

Original Article

Ultrasonographic Comparison of Ovarian Stromal Blood Flow between Fertile Women with Normal Ovaries and Infertile Women with Polycystic Ovary Syndrome

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Received: 1/16/2026

Accepted: 2/20/2026

Published: 2/28/2026

HOW TO CITE

Reemal Shahid et al. 2026. Ultrasonographic Comparison of Ovarian Stromal Blood Flow between Fertile Women with Normal Ovaries and Infertile Women with Polycystic Ovary Syndrome. Journal of Health, Wellness and Community Research. 4(4). DOI: <https://doi.org/10.61919/b5yb3b76>

ARTICLE INFORMATION

Author Contributions	Concept: RS, MNB; Design: RS, KN, MNB; Data Collection: RS, KN; Analysis: RS, KN, MNB; Drafting: RS, KN, MNB.
Ethical Approval	The study was approved by research ethical board of The Superior University, Lahore, Pakistan
Informed Consent	Written informed consent was obtained from all participants
Conflict of Interest	The authors declare no conflict of interest.
Funding	No external funding.
Data Availability	Available from the corresponding author on reasonable request.
AI Declaration	No generative AI was used for conceptualization, analysis, or content generation. AI use was limited to language refinement, and the authors remain fully responsible for the accuracy, originality, validity, and integrity of the manuscript's content.

ABSTRACT

Background: Polycystic ovary syndrome (PCOS) is characterized by ovulatory dysfunction, hyperandrogenism, and altered ovarian morphology. Doppler ultrasonography may provide additional information regarding ovarian stromal vascular characteristics, although Doppler indices are not established as standalone diagnostic criteria for PCOS. **Objective:** To compare ovarian stromal blood-flow indices, ovarian morphology, and reproductive hormones between fertile women with normal ovaries and infertile women with PCOS and to examine relationships among vascular, structural, and hormonal markers. **Methods:** A cross-sectional comparative study included 120 women aged 20–35 years: 60 fertile controls and 60 infertile women with PCOS diagnosed using Rotterdam criteria. Transvaginal Doppler ultrasonography was performed on cycle days 2–4. Pulsatility index (PI), resistance index (RI), systolic-to-diastolic (S/D) ratio, vascularization index (VI), flow index (FI), vascularization-flow index (VFI), antral follicle count (AFC), and ovarian volume were assessed. **Results:** Participants with PCOS had substantially greater AFC (36.50 ± 5.64 vs 15.43 ± 4.34 ; mean difference 21.07, 95% CI 19.25–22.89) and ovarian volume (11.99 ± 2.80 vs 6.11 ± 1.30 mL; mean difference 5.88, 95% CI 5.09–6.67), together with higher PI, RI, VI, FI, and VFI; all $p < 0.001$. FSH was lower, whereas LH and testosterone were higher in the PCOS group. VI correlated positively with AFC ($r = .667$), ovarian volume ($r = .596$), LH ($r = .612$), and testosterone ($r = .591$), whereas FSH was inversely related to VI ($r = -.614$) and FI ($r = -.557$); all $p < 0.001$. **Conclusion:** PCOS was associated with marked structural, hormonal, and stromal vascular differences. Doppler indices may provide complementary physiological information but require standardized prospective validation before use for diagnosis or fertility prediction. **Keywords:** Polycystic Ovary

Syndrome; Doppler Ultrasonography; Ovarian Stromal Blood Flow; Vascularization Index; Flow Index; Antral Follicle Count; Infertility.

INTRODUCTION

Polycystic ovary syndrome is one of the most common endocrine disorders affecting women of reproductive age and represents an important cause of ovulatory dysfunction and infertility. Its prevalence varies according to the population studied and the diagnostic criteria applied, with contemporary systematic evidence confirming a substantial global burden (1,2). PCOS is a heterogeneous disorder that may include irregular or absent ovulation, biochemical or clinical hyperandrogenism, polycystic ovarian morphology, insulin resistance, obesity, acne, hirsutism, and psychological burden (1,3). Current international recommendations retain ovulatory dysfunction, hyperandrogenism, and ovarian morphology as major diagnostic domains while emphasizing exclusion of alternative causes and appropriate application of ultrasound according to age and clinical circumstances (1).

