Can ovarian stromal blood flow predict the response to stimulation in polycystic ovary syndrome patients undergoing infertility treatment

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Abstract

Aim: To find out the difference in ovarian stromal blood flow in polycystic ovary syndrome (PCOS) and non-PCOS infertile patient and role of ovarian stromal blood flow as predictor of follicular response. **Design:** Prospective study. **Setting**: KJIVF and Laparoscopy Centre, Delhi. **Materials and methods**: Total 120 patients were recruited and divided into two equal groups. PCOS and non-PCOS infertile women of less than 35 years of age undergoing intrauterine insemination and *in vitro* fertilization (IVF) were included. Baseline and poststimulation two-dimensional transvaginal ultrasound with color and power Doppler was performed. Blood flow velocity waveforms with optimal flow were selected for measurement of systolic/diastolic ratio, peak systolic velocity (PSV), pulsatility index, and resistive index. **Intervention:** Color Doppler for ovarian stromal blood flow. **Statistical analysis:** Statistical testing was performed with the statistical package for the social science system version SPSS 17.0. **Results:** (a) Day 2/3 ovarian stromal PSV was significantly higher in PCOS women when compared with non-PCOS. (b) Positive correlation between ovarian stromal PSV and follicular response in patients with both PCOS and non-PCOS. **Conclusion:** Stromal vascularity in PCOS can be used as an additional criterion for the diagnosis of PCOS and ovarian stromal blood flow can be used as predictor of follicular response in IVF cycles especially in patients with PCOS.

Keywords: NON-PCOS, ovarian stromal blood flow, PCOS

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INTRODUCTION

Polycystic ovary syndrome (PCOS) is the commonest anovulatory disorder in infertility practice. Anovulation is the cause of infertility in 30% of the cases, and 90% of anovulation cases are actually caused by PCOS.[1]

In addition, patients with PCOS are more prone to develop ovarian hyperstimulation syndrome (OHSS) and Doppler may help in predicting OHSS.

Other than variety of paracrine and endocrine factors,[2] adequate blood supply plays an important role for normal ovarian function.[3] Ovarian stromal microvasculature has been assessed with the use of both color and power

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Doppler in normal as well as polycystic ovaries.[4] Some authors have found significantly higher vascularity among PCOS,[5-7] whereas others did not.[8,9] In addition, it can be used as a predictor of follicular response as described by few studies[10-13] but with no definite consensus.

Therefore, we conducted this study to gain insight into the ovarian stromal blood flow in infertile women with PCOS when compared with women with non-PCOS with normal ovarian reserve. In addition, our goal was to evaluate the association of Doppler indices to the follicular response to gonadotropin stimulation in controlled ovarian stimulation and to predict the response to stimulation during intrauterine insemination (IUI)/*in vitro* fertilization (IVF) cycles.

SUBJECTS AND METHODS

This was a prospective controlled study conducted at our center for a period of 6 months from November 2020 to April 2021.

Study population

All patients with infertility with PCOS and non-PCOS women attending the assisted reproductive technology (ART) center and meeting the inclusion criteria were selected.

Inclusion criteria:

(1) Patients with PCOS undergoing IUI or IVF cycles in study group
(2) Normal ovarian reserve patients undergoing IUI or IVF cycles in controlled group.
(3) Age less than 35 years.

Exclusion criteria:

(1) Patient with thin endometrium less than 7 mm
(2) Abnormal morphology
(3) High resistance flow and absent subendometrial blood flow on Doppler
(4) Immunologic factors such as antiphospholipid syndrome
(5) Endometriosis and other pelvic pathology
(6) History of investigation report suggestive of Koch.
(7) Deranged thyroid and prolactin levels.

Sample size

The total sample size was set as 120 [60 per group calculated from an effect size of 0.8, power of 80%, and of 0.05, where the standard deviation (SD) of two groups was 2.5].

Our sample size was based on Doppler measurement between patients with normal ovaries and those with polycystic ovaries. A previous study[13] using a similar protocol indicated that patient with polycystic ovaries had a higher mean ovarian stromal peak systolic velocity (PSV) than patients with normal ovaries.

