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Evaluating Ovarian Volume as a Diagnostic Marker for Polycystic Ovary Syndrome: A Comparative Study in Iraqi Women

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ABSTRACT

Background*: One of major problems in every day obstetrics and gynecology practice is the polycystic ovarian syndrome. Despite the fact that the disease has been described since many decades; the diagnosis of the disease is still difficult. Several guidelines have been introduced to highlights the pathognomonic criteria to diagnose the disease, but, still there is debate about the adoption and interpretation of these criteria including hyperandrogenemia, ovulation and menstrual irregularities and polycystic ovarian morphology.* ***Aim of the study****: to evaluate the role of ovarian volume measured by Doppler ultrasound in prediction of PCOS diagnosis.* ***Methodology****: The study, which is of case-control design, was carried out in the Maternity and Children Teaching Hospital at Al - Diwaniyah Province, Iraq. The study included 95 women with clinical diagnosis of polycystic ovary syndrome (in accordance with Rotterdam criteria) in addition to 90 healthy control women of comparable reproductive age range. Ultrasound examination was performed for all enrolled women. Size of ovary and ovarian morphological features were assessed and contrast was made between either study category.* ***Results****: The mean volume of ovaries in PCOS women was 9.13 ±1.89 ml; whereas, that of control group was 8.16 ±1.22 ml. This variation in average ovarian volume between the two categories was statistically significant ($p<0.001$). The proportion of women with ovarian volume > 10 ml was greater in a significant way in PCOS category in comparison with the category of control individuals, 23.2 % versus 4.4 %, respectively ($p <0.001$). The cutoff value was > 9.4 ml with a specificity of 86.7 %, a sensitivity of 36.4 % and an area under curve (AUC).* ***Conclusion****: The use of ovarian volume alone is not sufficient to diagnose women with PCOS and that the used of clinical features, biochemical features, hormonal assay and ultrasound examination are all needed to label a suspected woman with such a diagnosis.*

Keywords: *Ovarian Volume, Polycystic Ovary Syndrome, Doppler Ultrasound, Morphological Features.*

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INTRODUCTION

Worldwide, polycystic ovary syndrome (PCOS) is a highly frequent abnormality of endocrine system that affects females during reproductive lifetime (1, 2). The exact prevalence globally is variable based on the particular diagnostic features applied, thus ranges between 5 % up to 15 % are reported in various literature (3). Despite great variation in diagnostic criteria, there is general agreement worldwide about polycystic ovary morphology, elevated serum androgen biochemically or clinical features of such elevation and anovulation as features for diagnosis (4-6). Nevertheless, it is worth to mention that to label women as having such

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diagnosis, other causes that gives similar clinical features, such as non-classical congenital adrenal hyperplasia, hyperprolactinemia and thyroid disease must be first excluded (7, 8). The disease is fairly common, nevertheless, there is under-diagnosis and frequent visits to the same or different physician may be needed in order to establish the diagnosis with some time consumption and delay (9, 10).

Delay in the diagnosis may result in complications which can be difficult to treat and affect adversely the quality of life of affected women (10). Some of the complications associated with PCOS include type 2 diabetes, infertility, obesity, non-alcoholic fatty liver disease, depression, metabolic syndrome, cardiovascular disease, endometrial cancer, obstructive sleep apnea, and the risk of pregnancy complications (11, 12). Thus, raising awareness of novel PCOS features may enhance the disease ascertainment in patients and avert these complications (9,10). National Institutes of Health (NIH) defined diagnostic criteria in 1990, followed by The Rotterdam 2003, the American Society for Reproductive Medicine and the European Society for Human Reproduction and ESHRE which have refined the diagnosis into the four phenotypes A, B, C, and D. The A-phenotype is characterized by the full-blown picture of the disease. The B-phenotype is also known as non-PCOS kind. The ovulatory type is labeled as C-phenotypes and the last phenotype (D-Phenotype) is characterized by being hyperandrogenic (13).

The definition of PCOS was based on ultrasound examination in 2004, which is known as the Rotterdam criteria, in which the existence of one or more of the following was considered a diagnostic criterion: the volume of the ovary must be 10 ml or more or presence of 12 ovarian follicles varying in size between 2 to 9 mm (14). Later on, in 2018, a recommendation was made by ESHRE group regarding guidelines to define PCOS, and this recommendation was about the use of ultrasound transducers transvaginal with 8 MHz frequency bandwidth. Accordingly, the existence of >20 follicle per ovary is diagnostic without considering the volume of the entire ovary (15). Despite significant advancements in imaging, there is still minimal improvement when diagnosing PCOM even with an ovarian volume (OV) of 10 mL. FNPO is still preferred above OV for the diagnosis of PCOS (16) due to its higher accuracy and lower variability. But the reliability of the measurement when comparing OV with FNPO and the counted follicles per section showed greater intra-observer and inter-observer reliability (17). Because of these findings, OV may still be considered a relevant approach to the diagnosis of PCOS.