Ovarian morphology in PCOS reflects disordered follicular development and the accumulation of numerous small antral follicles, while ovarian volume may also be increased (1,4). These structural abnormalities occur within an ovarian stromal environment characterized by interacting endocrine, metabolic, and vascular alterations (3). The ovary possesses a dynamic vascular network that supports follicular development, hormone transport, steroidogenesis, and ovulation. Vascular endothelial growth factor and related signaling pathways have central roles in follicular angiogenesis, endothelial-cell activity, and the development of the ovarian microvasculature (5). Dysregulation of angiogenic pathways has also been implicated in PCOS pathophysiology, providing a biological rationale for investigating ovarian stromal vascularity in affected women (3,6).

Doppler ultrasonography permits non-invasive assessment of ovarian haemodynamic characteristics. Spectral Doppler measures such as PI and RI characterize aspects of arterial flow waveforms and vascular resistance, whereas three-dimensional power Doppler-derived VI, FI, and VFI provide quantitative measures related to vascular signal presence and flow-signal intensity within a defined tissue volume (7,8). These indices represent different haemodynamic properties and should not be regarded as interchangeable or interpreted as direct equivalents of absolute tissue perfusion (7,8).

Previous investigations have identified alterations in ovarian stromal blood-flow characteristics in women with PCOS, although the magnitude and direction of individual Doppler findings have varied across studies (9,10). Ng et al. directly compared fertile women with normal ovaries and infertile women with PCOS, providing an important precedent for the present comparative design (9). Earlier three-dimensional power Doppler research examined VI, FI, and VFI as potential quantitative markers of ovarian vascularity in PCOS (7). Differences in PCOS phenotype have subsequently been shown to influence three-dimensional ovarian and vascular parameters, while treatment-related changes in stromal blood flow have also been observed following metformin therapy (11,12). More recent research has continued to investigate three-dimensional power Doppler characteristics and their relationships with reproductive hormone concentrations, while meta-analytic evidence confirms substantial variability among published ovarian Doppler findings (10,13).

Despite this biological and imaging rationale, ovarian Doppler indices are not incorporated as standalone diagnostic criteria in contemporary evidence-based PCOS guidance (1). Their most appropriate current role is therefore as research measures or potentially complementary physiological markers rather than independent diagnostic tests. The present study compared ovarian structural, vascular, and hormonal measures between fertile women with normal ovaries and infertile women with PCOS and evaluated relationships among ovarian blood-flow indices, follicular burden, ovarian volume, and reproductive hormones.

MATERIALS AND METHODS

Study Design and Setting

A cross-sectional comparative study was conducted over six months at the gynecology and infertility outpatient department of Mian Meer Hospital and Al Nasr Laboratory.

Participants

A total of 120 women aged 20–35 years were recruited through purposive sampling. Participants were divided equally into two groups comprising 60 fertile women with normal ovarian function and normal ovaries and 60 infertile women with PCOS. Fertile controls had regular menstrual cycles and normal ovarian morphology on ultrasound. Women in the PCOS group had infertility and were diagnosed according to the 2003 Rotterdam criteria, which define PCOS on the basis of combinations of ovulatory dysfunction, hyperandrogenism, and polycystic ovarian morphology after exclusion of alternative causes (1,14).

Participants had not received hormonal therapy during the preceding three months. Women with recognized alternative causes of infertility, including endometriosis and uterine abnormalities, were excluded, as were those with major chronic medical conditions, pregnancy, hormonal contraception, or ovarian or pelvic tumors.

Ultrasonography and Doppler Assessment

Baseline transvaginal ultrasonography was performed during cycle days 2–4. Ovarian assessment included AFC and ovarian volume together with the spectral Doppler indices PI, RI, and S/D ratio and the vascular indices VI, FI, and VFI. The combined measurements were used to characterize spectral vascular impedance and stromal vascularity or flow-signal characteristics, recognizing that spectral Doppler indices and three-dimensional power Doppler vascular indices represent related but distinct components of ovarian vascular assessment (7,8).

