ORIGINAL RESEARCH ARTICLE

A Comparative Study and Correlation of Role of Sonological Features and Endocrinological Markers in Establishing Diagnosis In Clinically Suspected Cases of Polycystic Ovarian Disease

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A B S T R A C T

Introduction: Polycystic ovarian syndrome (PCOS) is a common endocrine disorder of women. The cardinal features are hyperandrogenism and oligo-anovulation. A nearly universal finding is an increased Gonadotropin releasing hormone pulse frequency which favors luteinizing hormone production over follicle stimulating hormone. Increased LH subsequently promotes theca cell production of androgens, while relative FSH deficiency reduces the ability of granulose cells to convert androgen into estrogen and impairs follicle maturation and ovulation. Ultrasonography is usually performed as a first step in the in clinically suspected cases of PCOD. Using hyperandrogenism to establish diagnosis of PCOD in suspected cases and then comparing them. Hence, the aim of the present study was to assess the role of sonographic features and hyperandrogenism in establishing diagnosis in PCOD patients.

Material and Methods: Total Fifty two (52) patients with suspected PCOD were evaluated using ultrasonological and clinical/biochemical signs of hyperandrogenism. Data regarding hyperandrogenism (clinically hirsutism and serum TT) and ultrasonography changes in ovaries were collected. Relevant clinical assessment included assessment of hirsutism if present as per modified Ferriman Gallwey score system.

Results: It was found that sonological changes were present in significant number of PCOD patients 77% with p value 0.0006, similarly clinical or hormonal hyperandrogenism were also present in significant number of patients 35% with p value 0.003.In only 6 patients both sonological and the hyperandrogenism were observed.

Conclusion: Ultrasonographic features of ovarian morphology have substantial diagnostic potential to distinguish between women with PCOS and healthy women

Keywords: Polycystic Ovarian Disease, Hyperandrogenism, Gonadotropin Releasing Hormone, Follicle Stimulating Hormone, Luteinizing Hormone

INTRODUCTION

PCOS was first described as a reproductive disorder comprising menstrual irregularity, in fertility, hirsutism and enlarged polycystic ovaries, by Stein and Leventhal in 1935. In 1960s the term polycystic ovary syndrome was introduced and it is still considered as the most appropriate polycystic ovary syndrome is a common endocrine disorder of women. The cardinal feature of PCOS is hyperandrogenism and Oilgo-ovulation. Etiology is unknown but it has long term health complications, having been associated with type 2 diabetes, risk factor for cardiovascular disease.[1] The metabolic abnormalities often associated with this syndrome are not included in definition of syndrome because it is still unclear whether they are intrinsic to the disease or not.[2] There is also growing evidence that women with PCOS are at increased risk of obstructive sleep apnoea, depression, non-alcoholic fatty disease and endometrial cancer. As such this disorder is a significant public health concern in the society, which therefore indicates to accurately identify the proportion of women affected. [3]

The heterogeneous origin of PCOS has been demonstrated by several studies. Abnormality in steroidogenesis and metabolism are present, but exact link between these two pathologic features remains to be clarified. In affected women, normal ovarian function is disturbed mostly by hyperandrogenism and by the elevated serum concentrations of luteinizing hormone (LH)[7-8] thus resulting in multiple small cysts.[4] A nearly universal finding in PCOS is an

increased gonadotropin-releasing hormone (GnRH) pulse frequency with favors LH production over follicle stimulating hormone (FSH).[5] The increased LH subsequently promotes theca cell production of androgens, while the relative FSH deficiency reduces the ability of granulose cells to convert androgen into estrogen and impairs follicle maturation and ovulation.[6]

Despite PCOS being considered the most common endocrine disorder in women reproductive age prevalence estimates are highly variable, ranging 2.2% to as high as 26% this disorder is logistically difficult with necessity to carry out blood or ultrasound tests. Secondly, considerable heterogeneity in the presentation of symptoms has contributed to lack of agreement over the diagnostic criteria used to define the condition. The criteria for PCOS in adolescents follow the same clinical guidelines as those for adults. Diagnosis, however, is complicated by the fact that it is often difficult to differentiate physiologic anovulation, common in girls immediately after menarche, from true ovulatory dysfunction.[7]