The formula for calculating sample size is as follows:

$$n = \frac{(\delta_1^2 + \delta_2^2) \cdot [Z_{1-\alpha/2} + Z_{1-\beta}]^2}{(M_1 - M_2)^2}$$

where $Z\alpha/2$ is the critical value of normal distribution at $\alpha/2$ (e.g., for a confidence level of 95%, *a* is 0.05, and the critical value is 1.96), Z_β is the critical value of the normal distribution at β (e.g., for a power of 80%, $b\beta$ is 0.2), and M_1 and M_2 are the expected sample mean of the two groups. *s*1 and *s*2 are the expected sample SD of the two groups.

The patients were divided into two groups.

Study group: Infertility patients with PCOS as defined by Rotterdam criteria.[14]

Control group: Non-PCOS infertility patients.

Rotterdam criteria: The presence of two from the following three diagnostic criteria:

(1) oligo- and/or anovulation,
(2) clinical and/or biochemical features of hyperandrogenism, and
(3) the presence of polycystic ovary morphology.

To make a diagnosis of polycystic ovaries, either 12 or more follicles measuring 2 to 9 mm in diameter or increased ovarian volume (10 cm^3) should be present on scanning. Written informed consent was taken from all the selected women in a language understood by them. All patients underwent transvaginal sonography on day 2 or day 3 of the menstrual cycles as routinely performed at our center. Single examiner performed the ultrasound and Doppler studies in all women to avoid interobserver variation. In addition, basal endocrine hormonal profiles were assessed as routinely performed at our center. After complete evaluation, patient underwent superovulation in IUI and controlled ovarian hyperstimulation in IVF cycles depending on the patient's age and previous response. Monitoring of follicular growth was carried out with serial ultrasound scans and the dose was adjusted according to the follicular response as routinely performed. In addition, all selected patients underwent repeat Doppler studies after gonadotropin stimulation on the day of human chorionic gonadotropin (HCG) administration. When three or more leading follicles at least 18 mm in diameter in IVF cycles and one leading follicle more than 18 mm in IUI cycles as measured by ultrasound, 5000 IU of HCG was administered.

Ovarian Doppler studies

Color and power Doppler ultrasound was performed to record of variance from Doppler flow with the use of two dimensional (2D) endovaginal probe of 5 to 9 MHz frequency. The areas of maximum color intensity represent the greatest Doppler frequency shifts for pulse Doppler examination. Blood flow velocity waveforms with optimal flow were selected for measurement of systolic/diastolic (S/D) ratio, PSV, pulsatility index (PI), and resistive index (RI). A recording was taken as satisfactory when there were at least three equally intense waveforms in a row. For each woman, the average of each index in stimulated ovary was calculated and used for statistical analysis.

Statistical analysis

Statistical testing was performed with the statistical package for the social science system version SPSS 17.0 (IBM). Continuous variables were presented as mean ± SD or median (interquartile range) for non-normally distributed data. Categorical variables were expressed as frequencies and percentages. The comparison of normally distributed continuous variables between the groups was performed using Student t test. Nominal categorical data between the groups were compared using Chi-squared test for Fisher exact test as appropriate. Non-normal distribution continuous variables were compared using Mann–Whitney U test. For all statistical tests, $P < 0.05$ was taken to indicate a significant difference.

Ethical clearance: Ethical clearance was taken from ethical committee.

Financial statement: Cost of Doppler was borne by our center.

RESULTS

In this study, a total of 120 subjects were recruited and divided into two equal groups: patients with PCOS and patients with non-PCOS with normal reserve.

Table 1 summarizes the basic characteristics of patients such as age, duration of infertility, etc., which were similar. No patients had severe obesity even in PCOS group. Equal number of patients underwent both the procedures, that is, IUI and IVF in both groups. Average number of follicles formed and the protocol used for superovulation/COH and mean dose of gonadotropin used were also similar in both of the groups. However, mean duration of gonadotropin stimulation was statistically significantly less in PCOS group than in non-PCOS group in patients undergoing IUI or IVF. Higher LH/FSH ratio and anti mullerian hormone (AMH) levels as high as 9 ng/mL were observed in PCOS group and the values were higher in patients with OHSS. Hormonal profile was normal in non-PCOS group.

