ORIGINAL ARTICLE

The role of ultrasound findings in detecting infertility in patients with polycystic ovary syndrome

Short title: The Role of Ultrasound in Patients with polycystic ovary syndrome

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ABSTRACT

Objective. Polycystic ovarian syndrome (PCOS) is women’s most common reproductive disorder in their childbearing years, with an estimated prevalence of 5–10%. In women with PCOS, the chance of having problems, including infertility, insulin resistance, and type 2 diabetes, increases significantly. The role of ultrasound in diagnosing PCOS is clear. In this study, we aimed to assess the diagnostic value of multiple ultrasound manifestations of PCOS in detecting infertility in patients with PCOS.

Materials and Methods. The study enrolled 246 patients with PCOS, of whom 171 (69%) had infertility and 75 (30%) were fertile. Patients underwent ultrasonography between Days 3 and 7 of the menstrual cycle to assess ovarian volume, total follicle count, follicle distribution pattern (peripherally distributed versus randomly distributed), and S/A ratio.

Results. The mean age of patients in the group without fertility problems was 28, and in patients with infertility, it was 31, but the difference was not significantly meaningful. The
sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of ovarian volume higher than 10cc for detecting infertility in patients with PCOS were 92%, 91%, 90%, and 90%, respectively. Our results show that peripherally distributed follicles and an increased ovarian volume of more than 10 cc exhibited the highest sensitivity, specificity, PPV, and NPV in detecting infertility in patients with PCOS compared with other ultrasound findings.

**Conclusions.** Peripherally distributed follicles and an increased ovarian volume of more than 10 cc could be used as an appropriate screening test for detecting infertility in patients with PCOS.

**Key words**
Polycystic ovarian syndrome; PCOS; infertility.

**Introduction:**

Polycystic ovarian syndrome (PCOS) is the most common reproductive disorder among women in their childbearing years, with an estimated prevalence of 5–10% [1-6]. It is characterized by a range of variable manifestations [7]. Evidence suggests that several vitamin imbalances and nutraceutical supplementation to counteract them may significantly affect women's health [8,9]. One of the most critical mechanisms of PCOS pathogenesis is insulin resistance. For this reason, insulin sensitizers, such as inositol isoforms, have gained increasing attention due to their safety profile and effectiveness [10].

The diagnosis of PCOS is typically based on a combination of clinical and endocrine characteristics, including elevated serum concentrations of luteinizing hormone (LH), testosterone (T), and androstenedione [11,12]. The 2003 ‘Rotterdam criteria’ allow for the diagnosis of PCOS when two out of three features are present: oligomenorrhea or anovulation, clinical or biochemical hyperandrogenism, and polycystic ovarian morphology (PCOM) observed through ultrasound examination [13-18]. In previous studies, polycystic ovary morphology (PCOM) was defined as enlarged ovaries with a mean volume of 12 cm³, characterized by an increased number of small follicles (2–8 mm) predominantly located at the periphery [19]. Other studies considered PCOM as 10 or more follicles measuring 2–8 mm in diameter arranged in a peripheral pattern around an echo-dense stroma [20,21].

Currently, the diagnosis of PCOS is typically made based on the Rotterdam criteria, which require the presence of at least two out of three criteria: (1) oligo- and/or anovulation, (2) hyperandrogenism (clinical and/or biochemical), and (3) polycystic ovary morphology (PCOM) observed through ultrasonography. PCOM is defined as 12 or more follicles measuring 2-9 mm in diameter and/or an increased ovarian volume >10 cm³ [22-26]. Additionally, several studies have investigated the role of the stroma/total area ratio (S/A ratio) in diagnosing PCOS [27-29].