Secondly ultrasound diagnosis of ovarian morphology is problematic in young girls. Tans-abdominal ovarian ultrasound, especially in obscene individuals, is less sensitive for identifying polycystic ovaries compared to trans-vaginal ultrasound which may be undesirable in virginal girls.[8]

Recently new criteria have immersed but existing prevalence estimates have been based on prior national institute of health (NIH) criteria (Rotterdam ESHRE: ASRM-sponsored PCOS consensus workshop group, 2004). Consequently, there exists the necessity to provide an estimate of PCOS prevalence that is what representative and takes into account the differences in diagnosing the disorder. NIH diagnostic criteria were based on consensus of experts who concluded that women have PCOS if they present with the combination of chronic oligo-ovulation or anovulation and clinical or biochemical sign of hyperandrogenism, with the exclusion of related disorders.[9]

The criteria for PCOS in adolescent girls follow the same clinical guidelines as those of adults. Diagnosis, however, is complicated by the fact that it is often difficult to differentiate physiologic anovulation, common in girls immediately after menarche from true ovulatory dysfunction. Secondly, ultrasound diagnosis of ovarian morphology is problematic in young girls. Trans-abdominal ovarian ultrasound, especially in obese individuals, is less sensitive for identifying polycystic ovaries compared to trans-vaginal ultrasound, which may be undesirable in virginal girls.[10] Moreover, polycystic ovarian morphology on ultrasound may be found in half of normal adolescent girls, suggesting that it could be a variant of normal or normal developmental stage during puberty.[11] Despite these problems, early recognition of the condition, particularly HA, in adolescent girls is critically important for understanding the under pinning of the disorder. Hence, the aim of the present study was to assess the role of sonographic features and hyperandrogenism in establishing diagnosis in PCOD patients.

MATERIAL AND METHODS

The present study was a prospective study conducted in the Department of Radio diagnosis and Department of Obstetrics and Gynecology, GSVM Medical College, Kanpur from December 2014 to October 2016. All the cases attending the Department of OBG, fulfilling the inclusion and exclusion criteria were selected and enrolled in the study after taking the informed written consent.

Data regarding hyperandrogenism (clinically hirsutism and serum TT) and ultrasonography changes in ovaries were collected. Women in reproductive age group;15-45 years, with menstrual irregularities; oligomenorrhea or amenorrhea and women with hyperandrogenism; assessed by hirsutism (assessed with modified Ferriman Gallwey score) with or without the other features like acne, alopecia were included in the current study. Women who have taken oral contraceptive pill within last 6 months, having other causes of infertility like hypothalamic hypogonadism, tuberculosis, endometriosis, hyperprolactinemia, having polycystic disease, ovarian and adrenal tumor (diagnosed by total testosterone or imaging modality and at least one ovarian follicle with diameter of greater than 10mm on ultrasound examination were completely excluded from the present study.

After taking appropriate history, patients were assessed clinically. Relevant clinical assessment included assessment of hirsutism if present (as per modified Ferriman Gallwey score system[12]) also the presence acne and alopecia. The Ferriman Gallwey score is a method of evaluating and quantifying hirsutism in women. The modified method uses 9 body areas to assess hair growth. The hair growth is rated from 0(no growth of terminal hair) to 4(extensive hair growth) in each of 9 locations. A patient score may therefore range from 0 to 36. While most experts refer to a modified score of 8 or more to diagnose hirsutism, some suggest a tally of 6 or more is enough to indicate hirsutism. Based on this score pattern and other clinical tests hirsutism can be evaluated as mild, moderate or severe. In this study, the score >6 has been considered for the cut off value to designate whether hirsutism is present or not. Also the presence of acne (if present in >2 areas) and alopecia was also recorded.