There were no significant differences in the baseline ovarian Doppler indices between right and left ovaries and so the mean value was calculated for each patient and

Table 1: Baseline characteristics of PCOS and non-PCOS group

Characteristics		PCOS (N = 60)	Non-PCOS (N = 60)	P-value
Mean age	(years)	27.5±3.52	26.8 ± 3.74	0.44
Mean duration of infertility	(years)	3.9 ± 2.76	4.2 ± 2.81	>0.5
BMI (kg/m^2)N (%)	(≤25)	35 (58.3)	38 (63.3)	0.65
	(>25)	25 (41.6)	22 (36.6)	
Procedure done$N$ (%)	IUI	30(50)	30 (50)	1.00
	IVF	30(50)	30 (50)	
Average number of follicles	IUI	1.7 ±.97	1.5 ± 0.68	>0.5
	IVF	12 ± 3.98	10.9 ± 2.9	
Mean dose of gonadotropin	IUI	547.5 ± 203.25	697.5 ± 302.1	0.20
	IVF	1687.5 ± 265.16	1912.5 ± 372.9	0.13
Mean duration of gonadotropin	IUI	9.2 ± 0.42	10.2 ± 0.78	0.002
	IVF	9.8 ± 0.42	11.0 ± 0.94	0.002
Superovulation/COH	Letrozole	12(20)	18 (30)	0.56
	Gonadotropin	34 (56.6)	31 (51.6)	
	Letrozole andgonadotropin	14 (23.3)	11 (18.3)	

PCOS, polycystic ovary syndrome; BMI, body mass index; IUI, intrauterine insemination; IVF, *in vitro* fertilization.

used for further analysis. Baseline and Doppler parameters after stimulation by HCG included PSV (cm/second), S/D ratio, RI, and PI.

Mean value of baseline PSV was significantly higher for PCOS group than non-PCOS group in Table 2. However, no significant difference in two groups poststimulation was found.

Patients with hyperresponse in PCOS group had statistically significantly increased PSV and decreased S/D ratio in comparison with normal response in baseline scan. Low S/D ratio is suggestive of low resistance flow in ovaries which was found in patients with hyperresponse [Table 3], even though there was no difference in RI or PI. However, there was no significant difference in Doppler parameters between PCOS and non-PCOS group in poststimulation.

Table 4 summarizes strong uphill correlation between PSV and follicular response at baseline in IVF subjects in both the groups. In addition, the correlation was found to be moderate uphill in IUI in both groups, whereas baseline RI showed mild downhill correlation with follicular response in IVF subjects. S/D and PI did not show any correlation in baseline in both groups.

The PSV was found to be significantly higher in subjects with body mass index (BMI) ≤ 25 at baseline than in subjects with BMI > 25 [Table 5], whereas baseline S/D ratio and PI were found to be significantly lower in subjects with BMI ≤ 25. However, no such significance was reached in poststimulation phase [Table 5].

Similarly, in PCOS group, patients with BMI ≤ 25 were found to be associated with higher baseline PSV values than patients with PCOS with BMI > 25 [Table 6].

Non-PCOS subjects with lower BMI showed significantly higher baseline PSV, whereas S/D ratio as well as RI was significantly lower [Table 7].

Table 8 compares changes in Doppler parameter on stimulation. PSV was found to be significantly increased and S/D ratio, RI, and PI were found to be significantly decreased poststimulation in total population as well as in PCOS and non-PCOS groups.

Table 2: Baseline ovarian stromal Doppler indices in the PCOS and non-PCOS group

	Doppler indices	PCOS	Non-PCOS	*P*-value
Baseline Doppler parameters	PSV (cm/second)	11.46 ± 2.4	9.07 ± 2.4	<0.0001
	S/D ratio	2.97 ± 0.53	3.16 ± 0.41	0.085
	RI	0.78 ± 0.69	0.79 ±0.08	0.675
	PI	1.4 ± 0.34	1.53 ± 0.24	0.104
Doppler parameters on the day of stimulation by HCG	PSV (cm/second)	15.33 ± 3.72	16.40 ± 4.34	0.243
	S/D ratio	2.42 ± 0.5	2.52 ± 0.39	0.282
	RI	0.60 ± 0.09	0.59 ± 0.07	0.621
	PI	1.06 ± 0.25	1.04 ± 0.25	0.742

PCOS, polycystic ovary syndrome; PSV, peak systolic velocity; HCG, human chorionic gonadotropin; PI, pulsatility index; RI, resistive index; S/D, systolic/diastolic.

