2.42) (follicle size $5.64 \pm .48$) and group III (age 39.86 ± 2.98) (follicle size $5.88 \pm .53$) in patients with PCOS. It was also noticed that; in this study the mean value of follicle size was smallest in age group II (age 31.78 ± 2.42). Journey to ovulation begins during late luteal phase of prior menstrual cycle, when certain 2-5 mm sized healthy follicles form a population, from which dominant follicles is to be selected for next cycle. During Day 1-5 of the menstrual cycle, a second process of 'follicular selection' begins, when among all recruited follicles, certain growing follicles of size 5-10 mm are selected, while rest of the follicles regress or become atretic. During Day 5-7 of the menstrual cycle, a process of 'dominance' begins, when a certain follicle of 10 mm size takes the control and becomes dominant and reaches 17-27 mm size just prior to ovulation. Almost nearing ovulation and it literally explodes to release the ovum morphologically, the characteristic feature of polycystic ovaries is an apparent failure to select a dominant follicle and the accumulation of antral follicles 2-8 mm in size. It is assumed that this appearance reflects an androgen-induced arrest in antral follicle development [Franks, S, et al., 2008].

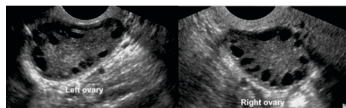


Figure :76US images of right and left ovaries demonstrate polycystic appearance, consisting of abundant hypointense central stroma with peripherally arranged follicles.

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