Women with PCOS have a significantly increased risk of various problems, including infertility, insulin resistance, and type 2 diabetes [27]. Some studies have explored the correlation between different ultrasound criteria of PCOS, particularly the pattern of follicle distribution in the ovary, and infertility in these patients. Therefore, the aim of the current study is to compare the reliability of different ultrasound features of PCOM, such as ovary volume, S/A ratio, and the pattern of follicle distribution (peripherally located versus random distribution), in predicting infertility in patients with PCOS.
Material and methods:

The competent Ethics Committee approved our cross-sectional study, and the study was conducted following the ethical standards established in the Declaration of Helsinki of 1946. Informed consent was obtained from all participants before enrollment. The data of patients were retrospectively reviewed from September 2016 to December 2019.

A total of 246 patients diagnosed with PCOS were enrolled in the study, with 171 (69%) experiencing infertility and 75 (30%) being fertile. Infertility was the inability to conceive after one year of unprotected intercourse. The inclusion criteria for the study were clinical and laboratory evidence of PCOS. Participants who had used hormonal contraception or fertility medications within the three months before enrollment were excluded from the study.

Ultrasound Technique:

Patients underwent ultrasonography between Days 3 and 7 of their menstrual cycle. The ultrasonography examinations were performed by a diagnostic radiologist with 17 years of experience in gynecologic ultrasonography using a Voluson E6 machine (GE Healthcare, Zipf, Austria) equipped with a 2–5 MHz abdominal probe and a 7.5-MHz transvaginal probe. The examinations took place at an educational, medical hospital. Importantly, the radiologist conducting the ultrasounds was blinded to the patient’s fertility history to avoid any bias. The ovaries were scanned in both the transverse and sagittal planes during the ultrasound examinations, covering the inner to outer margins. The following measurements were recorded for each patient:

- Ovarian volume (measurement of the size of the ovaries)
- Total follicle count (count of all follicles present in the ovaries)
- Follicle distribution pattern (peripherally distributed versus randomly distributed) (Figure 1A, 1B) - (evaluation of the arrangement of follicles within the ovaries)
- Stroma/area ratio (S/A ratio) (measurement of the stroma to total ovarian area ratio)

These parameters were assessed to evaluate the ultrasound manifestations of PCOS and their association with infertility in the patients. The calculation of ovarian volume was performed based on measurements of the largest and widest diameters of the ovaries in both the transverse and sagittal planes (as illustrated in Figure 2A). An ovarian volume greater than 10 cc was considered as higher than 10 cc, while a volume of 10 cc or less was classified as less than 10 cc. The follicle distribution pattern was assessed to determine whether the follicles were predominantly distributed in a "peripheral" pattern or randomly distributed within the stroma. The stroma/area ratio (S/A ratio) was calculated for each ovary, as demonstrated in Figure 2B. It was then categorized as either higher than 0.3 or less than 0.3. These measurements and assessments were conducted to evaluate the ultrasound manifestations of PCOS and their correlation with infertility in the patients.

Results:

Patient Characteristics:

The study included 246 women with PCOS, comprising 171 patients with infertility and 75 fertile women. The mean age of patients in the group without fertility problems was 28, while in
patients with infertility, it was 31; however, the difference was not statistically significant. The mean free androgen index of patients in the group without infertility was 11, and in the group facing fertility problems, it was 12. The menstrual cycle length in patients with infertility was significantly longer than the other group (78 versus 74) (P value < 0.05) (Table 1).

**Hormonal Profiles:**
All patients exhibited abnormal hormonal profiles, characterized by elevated serum LH and testosterone levels.

**Ultrasound Findings:**
Ultrasound examinations were successfully conducted for all patients, visualizing both ovaries using transabdominal and transvaginal scans. The sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of ultrasound considering ovarian volume higher than 10cc for detecting infertility in patients with PCOS were 92%, 91%, 90%, and 90%, respectively.

**Follicle Distribution Patterns:**
When comparing the diagnostic value of patterns of follicle distribution in ovaries, a higher sensitivity, specificity, PPV, and NPV were observed for peripherally distributed follicles versus random distribution, with values of 90%, 93%, 91%, and 92%, respectively, compared to 83%, 85%, 81%, and 83%.