Abundant are the studies on the associations of OV with PCOS (18), obesity (19), insulin resistance (20), androgenic activity (21, 22), metabolic syndrome (23), and AMH levels (22, 24, 25) among PCOS patients. Furthermore, while the Rotterdam criteria for PCOS specify cut-off OV of >10mL, it has been noticed that other studies due to cultural differences have suggested other boundaries for OV (13). This study aimed to find the usefulness of OV based on transvaginal ultrasonic imaging and its correlation with ovarian shape in PCOS-affected patients.

METHODS

Patients and methods

The current case-control research was carried out in the Maternity and Children Teaching Hospital at Al -Diwaniyah Province, Iraq. The study included 95 women with clinical diagnosis of PCOS based on criteria of Rotterdam in addition to 90 healthy control women of comparable reproductive age range. Ultrasound examination was performed for all enrolled women. Size of ovary and ovarian morphological features were assessed and

compared between either study groups. The inclusion criteria included PCOS women diagnosed by gynecologist specialist with no chronic medical illness and ≤ 40 years old. Women with chronic medical illness or >40 years old were excluded from the study. Ethical consideration was based on the ethical approval issued by the ethical committee pertaining to College of Medicine/ University of Al-Qadisiyah.

All participants were informed about the aim and the procedure of the current research and verbal consent was obtained. Excel part of Microsoft Office program and statistical package software (SPSS, version 16) formed the basis of statistical analysis and description. Minimum, maximum, standard deviation, and mean values have shown numerical variables in their whole. Qualitative data presented themselves as counts and proportions. Means between PCOS and control group were compared using an independent samples t-test. The Chi-square test let groups compare proportions. The ovarian volume cutoff value for predication of PCOS was derived from a receiver operating characteristic (ROC) curve. Considered a noteworthy cutoff value was the p-value of less than 0.05 or equal to it.

RESULTS

There was no statistically significant difference in average age between the subjects with PCOS and the control group (p = 0.061). The study incorporated 90 control women with a mean age of 27.76±5.9 years, and 95 women with PCOS aged 26.12±5.9 years on average. In the PCOS and control groups, moderate differences of their means body mass index (BMI) did not stand out within the sample, being 24.97 ± 4.02 kg/m2 and 25.07 ± 3.9 kg/m2 respectively (p = 0.381), as shown in table 1.

The comparison of ovarian volume calculated with the use of Doppler ultrasound in the PCOS and controls groups is presented in table 1 PCOS women's mean ovarian volume was 9.13 ± 1.89 ml while that of controls was 8.16 ± 1.22 ml. The difference in the means between the two populations was striking (p < 0.001). Moreover, proportion of women with ovarian volume greater than 10 ml was increased in the PCOS group when compared with controls, being 23.2 % and 4.4 % respectively (p <0.001). The limit value of ovarian volume for predicting PCOS was found by the ROC curve method, which results were illustrated in figure 1 and table 3. The limit value was > 9.4 ml with Area Under Curve (AUC) 0.640, sensitivity 36.4% and specificity 86.7%.

Table 1: Demographic characteristics contrasted between PCOS group and control group.

Characteristic	PCOS group *n* = 95	Control group *n* = 90	*p*
Age (years) Mean ±SD	26.12 ±5.92	27.76 ±5.93	0.061 I NS
Range	16 -39	17 -39	
BMI(kg/m^2) Mean ±SD	24.97 ±4.02	25.07 ±3.93	0.381 I NS
Range	19 -34	20 -32	

NS: not significant, **I:** independent samples t-test, **BMI:** body mass index **and SD:** standard deviation.

Table 2: Comparison of ovarian volume measured by Doppler ultrasound between PCOS group and control group.

Characteristic	PCOS group *n* = 95	Control group *n* = 90	*p*
Ovarian volume (ml) Mean ±SD	9.13 ±1.89	8.16 ±1.22	<0.001 I ***
Range	6.5 -12.8	6.5 -12.8	
≤ 10 ml	73 (76.8 %)	86 (95.6 %)	<0.001 C ***
> 10 ml	22 (23.2 %)	4 (4.4 %)	

***: significant at $p \leq 0.001$, **C**: chi-square test, **I:** independent samples *t*-test and **SD:** standard deviation.