Patients were assessed by Grey scale mode using 3.5MHz transducer with convex array on Medison Sonoace X 8 diagnostic ultrasound installed in department of radio diagnosis GSVM medical college Kanpur. Sonographic measurements were taken in real time, according to standard protocol (Figure 1). The highest possible magnification has been used. The ovaries were assessed for follicular count per ovary, measurement of ovarian volume and ovarian stromal echogenicity assessment. Follicular count per ovary was calculated as the total number of follicles measuring 2-9mm in diameter in each or bilateral ovaries. For the diagnosis of polycystic ovaries number of follicles should be 12 or more measuring 2-9mm in diameter in unilateral or bilateral ovaries. The mean follicular count have been calculated by counting the number of follicles in both polycystic ovaries and dividing by 2(if both are (polycystic) and counting the follicles only in single polycystic ovary (if changes seen only in single ovary).

The blood samples of the patients were assessed for evaluation of serum LH, FSH, TSH, PRL and TT. For stability of specimens centrifuge them and remove serum or

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plasma from cells within 2 hours of collection. Specimens were stored at room temperature for 8hrs or refrigerate at 2-8 degree Celsius for up to 5 days. If assays were not completed within 48 hours or the separated sample is to be stored beyond 48 hours, sample should be frozen at -20 degree Celsius or colder. Frozen samples should be thawed only once.

STATISTICAL ANALYSIS

The data was entered in to the Microsoft excel sheet and was analyzed with the help of SPSS software version 22. The descriptive statistics was applied to find out the percentage. The results were presented in the form of graphs, pie-charts and tables.

Age Group	MFC in PCOD pts with Polycystic Ovaries	MFC in PCOD pts with Normal Ovaries
15-25 years	12.4	8.5
26-35 years	12.7	8.8
36-45 years	12.3	7.0
Total	12.5	8.1

Table-1: Shows the distribution of data based on mean follicular count (MFC) in polycystic and normal ovaries in PCOD patients of different age groups

Age Group	MOV in PCOD pts with Polycystic Ovaries (in cc)	MOV in PCOD pts with Normal Ovaries
15-25 years	11.0	7.6
26-35 years	10.9	4.8
36-45 years	10.8	4.5
Total	10.9	5.6

Table-2: Shows the distribution of data based on mean ovarian volume (MOV) in polycystic and normal ovaries in PCOD patients in different age groups

Testosterone level	Number of Patients	Percentage
Raised	15	29%
Normal	37	71%
Total	52	100%

Table-3: Shows the number of PCOD patients with raised TT level among the study subjects

LH/FSH ratio	Number of Patients	Percentage
Ratio >2	20	38.4%
Ratio <2	32	61.6%
Total	52	100%

Table-4: Shows the number of PCOD patients with raised LH/FSH level among the study subjects

RESULTS

In the present study, it was found that the mean age of PCOD patients is 26±7.4 years. The youngest patient was of 17 years and the oldest one was of 40 years (Graph 1). The mean BMI is 23.5±4.1 with minimum being 18.9 and maximum

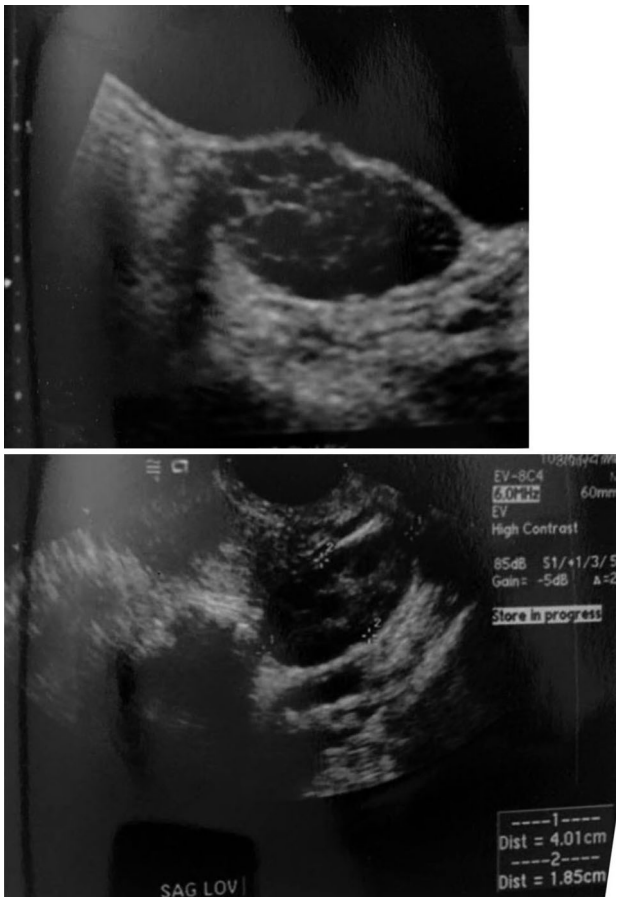
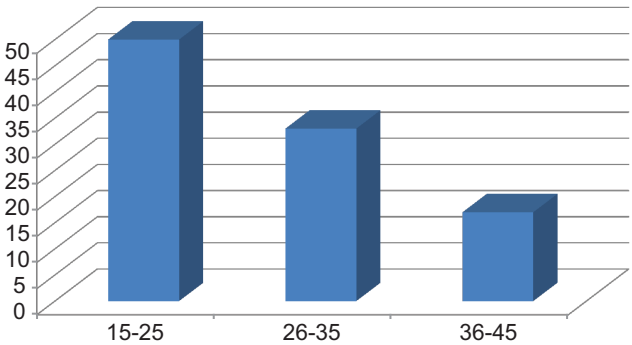