**Stroma/Area Ratio (S/A Ratio):**
Considering the S/A ratio higher than 0.3, ultrasound’s sensitivity, specificity, PPV, and NPV in detecting infertility were increased when compared with ovarian volume higher than 10cc.

**Combined Ultrasound Parameters:**
The highest sensitivity, specificity, PPV, and NPV of the ultrasound method for detecting infertility in patients with PCOS were obtained when considering the pattern of more than 12 follicles per ovary (peripherally distributed) along with ovarian volume higher than 10cc, with values of 98%, 97%, 96%, and 95%, respectively. However, with the same pattern (more than 12 follicles per ovary (peripherally distributed)) but with an ovarian volume less than 10cc, the sensitivity, specificity, PPV, and NPV of ultrasound for detecting infertility decreased to 82%, 84%, 78%, and 80%, respectively (Table 2).

**Discussion**
Polycystic ovary syndrome (PCOS) is a prevalent endocrine disorder among women [30]. The diagnosis of PCOS is typically based on at least two out of three criteria: oligo- or anovulation, clinical and/or biochemical signs of hyperandrogenism, and polycystic ovaries morphology observed through ultrasound examination [28]. The role of imaging in assessing various diseases is well-known [31-39]. Ultrasound is a commonly used non-invasive imaging modality for evaluating patients with PCOS.

The ultrasound criteria used to assess polycystic ovaries (PCO) in this study include the presence of 12 or more ovarian follicles measuring 2-9 mm in diameter, peripherally distributed ovarian follicles, an ovarian volume exceeding 10 cm3, and a highly echogenic ovarian stroma.
Infertility rates in individuals with PCOS are estimated to be 15 times higher than those without the condition [40].

Previous studies have investigated multiple ultrasound findings in patients with PCOS. However, few studies have investigated the correlation between ultrasound findings and infertility in patients with PCOS. This study aimed to determine the diagnostic value of different ultrasound manifestations in identifying infertility in patients with PCOS. In polycystic ovaries, the peripheral distribution of follicles has traditionally been recognized as a characteristic feature [41]. Our data revealed a higher sensitivity and specificity of ultrasound in detecting infertility among patients with PCOS when considering an ovarian volume cutoff point of 10 cc and the presence of at least 12 follicles with a peripheral distribution, consistent with previous studies [23,41,42]. Conversely, considering randomly distributed follicles per ovary resulted in lower sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) for detecting infertility in PCOS patients. Additionally, an increased stroma/area (S/A) ratio demonstrated a strong association with high sensitivity, specificity, PPV, and NPV for detecting infertility. These findings suggest that an increased central stroma of the ovary with peripherally distributed follicles is a significant predictor of infertility in patients with PCOS.

Based on our results, the combination of peripherally distributed follicles and an ovarian volume exceeding 10 cc showed the highest sensitivity, specificity, PPV, and NPV in detecting infertility among patients with PCOS compared to other ultrasound findings. Conversely, the lowest sensitivity and specificity were observed when considering peripherally distributed follicles alongside an ovarian volume of less than 10 cc. Regrettably, most of the studies conducted on patients with PCOS have focused on evaluating ultrasound findings rather than specifically assessing the diagnostic value of these findings in detecting infertility [22,28,30]. This study found that while considering the criteria of the number of follicles per ovary for PCOS, clinicians should pay more attention to the location of the follicles, which should be more peripherally distributed rather than randomly distributed.

Only a limited number of studies have investigated the relationship between ultrasound manifestations and infertility in patients with PCOS. This highlights the need for further research in this area to better understand the potential diagnostic value of ultrasound in identifying infertility in PCOS patients.

Conclusion:

Our study represents the first attempt to evaluate the significance of multiple ultrasound features of PCOS in detecting infertility among patients with the condition. According to our findings, peripherally distributed follicles with an ovarian volume exceeding 10 cc appears to be a promising screening test for identifying infertility in PCOS patients. However, it is crucial to acknowledge that these results should be validated through additional research involving larger sample sizes to ensure their reliability and generalizability. Further studies are necessary to confirm and build upon our findings to enhance our understanding of the diagnostic potential of ultrasound in assessing infertility in individuals with PCOS.

