



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

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ABSTRACT

Background: Polycystic ovary syndrome (PCOS) is one in every of the foremost common endocrine problems in adolescent and adult women, and significantly has reproductive and metabolic effects. 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 it is clear that 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 uterine 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 uterine area and endometrial thickness 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, the researcher observed an increase in uterine area from 19.92 ± 4.78 to 26.32 ± 3.80 ($p < 0.000$) and endometrial thickness from 6.96 ± 1.38 to $7.68 \pm .99$ ($p < 0.011$) in group III. The present study examined that UA and ET were considerably increased in the older age group. The current study noticed a positive correlation of age with endometrial thickness ($p < 0.011$) and uterine area ($p < 0.000$).

KEYWORDS : Uterus, Endometrium, Trans-abdominal ultrasound, trans-vaginal ultrasound

INTRODUCTION

General introduction

The endometrium is the inner epithelial layer, along with its mucous membrane, of the mammalian uterus. The endometrium consists of a simple columnar epithelium and an underlying thick connective tissue stroma. The mucosa is invaginated to form many simple tubular uterine glands. The glands extend through the entire thickness of the stroma. The stromal cells of the endometrium are embedded in a network of reticular fibres. The endometrium is subject to cyclic changes that result in menstruation.

Only the mucosa of the body of the uterus takes part in the menstrual cycle. It has a basal layer and a functional layer; the functional layer thickens and then is sloughed during the menstrual cycle or estrous cycle. The menstrual cycle is divided into the following phases: postmenstrual, proliferative, secretory, and menstrual. The cyclic changes in the endometrium take place under influence of hormones (estrogen and progesterone) produced by the ovary.

[Ovarian cycle. 24 December 2016. <https://en.wikipedia.org/wiki/Endometrium>.]

The functional layer is neighboring to the uterine cavity. This layer is built up after the end of menstruation during the first part of the previous menstrual cycle. Proliferation is induced with the resource of estrogen, and later changes during this layer area unit engendered via progesterone from the corpus luteum (luteal phase). It is tailored to supply associate degree superior setting for the implantation and growth of the embryo. This layer is totally shed throughout emission [Guyton, AC and Hall, JE, eds, 2006] [Blue Histology, Female reproductive system].

The basal layer, neighboring to the involuntary muscle and at a lower place the functional layer, is not shed at any time within the course of the oscillation, and from it the functional layer develops. Within the absence of progesterone, the arteries presenting blood to the functional layer constrict, with great care cells therein layer prove to be ischaemic and die, foremost to menstruation. It is possible to select out the part of the oscillation by means that of method of reference to each the gonad cycle (ovarian cycle) or the female internal reproductive organ cycle (uterine cycle) via looking at microscopic anatomy variations at each section, for instance:

[Table 1: Endometrial changes in different phases of ovarian cycle] [Guyton, AC and Hall, JE, eds, 2006]

Phase	Days	Thickness	Epithelium
Menstrual phase	1–5	Thin	Absent

Follicular phase	5–14	Intermediate	Columnar
Luteal phase	15–27	Thick	Columnar. Also visible are arcuate vessels of uterus
Ischemic phase	27–28		Columnar. Also visible are arcuate vessels of uterus

In 1935, Stein and Leventhal reported a series of 7 women who presented with oligo/amenorrhoea, hirsutism, obesity, infertility, and bilateral polycystic ovaries (Stein-Leventhal syndrome). Bilateral wedge resection of the enlarged ovaries was therapeutic in normalizing the menses and fertility of the women studied. They concluded that there was a primary ovarian defect, and the disorder was known as polycystic ovarian disease (PCOD). Today, PCOD has been associated with various metabolic disorders, and is now known as polycystic ovary syndrome (PCOS) [Stein, IF and Leventhal, ML, 1935].

With data controlled for age, women with PCOS are more frequently glucose intolerant or diabetic than are their non-PCOS counterparts. Impaired glucose tolerance is an independent risk factor for both type 2 diabetes mellitus and cardiovascular disease. [Legro, RS et al., 2005]. Women with PCOS are at a higher risk for endometrial hyperplasia and carcinoma. This is largely thought to be the result of unopposed estrogen associated with anovulatory cycles and the lack of progesterone-induced inhibition of proliferation and differentiation to secretory endometrium following ovulation. The degree of risk for endometrial carcinoma in women with PCOS is still being investigated [Navaratnarajah, R et al., 2008]. Breast and ovarian cancers have also been variably associated with PCOS [Balén, AH et al., 2003]. In fact, women with PCOS who undergo coronary computed tomography (CT) have more extensive coronary artery disease than do age-matched control subjects [Christian, RC et al., 2003] and in the premenopausal years, have a higher prevalence of subclinical carotid atherosclerosis [Talbot, EO et al., 2000]. This increased atherosclerotic burden leads to an increased risk of vascular complications, such as myocardial infarction [Dahlgren, E et al., 1992].