Table 3: Association of baseline Doppler parameter to follicular response in PCOS group of normal response and hyperresponse in *in vitro* fertilization patients

	Doppler indices	PCOS normal response	PCOS hyperresponse	*P*-value
Baseline Doppler parameters	PSV (cm/second)	10.69 ± 1.92	14.21 ± 1.67	0.002
	S/D ratio	3.32 ± 0.57	2.52 ± 0.56	0.017
	RI	0.81 ± 0.05	0.82 ± 0.03	0.592
	PI	1.44 ± 0.33	1.38 ± 0.26	0.649

PCOS, polycystic ovary syndrome; PSV, peak systolic velocity; PI, pulsatility index; RI, resistive index; S/D, systolic/diastolic.

Table 4: Doppler parameters in patients undergoing IUI and IVF in PCOS and non-PCOS group

Doppler parameters		PCOS		Non-PCOS	
		IUI (*N* = 30)	IVF (*N* = 30)	IUI (*N* = 30)	IVF (*N* = 30)
Baseline	PSV (cm/second)	0.758*	0.888*	0.670*	0.823*
	S/D ratio	0.451	0.416	−0.305	− 0.315
	RI	−0.113	−0.122	−0.353	− 0.591*
	PI	−0.082	− 0.118	0.167	0.193

PCOS, polycystic ovary syndrome; PSV, peak systolic velocity; IVF, *in vitro* fertilization; IUI, intrauterine insemination; PI, pulsatility index; RI, resistive index; S/D, systolic/diastolic. *$P < 0.05$.

Table 5: Association of Doppler parameters with BMI in total study population

Doppler parameters baseline	Doppler parameters	BMI $\leq$ 25(N = 73)	BMI $>$ 25(N = 47)	P-value
	PSV (cm/second)	11.04 ± 2.76	9.10 ± 2.21	0.001
S/D ratio	2.94 ± 0.49	3.25 ± 0.41	0.004	
RI	0.78 ± 0.07	0.80 ± 0.08	0.145	
PI	1.40 ± 0.29	1.60 ± 0.28	0.004	

BMI, body mass index; PSV, peak systolic velocity; PI, pulsatility index; RI, resistive index; S/D, systolic/diastolic.

Table 6: Association of Doppler parameters with BMI in patient with PCOS

Doppler parameters baseline	Doppler parameters	BMI $\leq$ 25(N = 35)	BMI $>$ 25(N = 25)	P-value
	PSV (cm/second)	12.42 ± 2.35	10.20 ± 1.89	0.03
S/D ratio	2.84 ± 0.57	3.15 ± 0.43	0.072	
RI	0.79 ± 0.04	0.78 ± 0.09	0.770	
PI	1.31 ± 0.29	1.58 ± 0.36	0.014	

BMI, body mass index; PCOS, polycystic ovary syndrome; PSV, peak systolic velocity; PI, pulsatility index; RI, resistive index; S/D, systolic/diastolic.

Table 7: Association of Doppler parameters with BMI in patient with non-PCOS

Doppler parameters baseline	Doppler parameters	BMI $\leq$ 25(N = 38)	BMI $>$ 25(N = 22)	P-Value
	PSV (cm/s)	9.8 ± 2.54	7.86 ± 1.90	0.015
S/D ratio	3.03 ± 0.38	3.37 ± 0.37	0.010	
RI	0.77 ± 0.091	0.83 ± 0.06	0.028	
PI	1.48 ± 0.27	1.62 ± 0.16	0.087	

PCOS, polycystic ovary syndrome; BMI, body mass index; PSV, peak systolic velocity; PI, pulsatility index; RI, resistive index; S/D, systolic/diastolic.