Authors contribution

Study design, clinical participation, supervision.

**Funding**

None.

**Study registration**

N/A

**Disclosure of interests**

The authors declare that they have no conflict of interests.

**Ethical approval**

The study received approval from the local Ethics Committee with the IRB number [IR.SBMU.REC.9714], and it was conducted in accordance with the ethical standards established in the Declaration of Helsinki of 1946

**Informed consent**

Informed consent was obtained from all individual participants included in the study

**Data sharing**

Data are available under reasonable request to the corresponding author

**References:**


Table 1. A comparison of clinical, hormonal features in women with PCOS with and without fertility problems.

<table>
<thead>
<tr>
<th></th>
<th>Patients with PCOS without fertility problems (n = 75)</th>
<th>Patients with PCOS with infertility (n = 171)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>28 (23–35)</td>
<td>31 (25–38)</td>
<td>0.204</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>30.1 (23.7–37.3)</td>
<td>31.1 (23.7–37.3)</td>
<td>0.008</td>
</tr>
<tr>
<td>Menstrual cycle length (d)</td>
<td>74 (46–128)</td>
<td>78 (46–128)</td>
<td>0.005</td>
</tr>
<tr>
<td>Total testosterone (nmol/l)</td>
<td>3.12 (2.50–4.50)</td>
<td>3.38 (2.50–4.50)</td>
<td>0.004</td>
</tr>
<tr>
<td>Free androgen index</td>
<td>11 (6–18)</td>
<td>12 (6–18)</td>
<td>0.009</td>
</tr>
</tbody>
</table>

Median values are presented with 25–75th quartiles in parentheses.

Table 2. Reliability of ultrasound findings in predicting infertility in patients with PCOS.

<table>
<thead>
<tr>
<th></th>
<th>Sensitivity% (95% CI)</th>
<th>Specificity% (95% CI)</th>
<th>PPV% (95% CI)</th>
<th>NPV% (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ovarian volume&gt;10cc</td>
<td>92% (71-99)</td>
<td>91% (70-98)</td>
<td>90% (68-97)</td>
<td>90% (68-97)</td>
</tr>
<tr>
<td>&gt;12 follicles per ovary (peripherally distributed)</td>
<td>90% (69-97)</td>
<td>93% (81-99)</td>
<td>91% (69-99)</td>
<td>92% (71-98)</td>
</tr>
<tr>
<td>&gt;12 follicles per ovary (randomly distributed)</td>
<td>83% (74-92)</td>
<td>85% (72-93)</td>
<td>81% (71-91)</td>
<td>83% (72-92)</td>
</tr>
<tr>
<td>S/A &gt;0.3</td>
<td>92% (71-99)</td>
<td>93% (81-99)</td>
<td>96% (85-99)</td>
<td>93% (83-99)</td>
</tr>
<tr>
<td>&gt;12 follicles per ovary (peripherally distributed) along with Ovarian volume&gt;10cc</td>
<td>98% (85-99)</td>
<td>97% (87-99)</td>
<td>96% (86-99)</td>
<td>95% (86-99)</td>
</tr>
<tr>
<td>&gt;12 follicles per ovary (peripherally distributed) along with Ovarian volume&lt;10cc</td>
<td>82% (75-93)</td>
<td>84% (71-94)</td>
<td>78% (69-85)</td>
<td>80% (75-86)</td>
</tr>
</tbody>
</table>
**Figure 1.** Demonstrates polycystic ovary with (A) randomly distributed follicles and (B) peripherally located follicles.

**Figure 2.** (A) Measuring the dimensions of the polycystic ovary with the pattern of peripherally located follicles, note the enlarged ovary. (B) Demonstrating the method of measuring the S/A ratio in the ovary in the same patient.