The mucous membrane in ladies with PCOS is laid low with secretion and metabolic abnormalities that contribute to some catamenial abnormalities discovered in those ladies [Giudice, L.C., 2006]. The mucous membrane of PCOS patients has high levels of insulin-like growth factor-1 (IGF-1) activity [Wu, M.-H., et al. (2004)], minimized concentrations of sex hormone-binding globulin (SHBG) [Jayagopal, V., et al. (2003)], up-regulation of mucosa aromatase, hyperandrogenemia and hyperinsulinemia. Consequently, those molecular changes increase the potential for growth changes at

intervals the mucous membrane [Chittenden, B., et al. 2009].

Endometrial Hyperplasia (EH) is associate degree abnormal proliferation of mucosa stroma and glands and represents a spectrum of mucosa changes starting from glandular atypia to frank pathologic process, that solely may be determined by a diagnostic assay. Up to simple fraction of mucosa carcinomas area unit assumed to be preceded by dysplasia [Kurman, R.J et al., 1985]. On the opposite hand, studies advised that the prevalence of endometrial carcinoma among PCOS cases is not on top of those of the final population [Holm, N.S.L., et al., 2012]. Ravn, P., et al., 2012 also suggested that the prevalence of endometrial cancer among PCOS cases is not higher than those of the general population [Ravn, P., et al., 2012]. The prevalence of endometrial carcinoma in ladies with PCOS is calculable to be around 20% to 37% [Navaratnarajah, R., 2008] that will increase even a lot of in corpulent ladies with PCOS [Calle, E.E., et al., 2003]. In distinction, a recent review explicit that this risk is overestimated [Fanta, M. 2013]. Shah, B et al, (2010) reported that in their study 31.4% of adolescent women tormented by PCOS had mucosa thickness of >7mm. therefore, there is a 4sturdy link of PCO with ET within the younger age organisation. Therefore, this association got to be recognized as early as viable to stay removed from cancerous changes.

Physiological changes that occur in such instances of PCOS area unit as a result of whereas this case takes , the process of ovulation is affected and stopped , [Nazir, F et al.,2011] that in flip results in the mucosa lining not being shed, as a result of it is miles uncovered notably to eostrogen, succeeding at intervals the thickening of the mucous membrane and, as a end product, larger hazard of mucosa most cancers [Kenneth, MN, John, SP and Eran, BL, 2001]. P. Lam et al. (2009) discovered out that reduced subendometrial blood drift on the begin of the oscillation in ladies with PCOS hispid, suggesting that hyperandrogenism might to boot have an enormous unhealthy impact on mucosa insertion. Eryilmaz, O.G., et al. (2012) represented that there is a rise in mucosa thickness at some stage within the oscillation in unimpregnated sufferers with PCOS, when in distinction to unimpregnated patients while not PCOS.

In their observe, Anthony P. Cheung(2001) examined that in anovulatory, infertile women with PCOS, mucosa thickness abundant but 7 millimeter or intermenstrual interval less than 3 months(more than four catamenial periods in line with year) is associated with proliferative mucous membrane simplest . In the end, when those criteria area unit gift, no mucosa dysplasia is expected. Compared, the hazard of finding endometrial dysplasia on mucosa diagnostic assay is expected to upward thrust via 34.6%. Further, the risk of mucosa dysplasia is expected to upward thrust by 43.2% (OR 1.432) while the amount of amenorrhea increases from 5 to 6 months if the mucosa thicknessis command constant.

Nagamani, P and Levine, D, (2007) sent that mucosa thickness of <6mm can seldom be able to conceive clearly and it is miles vital to remember that secretion various remedy (HRT) is one in every of the foremost common components in unimpregnated women that is idea to relate to improved UA and ET.

Patients And Techniques Study Methodology

On this empiric crossectional examine hundred and fifty married or single adolescent and adult women with PCOS had been divided into three age-primarily based groups of fifty every: 12 – 28 years (group I), 29-36 years (group II) and 37-50 years (group III). This study was completed 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 became finished on a whole vesica. TVS became completed on an empty vesica high-quality if the affected character turned into diagnosed with PCO at some point of TAS [Usmani A, 2012]. Physical examination was performed in each person by a medical health professional person. All PCOS subjects were tested by victimization method of a senior ultrasound specialist and patients had been evaluated with the help of transabdominal and transvaginal US.

Diagnosis of PCOS was based on the 2003 Rotterdam ESHRE/ASRMSponsored PCOS Consensus criteria [Welt, CK et al., 2006],

which include at least two of the following: (i) oligo- and/or anovulation (ANOV), (ii) biochemical hyperandrogenemia and/or hyperandrogenism (clinical signs of high androgen levels) (HA), and (iii) polycystic ovaries on ultrasound (PCO) with 12 or more follicles of 2 - 9 mm diameter in one ovary. Clinical variables such as age, body weight and height were assessed in all subjects. Body mass index (BMI) was calculated as weight (kg) divided by the square of height (m²). Biochemical hyperandrogenemia is defined as serum testosterone levels and/or serum Free Androgen Index being higher than two standard deviations above the mean levels of a normal control population. Clinical hyperandrogenism is defined as the presence of hirsutism, acne, or androgenic alopecia. Hirsutism is assessed by Ferriman-Gallwey scale (patients with scores of 8 or greater were considered hirsute [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, severe bodily hobby, associate degree gonad mass or cyst (extra than ten millimeter in diameter) detected with the helpful resource of ultrasound examination on this have a take a glance at were excluded.