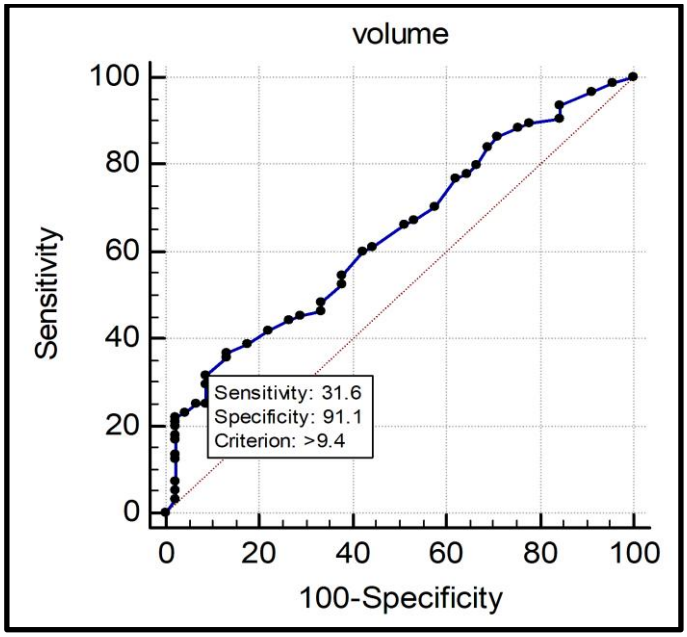

Figure 1: Receiver operating characteristic (ROC) curve analysis to calculate the ovarian volume cutoff value for prediction of PCOS.

Table 3: The statistical features of ROC curve.

Characteristic	Result
Cutoff value	> 9.4 ml
Accuracy %	64.0
Specificity %	86.7
Sensitivity %	36.4
p-value	<0.001***
AUC	0.640
95 % CI	0.566 to 0.709

***: significant at $p \leq 0.001$, **CI**: confidence interval, and **AUC**: area under the curve.

DISCUSSION

One of major problems in every day obstetrics and gynecology practice is the polycystic ovarian syndrome. Despite the fact that the disease has been described since many decades; the diagnosis of the disease is still difficult. Several guidelines have been introduced to highlights the pathognomonic criteria to diagnose the disease, but, still there is debate about the adoption and interpretation of these criteria including hyperandrogenemia, ovulation and menstrual irregularities and polycystic ovarian morphology.

The use of ultrasound to measure ovarian volume and use this criterion in the detection of PCOS has been evaluated by many researchers and the results was somewhat controversial. In this study we included 95 women with PCOS and 90 women who served as a control group. We found that overall the mean ovarian volume was higher significantly in PCOS women in comparison with control women and that significant proportion of PCOS women had a volume of > 10 ml. However, the proportion of those women was less than quarter of enrolled PCOS patients (23.2 % only), thus, we suggested that another better cutoff value might exist to predict a diagnosis of PCOS with higher sensitivity. We, thus, performed ROC curve analysis and found that 9.4 ml cutoff value is better predictor than the 10 ml already mention in the vast majority of previous literature. Nevertheless, this new predictor was again of poor sensitivity (36.4 %).

Therefore, our results are referring to that the use of ovarian volume alone is not sufficient to diagnose women with PCOS and that the used of clinical features, biochemical features, hormonal assay and ultrasound examination are all needed to label a suspected woman with such a diagnosis. The criteria adopted by The Rotterdam consensus in 2004 with respect to diagnosis of PCOS were based on two principal findings using ultrasound examination: The presence of 12 follicles or more (ranging in size between 2 and 9 mm) per ovary giving rise to a cystic morphology and/or a size of an ovary that is equal to or more than 10 ml (14). However, in 2018, a recommendation was made by ESHRE PCOS guideline committee, and this recommendation included the following statements: The use of 8 MHz frequency bandwidth transvaginal ultrasound transducers, the presence of > 20 follicles per an ovary and an ovarian volume of≥ 10 mL (15). It is noteworthy that despite significant advancements in imaging modalities, the characterization of cystic ovarian morphology remains the same at an ovarian volume of ≥10 mL (16). Furthermore, because demographic characteristics vary, several research groups have proposed different cut-off values for ovarian volume despite the Rotterdam criteria for PCOS including an ovarian volume of >10 mL (13).

Lower ovarian volume in PCOS-afflicted Asian women was previously noted (26) and was thought to vary across women in different ethnic subgroups of women (27, 28). Moreover, a woman's ovarian volume changes during her reproductive life; it peaks in size around adolescence, then decreases in maturity, and abruptly contracts during menopause (29, 30). Consequently, the variation in mean ovarian volume amongst studies may be explained by the age difference (13). According to earlier research, women with PCOS had a higher mean ovarian volume than those without PCOS (31, 32).

PCOS patients' ovaries typically displayed a higher number of tiny antral follicles along with varying degrees of cortical thickening, stromal hyperplasia and hypertrophy, and thecal cell hyperplasia and hypertrophy. These findings led to an increase in the ovarian volume (4, 33). In order to improve the sensitivity of the polycystic ovary definition, a number of studies that were based

on the Rotterdam consensus recommended a lower cut-off for ovarian volume, ranging from 6.4 to 7.5 mL (34, 35, 36). Variations in demographic variables, specifically related to ethnicity, obesity, blood insulin level, and the techniques employed to calculate the ovarian volume, may account for these discrepancies (29, 30, 37).

CONCLUSION

The use of ovarian volume alone is not sufficient to diagnose women with PCOS, and that the use of clinical features, biochemical features, hormonal assay, and ultrasound examination are all needed to label a suspected woman with such a diagnosis.

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