Table 8: Comparison of changes in Doppler parameter on stimulation

Group	Parameter	Day 2	Poststimulation	P-value
Total (N = 120)	PSV (cm/second)	10.27 ± 2.71	15.87 ± 4.05	<0.0001
	S/D ratio	3.06 ± 0.48	2.47 ± 0.45	<0.0001
	RI	0.79 ± 0.07	0.59 ± 0.08	<0.0001
	PI	1.48 ± 0.36	1.05 ± 0.25	<0.0001
PCOS (N = 60)	PSV (cm/second)	11.46 ± 2.40	15.33 ± 3.72	<0.0001
	S/D ratio	2.97 ± 0.53	2.41 ± 0.78	<0.0001
	RI	0.78 ± s0.06	0.60 ± 0.09	<0.0001
	PI	1.42 ± 0.35	1.06 ± 0.25	<0.0001
Non-PCOS(N = 60)	PSV (cm/second)	9.07 ± 2.48	16.04 ± 4.34	<0.0001
	S/D ratio	3.16 ± 0.41	2.52 ± 0.039	<0.0001
	RI	0.79 ± 0.08	0.59 ±0.04	<0.0001
	PI	1.53 ± 0.24	1.04 ± 0.25	<0.0001

PCOS, polycystic ovary syndrome; PSV, peak systolic velocity; PI, pulsatility index; S/D, systolic/diastolic.

DISCUSSION

Monitoring of stimulated cycles is performed primarily by 2D ultrasound. Most scans are carried out in gray scale. Additionally, color and power Doppler has been observed as prognostic tool. With newer machines having better resolution, power pulse Doppler, virtual organ computer-aided analysis imaging program may further simplify monitoring.

This study was aimed to compare the ovarian stromal vascularity among PCOS and normal reserve non-PCOS group and to assess the role of ovarian stromal blood flow in predicting ovarian follicular response in patients undergoing ovarian stimulation.

When we recorded and compared baseline ovarian Doppler parameters, significantly higher baseline PSV was found among PCOS women when compared with non-PCOS women. Panchal and Nagori[15] also suggested stromal PSV of 5-10 cm/second in normal ovaries with normal reserve and response. They also stated that if ovarian stromal PSV is >10 cm/second, then ovaries are prone to hyperstimulation. In our study, six patients from PCOS group undergoing IVF had hyperresponse and were found to have statistically significantly increased mean PSV and decreased S/D ratio in comparison with patients with normal response in PCOS group. No difference was found between RI and PI in these patients. No patient in IUI group had hyperresponse because of strict protocol and monitoring.

Pan *et al.* in their study compared and quantified three-dimensional power Doppler parameters in patients with PCOS to patients with non-PCOS.[16] They found significantly increased ovarian stromal vascular flow index (VFI) 2.1 ± 1.32 than 0.80 ± 0.97, flow index (FI) 50.26 ± 3.02 than 44.44 ± 5.42, vascularization index (VI) 3.99 ± 2.38 than 1.44 ± 1.20, and ovarian volume 12.9 ± 4.27 than 6.10 ± 3.14 in PCOS group than in non-PCOS group.

Considering the fact that adequate blood flow is necessary for follicular development and polycystic ovaries are highly sensitive to gonadotropin treatment, it can be inferenced that inherent higher ovarian stromal vascularity may be responsible, for the exaggerated response to ovarian stimulation in patients with PCOS.[17] Engmann *et al.*[18] also demonstrated significantly higher ovarian stromal PSV among PCOS women on baseline in early follicular phase, on the HCG administration day, and even after pituitary downregulation. Additionally, LH in patients with PCOS varied from 2.1 IU/L to 6.2 IU/L with mean value of 2.6 IU/L, whereas in patients with non–PCOS, it was normal.

We found no significant difference in PI, RI, and S/D ratios between two groups which was in accordance with the study by Younis *et al.*[13] Younesi *et al.*[19] also found no significant difference in RI. But in contrast, Ozkan *et al.*[20] reported significantly lower PI, RI, and S/D ratios in PCOS group than in normal patients in bilateral ovarian arteries.

In our study, we found that there was significant difference between baseline and poststimulation Doppler parameters. We found that PSV was increased, whereas S/D ratio, RI, and PI were decreased significantly. Pinkas *et al.*[21] also documented decrease in RI and PI on prestimulation and on HCG day.

In the present study, positive correlation was detected between baseline ovarian stromal PSV and follicular response among both the groups similar to previous studies. Zaidi *et al.*[10] demonstrated that mean ovarian PSV was significantly correlated with the ovarian follicular response, after adjusting for the confounding factors. In poor response, group mean ovarian stromal PSV was significantly lower when compared with PCOS women. We could not compare this with poor response group because none of our patient has shown poor response on stimulation. Engmann *et al.*[18] also suggested association between ovarian stromal blood flow PSV and the number of oocytes retrieved.