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 95% confidence interval .Test for normality was done using Kolmogorov-Smirnov test. Bonferroni correction for multiple comparisons was applied. Values are considered to be statistically significant at $p < 0.05$]

The uterine area and mucosa thickness were determined by trans-abdominal and trans-vaginal scans. Uterine area and endometrial thickness: The uterine area was calculated by the formula uterine length X anteroposterior diameter in cm². The uterine length from the top of the fundus to the cervix and the anteroposterior diameter can be measured by TAS. Endometrial thickness (double layer) was considered as the widest distance from the reflective interface between the endometrium and the myometrium of opposite sides on a sagittal view of the uterus reported in millimeters (mm). The endometrial thickness was measured in mm by TVS [Shah, B, Parnell, L and Milla, S, 2010].

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 crossectional 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 I), 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 $\pm$ 3.14 years, group II was 31.78 $\pm$ 2.42 years and 39.86 $\pm$ 2.98 years in group III. The researcher observed an increase in uterine area from 19.92 $\pm$ 4.78 to 26.32 $\pm$ 3.80 ($p < 0.000$) and endometrial thickness from 6.96 $\pm$ 1.38 to 7.68 $\pm$.99 ($p < 0.011$) in group III. The present study examined that UA and ET were considerably increased in the older age group.

The current study noticed a positive correlation of age with endometrial thickness ($p < 0.011$) (Figure-1), uterine area ($p < 0.000$) (Figure-2)

Table: 2: Morphological changes in 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
UTERINE AREA	19.92±4.78	22.21±4.20	26.32±3.80	.000
ENDOMETRIAL THICKNESS	6.96±1.38	7.36±1.13	7.68±0.99	.011

Values are expressed as mean±SD: compared by One Way Anova $p < 0.05$ is considered significant 95% confidence interval. Uterine area in cm^2 , endometrial thickness in mm.

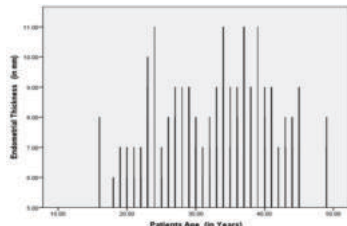


Figure 1: Picture depicting the outcome of age on endometrial thickening.

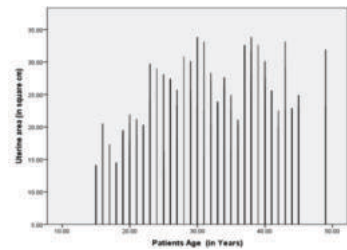


Figure 2: Picture showing a positive correlation of uterine area with age

DISCUSSION

The objective of the study was to determine the morphological changes in uterus in different age groups of adolescent and adult women with polycystic ovary syndrome. The researcher observed a substantial increase in uterine area from 19.92 ± 4.78 to 26.32 ± 3.80 ($p < 0.000$) and endometrial thickness from 6.96 ± 1.38 to 7.68 ± 0.99 ($p < 0.011$) in group III. The present study reports that UA ($p < 0.000$) and ET ($p < 0.011$) increase with age in women having PCOS. The current study is supported by the findings of Usmani, A et al. 2014. Their study revealed that ET and UA were more in the elder group and increased uterine area could be due to the presence of PCOS. In their experimental study 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. Because of the special stages of the menstrual cycle the mucous membrane of the uterus indicates variations in thickness. Those variations in thickness vary from 3mm, that is usually visible once emission, to 15mm throughout the luteal phase section. However, this thickness usually reduces once climacteric. Uncommon mucosa thickness has been associated with weight issues, PCOS and diabetes [Goldstein, SR, 2010] [Bu, Z, 2012]. The mucous membrane in ladies with PCOS is laid low with secretion and metabolic abnormalities that contribute to some catamenial abnormalities discovered in those ladies [Giudice, L.C., 2006]. The mucous membrane of PCOS patients has high levels of insulin-like growth factor-1 (IGF-1) activity [Wu, M.-H., et al. (2004)], minimized concentrations of sex hormone-binding simple protein (SHBG) [Jayagopal, V., et al. (2003)], up-regulation of mucosa aromatase, hyperandrogenemia and hyperinsulinemia. Consequently, those molecular changes increase the potential for growth changes at intervals the mucous membrane [Chittenden, B., et al. 2009]. The endometrium of women with PCOS is considered a model of dysfunctional endometrium, demonstrating over expression of androgen receptors, and failing to regulate estrogen receptors (ERs), when compared to normal women [Gregory CW et al. 2002].

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