Clinical and Hormonal Variables

Demographic and clinical variables included age, BMI, marital status, menstrual-cycle regularity, menstrual-flow pattern, dysmenorrhoea, age at menarche, bleeding duration, infertility history, and family history of PCOS. Hormonal assessment included follicle-stimulating hormone (FSH), luteinizing hormone (LH), testosterone, and anti-Müllerian hormone (AMH).

Statistical Analysis

Statistical analysis was performed using SPSS version 25. Descriptive data were summarized as mean±SD for continuous variables and n (%) for categorical variables. Independent-samples comparisons and Pearson correlation analyses were used to evaluate between-group differences and relationships among study variables. Group comparisons were additionally evaluated using Welch independent-samples t tests based on the group means, standard deviations, and sample sizes. Mean differences and corresponding 95% confidence intervals were calculated using n=60 participants per group. Two-sided p values for Pearson correlation coefficients were calculated using the corresponding r values and an analytical sample of 120 participants. A p value <0.05 was considered statistically significant.

Ethical Considerations

Ethical approval was obtained from the Institutional Review Board of Superior University, Lahore, Pakistan. Written informed consent was obtained from all participants after explanation of the study procedures, and participant confidentiality was maintained throughout the study.

RESULTS

Participant Characteristics

The mean age of the 120 participants was 27.72±4.65 years, with an age range of 20–35 years. Fifty-seven participants (47.5%) were married and 63 (52.5%) were unmarried. BMI distribution showed that 6 participants (5.0%) were underweight, 62 (51.7%) had normal weight, 35 (29.2%) were overweight, and 17 (14.2%) were obese. Irregular menstrual cycles were reported by 65 participants (54.2%), whereas 55 (45.8%) reported regular cycles. Mean menstrual-bleeding duration was 4.91±1.28 days, and mean age at menarche was 13.00±1.44 years. Dysmenorrhoea was reported by 38/60 women with PCOS and 23/60 fertile controls.

Between-Group Structural, Doppler, and Hormonal Findings

Women with PCOS had substantially higher antral follicle counts and ovarian volumes than fertile controls. All displayed Doppler indices were also higher in the PCOS group. FSH was lower, whereas LH and testosterone were markedly higher in women with PCOS.

Table 1. Participant Characteristics

Characteristic	Result
Total sample	120
PCOS	60
Fertile controls	60
Age, years	27.72±4.65
Age range	20–35
Married	57 (47.5%)
Unmarried	63 (52.5%)
Underweight BMI	6 (5.0%)
Normal BMI	62 (51.7%)
Overweight BMI	35 (29.2%)
Obese BMI	17 (14.2%)
Irregular menstrual cycles	65 (54.2%)
Regular menstrual cycles	55 (45.8%)
Bleeding duration, days	4.91±1.28
Age at menarche, years	13.00±1.44
Dysmenorrhoea, PCOS	38/60 (63.3%)
Dysmenorrhoea, controls	23/60 (38.3%)

A 2×2 analysis of dysmenorrhoea yielded a crude odds ratio of approximately 2.78, with Fisher exact $p=.010$.

Table 2. PCOS Versus Fertile Controls

Outcome	PCOS, Mean±SD	Controls, Mean±SD	Mean Difference (95% CI)	p value
Antral follicle count	36.50±5.64	15.43±4.34	+21.07 (19.25 to 22.89)	<.001
Ovarian volume, mL	11.99±2.80	6.11±1.30	+5.88 (5.09 to 6.67)	<.001
Pulsatility index	2.50±0.23	1.38±0.23	+1.12 (1.04 to 1.20)	<.001
Resistance index	0.64±0.05	0.41±0.05	+0.23 (0.21 to 0.25)	<.001
S/D ratio	3.20±0.45	2.48±0.29	+0.72 (0.58 to 0.86)	<.001
Vascularization index	1.63±0.39	0.96±0.29	+0.67 (0.55 to 0.79)	<.001
Flow index	2.53±0.56	1.79±0.41	+0.74 (0.56 to 0.92)	<.001
Vascularization–flow index	2.83±0.59	2.21±0.43	+0.62 (0.43 to 0.81)	<.001
Serum FSH, IU/L	2.84±1.15	7.40±1.34	−4.56 (−5.01 to −4.11)	<.001
Serum LH, IU/L	15.50±2.98	5.71±2.20	+9.79 (8.84 to 10.74)	<.001
Serum testosterone	113.5±30.7	27.7±14.6	+85.8 (77.1 to 94.5)	<.001

Substantial between-group differences were therefore observed for all displayed structural, Doppler, and hormonal outcomes.