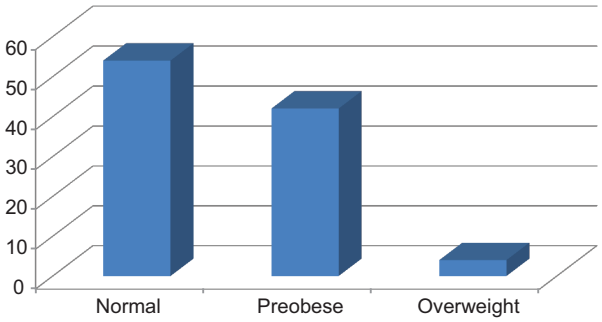
Figure-1: Shows the Ultrasonographic image of polycystic right ovary and left ovary showing multiple sub-centimetric follicles arranged peripherally.



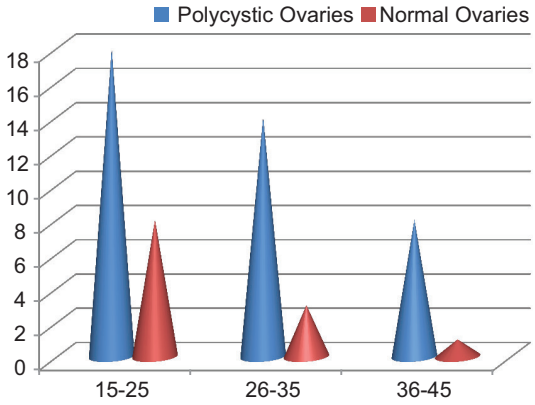
Graph-1: Shows the distribution of data based on age-group among the study subjects

Sonological changes in ovaries	Number of Patients	Percentage
PCOD with ovarian changes only	34	65%
PCOD with hyperandrogenism only	12	23%
PCOD with both ovarian changes and hyperandrogenism	6	12%

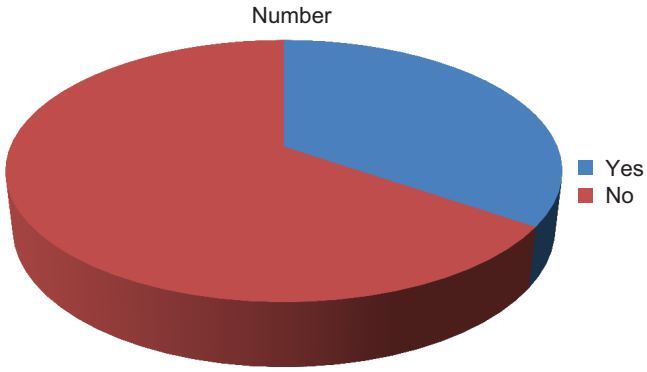
Table-5: Shows the distribution of PCOD patients having polycystic ovaries only, having hyperandrogenism only and having both polycystic ovaries and hyperandrogenism