On the other hand, Ng *et al.*[9] demonstrated that ovarian stromal blood flow indices have no role in predicting the ovarian follicular response. They also observed that normal weight BMI PCOS women were found to have significantly higher total ovarian VI/FI/VFI than overweight PCOS women. So they concluded that normal weight PCOS women had significantly higher vascularization indices when compared with overweight PCOS. Similarly, we also noted that PSV was found to be significantly higher in the subjects with BMI ≤ 25 at both baseline and poststimulation in both the groups, whereas S/D ratio and PI were found to be significantly lower in these patients. However, in PCOS group, all patients had BMI varying between 25 and 27 and in non-PCOS group, the BMI varied between 25 and 25.6. Hence, only minimal deranged BMI patients were recruited. Similar to our study, Arora *et al.*[22] positively correlated the predictive value of ovarian stromal blood flow with follicular response.Our results also showed that ovarian stromal blood flow helps in predicting clinical pregnancy in non-PCOS women with normal ovarian reserve undergoing IVF cycle. Baseline PSV was found to be significantly higher among pregnant women in this group; however, it was not significant in PCOS group or in total patients. It may be an incidental finding and requires more data for any consensus. In one previous study which has showed the role of stromal blood flow for prediction of pregnancy, stromal ovarian PSV was found to be significantly higher in the conception PCOS group when compared with the non-conception group.[18] However Younis *et al.*[13] concluded that ovarian stromal blood flow has no role in predicting IVF outcome. More studies are needed before reaching a definite conclusion on this issue.

Strength of the study:
(1) Prospective study
(2) Similar baseline characteristics of both the groups such as age and mean duration of infertility.
(3) Monitoring by 2D power Doppler ultrasound which is the mainstay of patient's monitoring in almost all centers.
(4) Ultrasounds performed by a single operator that limits the interobserver bias.

Limitations of the study:
(1) Small sample size.
(2) No poor responders/anovulation during study period.

CONCLUSION

(1) Baseline ovarian stromal PSV was found to be significantly higher for PCOS group (11.46 ± 2.4)

compared to normal reserve non-PCOS group. Higher PSV suggests higher ovarian stromal vascularity in PCOS which could be used as an additional criterion for diagnosis of PCOS.

(2) No significant difference was found between RI, PI, and S/D between two groups.

(3) Baseline PSV in patients with hyperresponse in PCOS group was higher (14.21 ± 1.67) and S/D ratio was lower (2.52 ± 0.56) compared to normal response group.

(4) Baseline PSV was found to be significantly higher in subjects with BMI ≤ 25, whereas S/D ratio and PI were found to be significantly lower when compared with subjects with BMI ≥ 25 but it could not be correlated with any difference in ovarian follicular response between these groups.

(5) Strong positive correlation was detected between baseline PSV and ovarian follicular response after gonadotropin stimulation in IVF subjects among both the groups, hence could be used as a predictor for predicting follicular response in IVF cycles.

(6) More studies with wider sample size are needed before reaching to any definite conclusion.