Correlations With Ovarian Vascular Indices

Pearson correlation analysis demonstrated multiple relationships between clinical, structural, hormonal, and ovarian vascular variables. The strongest positive relationship was observed between VI and AFC, while FSH showed consistent inverse relationships with all three vascular indices.

Table 3. Pearson Correlations With VI, FI, and VFI

Marker	VI: r; p	FI: r; p	VFI: r; p
BMI	0.259; .004	0.151; .100	0.173; .059
Antral follicle count	0.667; <.001	0.540; <.001	0.466; <.001
Ovarian volume	0.596; <.001	0.510; <.001	0.331; <.001
Resistance index	0.634; <.001	0.514; <.001	0.470; <.001
Pulsatility index	0.604; <.001	0.534; <.001	0.450; <.001
S/D ratio	0.495; <.001	0.391; <.001	0.432; <.001
Serum FSH	−0.614; <.001	−0.557; <.001	−0.455; <.001
Serum LH	0.612; <.001	0.496; <.001	0.428; <.001
Serum testosterone	0.591; <.001	0.533; <.001	0.476; <.001
Serum AMH	0.492; <.001	0.527; <.001	0.322; <.001

The strongest positive correlation was between VI and AFC ($r=.667$, $p<.001$). VI also showed strong positive relationships with ovarian volume, PI, RI, LH, and testosterone. FSH was inversely related to VI, FI, and VFI. BMI showed a modest positive correlation with VI but was not significantly correlated with FI or VFI.

DISCUSSION

The present study identified marked structural, hormonal, and Doppler differences between infertile women with PCOS and fertile women with normal ovaries. Women with PCOS had substantially larger ovaries and more than twice the mean AFC of controls. FSH concentrations were lower, whereas LH and testosterone were substantially higher in the PCOS group. Collectively, these findings characterize a study population with pronounced morphological and endocrine differences consistent with the recognized PCOS phenotype (1,3,4).

The structural findings are consistent with established ovarian features of PCOS, particularly increased follicular number and ovarian volume, although contemporary interpretation of ovarian morphology depends on ultrasound technology, age, and clinical context (1,4). Abnormal follicular development and failure of normal follicular selection contribute to the accumulation of multiple small antral follicles, while ovarian stromal and endocrine alterations form part of the broader pathophysiological environment of PCOS (1,3). The observed endocrine pattern is also biologically consistent with PCOS, in which ovarian androgen excess and altered hypothalamic-pituitary-ovarian signaling may contribute to reproductive dysfunction, although hormonal expression varies considerably across phenotypes (1,3).

The Doppler findings require more nuanced interpretation. VI, FI, and VFI were all higher in women with PCOS, indicating greater measured vascular presence and Doppler flow-signal characteristics within the ovarian stroma. PI, RI, and the S/D ratio were also higher. Because three-dimensional power Doppler indices and spectral resistance indices represent different haemodynamic properties, their concurrent elevation should not be reduced to a single description of “increased blood flow” (7,8). The findings are more appropriately interpreted as an altered ovarian stromal vascular phenotype in which vascularity or flow-signal measures and spectral resistance measures were simultaneously increased. This distinction is important because the individual Doppler indices are not interchangeable measures of absolute tissue perfusion and may respond differently to vascular architecture, blood-flow characteristics, and acquisition conditions (7,8).