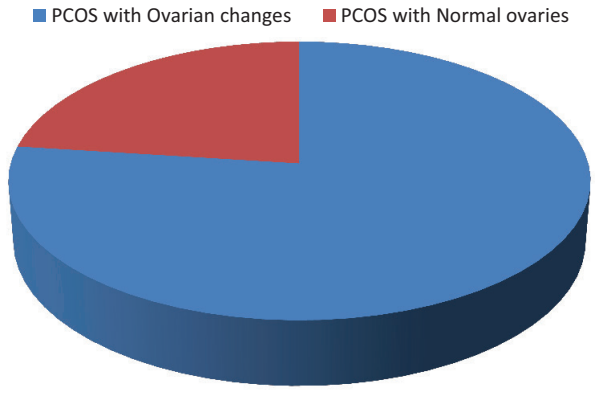
Graph-2: Shows the distribution of data based on BMI (wt in kg/ ht in meters) among the study subjects



Graph-3: Shows the age-wise distribution of data based on polycystic ovaries in PCOD patients at the time of presentation



Piechart-1: Shows the distribution of hirsutism in PCOD patients assessed with MFG scoring system



Piechart-2: Shows the distribution of PCOS patients with sonological changes in either or bilateral ovaries

being 31.0 (Graph 2). The number of PCOD patients who were assessed as per the MFG scoring system for which the hirsutism the cut off value taken is >6. Maximum number of patients belonged to the 15-25 years of age group (Graph 3). About 36% were present with hirsutism and 64% without hirsutism (Pie chart 1). About 40 (77%) patients were found to be with PCOS with ovarian changes and about 23% with PCOS were found to be with normal changes (Pie chart 2).

The mean follicular count in polycystic ovaries is 12.5±1.2 with lowest in 35-45 years of age group (MFC=12.3) and maximum in 26-35 years age group (MFC=12.7). In normal ovaries the MFC is 8.1 (Table 1).The MOV is mean ovarian volume in polycystic ovaries was found to be 10.9cc±1.1 with lowest in 35-45 years age group (MOV = 10.8cc) and maximum in 15-25 years age group (11.0cc). In normal ovaries the MOV is 5.6cc (Table2). About 15(29%) patients have raised level of total testosterone whereas about 37(71%) patients were found to have normal range (Table 3). The raised LH/FSH ratio of >2 was found to be 38.4% and LH/FSH ratio of <2 was found to be 61.6% (Table 4). Patients with only polycystic ovaries were 65%, with hyperandrogenism there were only 23% and with both polycystic and hyperandrogenism were 12% (Table 5).

DISCUSSION

PCOS is an exceptionally common disorder of premenopausal women characterized by hyperandrogenism and chronic anovulation.[13,14] A total of 52 clinically suspected patients for PCOS were evaluated using ultrasonological and clinical/ biochemical signs of hyperandrogenism. All patients were having complaints of menstrual irregularity presenting as oligomenorrhea as well as amenorrhea since 5.7months (±2.1 months). The mean age for patients was 26±7.4years and majority of patients were young belonging to 15-25 years age group.

The distribution of BMI showed that significant number of patients 46% were overweight or obese. The mean BMI was 23.5±4.1.patients having BMI within normal range were 56%. In the study conducted by Balen et al found the 41.8% patients were normal in weight and 52.9% were overweight or obese and 5.3% were underweight. Patients were assessed clinically for hirsutism and also other signs of hyperandrogenism like acne and alopecia. In an effort to reduce some of subjectivity associated with the clinical evolution of hirsutism, excessive hair growth in women is generally quantified by modified Ferriman-Gallwey scoring system.[15]

Sanchon et al evaluated that a cut off value of hirsutism score was increased from 8 or above to 10 or above latter is the figure that corresponds to 95th percentile of premenopausal women.[16] In the present study hirsutism was found to be present in 19 patients. Associated findings included acne (was included only if present in more than 2 areas) and also the alopecia. In this study sonological changes were observed in form of follicular count (MFC) in both the ovaries on dynamic scanning. Ovarian volume was measured and stromal echogenicity of ovarian stroma was also observed. The ovarian changes were seen in 40 patients (77%, p value 0.0001).