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Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Balen AH, Rutherford AJ. Managing anovulatory infertility and polycystic ovary syndrome. BMJ 2007;335:663-6.
2. McGee EA, Hsueh AJ. Initial and cyclic recruitment of ovarian follicles. Endocr Rev 2000;21:200-14.
3. Redmer DA, Reynolds LP. Angiogenesis in the ovary. Rev Reprod 1996;1:182-92.
4. Guerriero S, Ajossa S, Lai MP, Risalvato A, Paoletti AM, Melis GB. Clinical applications of colour Doppler energy imaging in the female reproductive tract and pregnancy. Hum Reprod Update 1999;5:515-29.
5. Zaidi J, Campbell S, Pittrof R, Kyei-Mensah A, Shaker A, Jacobs HS, *et al.* Ovarian stromal blood flow in women with polycystic ovaries – a possible new marker for diagnosis? Hum Reprod 1995;10:1992-6.
6. Battaglia C, Artini PG, D'Ambrogio G, Genazzani AD, Genazzani AR. The role of color Doppler imaging in the diagnosis of polycystic ovary syndrome. Am J Obstet Gynecol 1995; 172(Pt 1): 108-13.
7. Lam PM, Johnson IR, Raine-Fenning NJ. Three-dimensional ultrasound features of the polycystic ovary and the effect of different phenotypic expressions on these parameters. Hum Reprod 2007;22:3116-23.
8. Järvelä IY, Mason HD, Sladkevicius P, *et al.* Characterization of normal and polycystic ovaries using three-dimensional power Doppler ultrasonography. J Assist Reprod Genet 2002;19:582-90.
9. Ng EHY, Chan CCW, Yeung WSB, Ho PC. Comparison of ovarian stromal blood flow between fertile women with normal ovaries and infertile women with polycystic ovary syndrome. Hum Reprod 2005;20:1881-6.
10. Zaidi J, Barber J, Kyei-Mensah A, Bekir J, Campbell S, Tan SL. Relationship of ovarian stromal blood flow at the baseline ultrasound scan to subsequent follicular response in an in vitro fertilization program. Obstet Gynecol 1996;88:779-84.
11. Bassil S, Wyns C, Toussaint-Demylle D, Nisolle M, Gordts S, Donnez J. The relationship between ovarian vascularity and the duration of stimulation in in-vitro fertilization. Hum Reprod 1997;12:1240-5.
12. Younis JS, Haddad S, Matilsky M, Radin O, Ben-Ami M. Undetectable basal ovarian stromal blood flow in infertile women is related to low ovarian reserve. Gynecol Endocrinol 2007;23:284-9.
13. Younis JS, Jadaon JE, Haddad S, Izhaki I, Ben-Ami M. Prospective evaluation of basal stromal Doppler studies in women with good ovarian reserve and infertility undergoing in vitro fertilization-embryo transfer treatment: patients with polycystic ovary syndrome versus ovulatory patients. Fertil Steril 2011;95:1754-8.
14. Rotterdam ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group. Revised 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome. Fertil Steril 2004;81:19-25.
15. Panchal S, Nagori CB. Ultrasound in infertility. Donald Sch J Ultrasound Obstet Gynecol 2015;9:100-10.
16. Pan HA, Wu MH, Cheng YC, Li CH, Chang FM. Quantification of Doppler signal in polycystic ovary syndrome using three-dimensional power Doppler ultrasonography: a possible new marker for diagnosis. Hum Reprod 2002;17:201-6.
17. Pinkas H, Mashiach R, Rabinerson D, *et al.* Doppler parameters of uterine and ovarian stromal blood flow in women with polycystic ovary syndrome and normally ovulating women undergoing controlled ovarian stimulation: uterine and ovarian blood flow in women with PCOS. Ultrasound Obstet Gynecol 1998;12:197-200.
18. Engmann L, Sladkevicius P, Agrawal R, Bekir J, Campbell S, Tan SL. The pattern of changes in ovarian stromal and uterine artery blood flow velocities during in vitro fertilization treatment and its relationship with outcome of the cycle: Ovarian and uterine artery blood flow during IVF. Ultrasound Obstet Gynecol 1999;13:26-33.
19. Younesi L, Safarpour Lima Z, Akbari Sene A, Hosseini Jebelli Z, Amjad G. Comparison of uterine and ovarian stromal blood flow in patients with polycystic ovarian syndrome. Endocr Connect 2019;8:50-6.
20. Ozkan S, Vural B, Calişkan E, Bodur H, Türköz E, Vural F. Color Doppler sonographic analysis of uterine and ovarian artery blood flow in women with polycystic ovary syndrome. J Clin Ultrasound 2007;35:305-13.
21. Pinkas H, Mashiach R, Rabinerson D, *et al.* Doppler parameters of uterine and ovarian stromal blood flow in women with polycystic ovary syndrome and normally ovulating women undergoing controlled ovarian stimulation: Uterine and ovarian blood flow in women with PCOS. Ultrasound Obstet Gynecol 1998;12:197-200.
22. Arora A, Gainder S, Dhaliwal L, Suri V. Clinical significance of ovarian stromal blood flow in assessment of ovarian response in stimulated cycle for in vitro fertilization. Int J Reprod Contracept Obstet Gynecol 2015;4:1380-3.