Published findings concerning ovarian haemodynamics in PCOS have not been completely uniform. Ng et al. demonstrated differences in ovarian stromal blood-flow characteristics between fertile controls and infertile women with PCOS, although not every three-dimensional vascular measure differed after adjustment (9). Pan et al. identified quantitative differences in three-dimensional power Doppler measurements in PCOS, while subsequent research demonstrated that ovarian morphology and PCOS phenotype may influence three-dimensional sonographic and vascular parameters (7,11). Treatment-related alterations in ovarian stromal blood flow have also been demonstrated following metformin therapy (12). More recent investigation has continued to identify relationships between three-dimensional power Doppler characteristics, PCOS status, and reproductive hormone concentrations (13). Meta-analytic evidence further demonstrates substantial heterogeneity in ovarian Doppler findings, supporting cautious interpretation of individual indices across different clinical and technical settings (10).

Differences among published studies may reflect PCOS phenotype, BMI, ethnicity, fertility status, cycle timing, ultrasound technology, Doppler acquisition settings, and the specific vascular index under investigation (10,11). This methodological heterogeneity is particularly relevant to comparisons involving VI, FI, and VFI because three-dimensional power Doppler indices are affected by acquisition and processing parameters rather than functioning as machine-independent physiological measurements (8). Standardization of acquisition conditions is therefore important when these measures are compared across populations or evaluated as potential clinical markers.

The strongest correlation observed in the present study was between VI and AFC. VI, FI, and VFI were positively associated with AFC and ovarian volume, suggesting that greater stromal vascular signals co-occurred with the structural characteristics that distinguished the PCOS group. VI was also positively related to LH and testosterone and inversely related to FSH. These relationships are biologically plausible because follicular development, steroidogenesis, ovarian stromal function, and vascular regulation are interconnected processes, while angiogenic signaling has been implicated in PCOS-related ovarian dysfunction (3,5,6). Recent three-dimensional Doppler research has similarly examined relationships between ovarian vascular measurements and circulating reproductive hormone concentrations in women with PCOS (13).

Interpretation of the correlations nevertheless requires consideration of the marked separation between the PCOS and fertile-control groups. When two groups differ substantially in both the predictor and

outcome variables, correlations calculated across the combined sample may reflect between-group separation as well as relationships operating within each group. Aggregated associations can therefore differ materially from subgroup-specific associations, an issue illustrated by Simpson's paradox and related forms of confounding in clinical research (15). The observed correlations consequently do not establish that increasing AFC, LH, or testosterone within women with PCOS independently predicts increasing ovarian vascularity. Within-group correlation analyses and appropriately specified multivariable models would be required to evaluate these relationships more directly.

BMI showed a comparatively weak relationship with the ovarian vascular measurements. BMI correlated modestly with VI but was not significantly related to FI or VFI. This pattern suggests that body size alone is unlikely to account for the pronounced differences in stromal Doppler measurements between the two groups. Nevertheless, metabolic disturbances are closely integrated with the pathophysiology of PCOS, particularly insulin resistance, hyperinsulinemia, obesity, and associated metabolic abnormalities (1,3). More comprehensive assessment of insulin resistance, glucose metabolism, lipid profile, and inflammatory markers would help distinguish intrinsic ovarian effects of PCOS from vascular changes associated with broader metabolic dysfunction.

Dysmenorrhoea also differed between the groups, occurring in approximately 63% of women with PCOS and 38% of fertile controls. Dysmenorrhoea is not among the defining diagnostic domains of PCOS (1). The observed association may therefore reflect accompanying menstrual characteristics or other gynecological factors rather than a direct manifestation of PCOS itself. Because the study was cross-sectional, a mechanistic relationship between PCOS and dysmenorrhoea cannot be established from these findings.

Several features strengthen the study. Equal-sized comparison groups facilitated balanced between-group evaluation, and imaging was performed within an early-cycle window to reduce variation related to menstrual-cycle timing. Structural, vascular, and hormonal characteristics were assessed within the same cohort, permitting simultaneous examination of ovarian morphology, spectral Doppler parameters, three-dimensional vascular indices, and reproductive hormones. This multidimensional approach provides a more integrated characterization of the PCOS phenotype than assessment of ovarian morphology alone.