Also in a study done by Susan et al, they found that intra-observer variability in a analysis studied 54 scans in which images of polycystic and normal ovaries were duplicated and randomized for evaluation by 4 observers agreed on a diagnosis of PCOS only 51% of the time and agreed with themselves only 69% of the time the changes either in single ovary were considered to have polycystic ovaries.[17]

The mean follicular count in polycystic ovaries is 12.5±1.2 (n=40) with lowest in 35-45 years age group (MFC=12.3) and maximum in 15-25 years age group (12.7). In normal ovaries the MFC is 8.1 ±1.1 follicular counts were higher in polycystic ovaries of younger age group (45%) as compared to polycystic ovaries of other age group. The current ultrasonography guidelines, supported by ESHRE/ASRM consensus group, define polycystic ovary as containing 12 or more follicles measuring 2-9mm and/or the cut off of ≥12 follicles throughout the entire ovary was based on a single report demonstrating this value to have 99% specificity and 75% sensitivity in distinguish between polycystic and normal ovaries.

Mean ovarian volume in polycystic ovaries is 10.9cc ±1.1 (n=40) with lowest is 35-45 years age group (MOV=10.9cc) and maximum in 15-25years age group (11cc). In PCOS patients with normal appearing ovaries the MOV is 5.1cc±2.0.The cut-off value of increased ovarian volume was based on cumulative evidence reporting a larger mean volume of >10cm^3 for polycystic ovaries. In a study conducted by Lujan et al,[18] they analyzed that estimates of OV were associated with highest levels of reliability, which was not entirely surprising since the quotients for OV rely on few measurements while estimates of the follicle counts are more numerous and by virtue prone to more error. While measurements of OV were associated with highest levels of inter and intra-observer reliability, diagnostic accuracy and diagnostic confidence for this parameter were lowest reflecting the greater likelihood of overlap in OV among controls and women with PCOS.

Despite this, OV should still be considered a helpful parameter when evaluating ovarian morphology. In obese patients with PCOS it may be possible to gauge the limits of the ovary for measurements of OV and determination of polycystic ovarian morphology. The stromal echogenicity also found to be increased in patients with polycystic ovaries (n=40). The only polycystic ovaries were found in 34 patients (65%), only hyperandrogenism found in 12 patients (23%) and both features were present in 6 patients (12%). Patients were evaluated for hormonal levels measuring LH, FSH, PRL, TSH and TT. To be of value the normal range for all hormones should be precisely defines in a group of regularly ovulating women in the early follicular phase of the cycle for the assay used in each laboratory.

In a study done by Marla et al, serum levels of free testosterone and not total testosterone were more frequently elevated in women with PCOS. Serum free testosterone is therefore considered to be the more sensitive biochemical marker supporting the diagnosis of PCOS. Measurements of testosterone in serum include a portion bound to SHBG. Because PCOS is often associated with decreased SHBG levels (because of obesity and insulin resistance), increased testosterone clearance does not allow for an accurate reflection of increased androgens production.[19] The most accurate method of measuring free testosterone in serum is equilibrium dialysis, yet very few laboratories have adopted this standard because the process is complicated, expensive and labour intensive. The serum levels of TSH and PRL were within the normal ranges. FSH level is increased in 4 patients (8%).The mean value of FSH in study patients was 6.3±0.9 and maximum to be 8.2.The LH levels were raised in 5 patients (9%) with mean value 11.9±1.7. However the level of LH FSH ratio was found to be more than 2 in 20 patients. It was observed that although the LH was found to be raised in only 5 patients but the LH/FSH ratio was found to be raised in 20 patients. This showed that most of the patients who had increased LH/FSH ratio have LH levels toward higher level within the normal range.

CONCLUSION

On comparative analysis of the sonological and hormonal data of the study we found that sonological changes were present in significant number of PCOD patients 77% with p value 0.0006, similarly clinical or hormonal hyperandrogenism were also present in significant number of patients 35% with p value 0.003. In very few cases, both sonological and hyperandrogenism was observed. Thus, ultrasonographic features of ovarian morphology have substantial diagnostic potential to distinguish between women PCOS and healthy women.

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