Important limitations should also be considered. The cross-sectional design precludes determination of temporal or causal relationships, while purposive sampling from a limited number of clinical sites constrains generalizability. The comparison also combines PCOS status with fertility status because the PCOS group consisted of infertile women whereas the controls were fertile. Fertility status may therefore contribute to observed between-group differences and limits attribution of all vascular, structural, and hormonal findings exclusively to PCOS.

The pooled correlation analysis provides another important limitation because associations calculated across two strongly separated groups may partly reflect between-group differences rather than within-group biological relationships (15). In addition, some inferential analyses were based on group-level summary statistics, which limits the scope for participant-level adjustment and more detailed multivariable modeling. These considerations are particularly important when interpreting correlations between vascular indices and structural or hormonal variables.

Technical standardization of Doppler acquisition is also important. VI, FI, and VFI are sensitive to acquisition and processing conditions, including gain, pulse-repetition frequency, flow characteristics, acquisition volume, and definition of the analyzed region, and experimental evidence has demonstrated that instrument settings can materially affect measured vascular indices (8). Greater standardization of Doppler acquisition parameters and formal assessment of intraobserver and interobserver reproducibility would strengthen comparison across studies and improve evaluation of these measurements as potential clinical markers (8,10).

Current international PCOS guidance does not recommend ovarian Doppler indices as standalone diagnostic criteria (1). The present findings therefore support continued investigation of ovarian haemodynamics rather than immediate incorporation of Doppler vascular indices into routine diagnostic algorithms. Prospective studies employing standardized acquisition protocols and appropriate comparison groups could determine whether stromal vascular indices provide incremental information regarding ovulation-induction response, assisted-reproduction outcomes, or excessive ovarian response beyond established clinical, biochemical, and morphological measures.

CONCLUSION

Infertile women with PCOS demonstrated substantially greater antral follicle counts and ovarian volumes, higher VI, FI, and VFI, higher spectral PI and RI, lower FSH, and higher LH and testosterone than fertile controls. Ovarian vascularity indices were strongly associated with structural and hormonal characteristics, particularly AFC, ovarian volume, FSH, LH, and testosterone.

These relationships demonstrate an integrated structural, endocrine, and vascular PCOS phenotype but do not establish causation, within-PCOS associations, or independent diagnostic performance. Doppler ultrasonography is a promising research adjunct for characterizing ovarian haemodynamics, but standardized acquisition, within-group validation, and prospective outcome studies are required before vascular indices can be used as standalone diagnostic tests or treatment-response predictors.

STRENGTHS AND LIMITATIONS

The study used equal-sized comparison groups and assessed ovarian structure, vascularity, and reproductive hormones within the same cohort. Imaging was performed in an early-cycle window intended to reduce cycle-related variation, while the combined evaluation of morphological, spectral Doppler, three-dimensional vascular, and hormonal characteristics enabled multidimensional assessment of the study population.

The cross-sectional design prevents determination of temporal or causal relationships. The PCOS group was infertile whereas controls were fertile, creating potential confounding between fertility status and PCOS. Purposive sampling limits generalizability, and metabolic influences such as insulin resistance were not comprehensively characterized. Correlations were calculated across the two groups and may therefore partly represent between-group separation rather than within-group biological relationships. Some inferential analyses were based on group-level summary statistics, limiting participant-level adjustment. Technical standardization and reproducibility assessment of Doppler acquisition also represent important considerations when interpreting and comparing the vascular indices.

RECOMMENDATIONS

Future studies should include fertile and infertile comparison groups both with and without PCOS where feasible to distinguish PCOS-related vascular differences from those associated with infertility. Machine settings and three-dimensional Doppler acquisition protocols should be standardized and fully specified, and intraobserver and interobserver reproducibility of VI, FI, VFI, PI, and RI should be quantified.

Within-PCOS correlations and multivariable analyses should account for potentially influential variables including age, BMI, insulin resistance, phenotype, and hormonal treatment. Prospective research should further determine whether baseline stromal Doppler measures provide clinically useful information regarding ovulation-induction response, IVF outcomes, or ovarian hyper-response.

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