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ORIGINAL ARTICLE

A Comparative Study on Quantitative Assessment of Blood Flow and Vascularization in Polycystic Ovary Syndrome Patients and Normal Women Using Three-Dimensional Power Doppler Ultrasonography

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Abstract

Purpose of the Study To compare the quantitative assessment of blood flow and vascularization of ovaries in polycystic ovary syndrome patients and normal women using three-dimensional power Doppler ultrasonography.

Methods This cross-sectional quantitative study was conducted on women of reproductive age group (15–45 years) attending Gynaecology OPD AIMSR, Bathinda, Punjab. Thirty women were enrolled in polycystic ovarian syndrome (PCOS) group and 30 healthy women in control group. Women were categorized as polycystic ovary syndrome according to Rotterdam's criteria. The women with PCOS underwent transvaginal USG Doppler on day 6 of the cycle using 3D power Doppler USG equipment (GE

Voluson E8), and vascularization index (VI), flow index (FI) and vascularization flow index (VFI) were measured.
Results The mean values of VI, FI and VFI measured by power Doppler ultrasonography were significantly increased (P value = 0.000) in women with PCOS when compared with healthy women.
Conclusion This study suggests that blood flow and vascularization measured by 3D power Doppler ultrasonography in ovaries of polycystic ovary syndrome patients were significantly more than the ovaries of normal women.

Keywords Polycystic ovary syndrome · Three-dimensional power Doppler ultrasonography · Vascularization index (VI) · Flow index (FI) · Vascularization flow index (VFI)

Introduction

Polycystic ovarian syndrome (PCOS) is one of the most common endocrine disorders affecting female fertility, although its etiology remains unknown. The criteria for diagnosis and definition of polycystic ovary disease are as heterogeneous as the pathology itself. So, it is the time for the development of a more objective method for the definition of PCOS.

The blood flow and the vascular pattern of an organ are directly related to its morphology and function. Ultrasonography may be used as a valuable tool to detect the same. With the recent advent of 3D power Doppler ultrasonography, it is now possible to quantify blood flow information of ovaries in the form of vascularization index (VI) representing vessels in tissues showing the flow signals, flow index (FI) representing intensity of flow and vascularization flow index (VFI) representing combination of VI and FI.

The aim of the present study was to evaluate the characteristics of polycystic ovaries compared to normal ovaries using 3D power Doppler ultrasonography with the purpose that this information might provide an additional parameter for the ultrasound diagnosis of the PCOS, hence may prove a new objective method for the diagnosis of PCOS.

Aim and Objective

Aim

To compare the quantitative assessment of blood flow and vascularization of ovaries in polycystic ovary syndrome patients and normal women using three-dimensional power Doppler ultrasonography.

Materials and Methods

This cross-sectional study was carried out in the Department of Obstetrics and Gynaecology and Department of Radiodiagnosis, AIMSR, Bathinda, which is a tertiary care teaching hospital in the state of Punjab. The study was carried out from July 2015 to Oct 2016 after obtaining clearance from the scientific and ethical committee of the hospital. A written informed consent was taken from the participants before enrollment.

Inclusion Criteria

Cases were included in the study based on Rotterdam's criteria (Table 1).

Exclusion Criteria

1. Women with history of use of oral contraceptives, corticosteroids, antipsychotic drugs or antidiabetic drugs in the last 3 months
2. Patients with other known causes of hyperandrogenism like Cushing syndrome, late onset adrenal hyperplasia, androgen-secreting tumor or hyperprolactinemia.
3. Patients with untreated hypothyroidism, renal, hepatic, cardiac or pulmonary disease.
4. Smokers or alcoholics.
5. All pregnant women.

Formula for quantitative observational study was used for sample size calculation. Sample size turned out to be 29 patients in each group. We enrolled 30 patients in each group for the study.

Methods

A detailed history from all the subjects was taken and clinical examination performed. On day 2 of the menstrual cycle, fasting blood samples were collected from all the subjects in plain vial for estimation of luteinizing hormone (LH), follicle-stimulating hormone (FSH), estradiol, testosterone, dehydroepiandrosterone sulfate (DHEAS), prolactin, thyroid-stimulating hormone (TSH), insulin and blood glucose (FBS). Hormonal levels were measured by

Table 1 Rotterdam's criteria [1]

Two of the three criteria below and exclusion of other etiologies (e.g., congenital hyperplasia, androgenic tumors, cushing syndrome)
1. Oligo and/or anovulation
2. Clinical and/or biochemical signs of hyperandrogenism
3. Polycystic ovaries

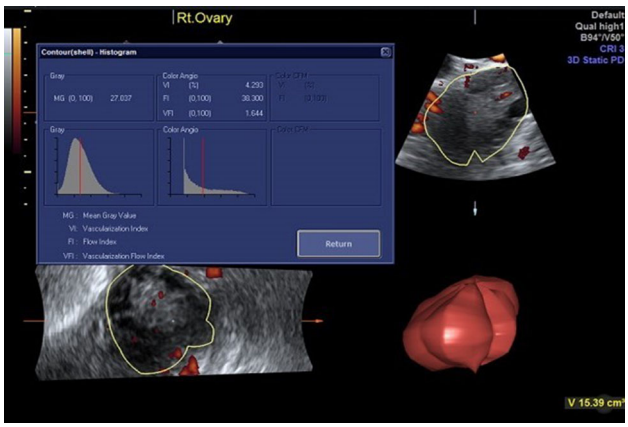

Fig. 1 Power Doppler ultrasonography histogram

Tosoh AIA 360 automatic hormone analyzer (Immunoflorescence), and blood glucose was measured using automated analyzer A15-Biosystems (Spectrophotometry).

Normal reference value taken for LH was 1.7–13.3 mIU/ml, FSH was 4.5–11.0 mIU/ml, S. estradiol was 40.7–220.4 pg/ml, S. testosterone was 9.0–56.0 ng/dl, DHEAS was 65–524 µg/dl, fasting insulin was 1.1–17.0 µg/ml, fasting glucose was 70–100 mg/dl, HOMA IR was ≤ 2, TSH was 0.39–6.2 µIU/ml and S. prolactin was 2.1–47.6 ng/ml.

The Rotterdam's consensus defined the polycystic ovary as having 12 or more follicles, measuring between 2 and 9 mm, and/or an ovarian volume (OV) > 10 cm^3. Only one ovary meeting these criteria is sufficient to establish the presence of polycystic ovaries [1].

Transvaginal 3D power Doppler ultrasonography (GE Voluson E8) was performed on day 6 of the cycle to measure total ovarian volume, follicular size and number, endometrial thickness, vascularization index (VI), flow index (FI) and vascularization flow index (VFI) using Virtual Organ Computer-aided Analysis (VOCAL) imaging program (Fig. 1).

Table 2 Clinical characteristics of cases and control groups

Variable		Group 1	Group 2	Significance
Age	Mean ± SD	26.37 ± 3.855	23.83 ± 4.949	NS
Menstrual history				
Regular		1	30	S
Irregular		29	0	S
H/o weight gain		4	4	NS
H/o stress		16	0	S
Height	Mean ± SD	156.23 ± 3.15	157.53 ± 5.69	NS
Weight	Mean ± SD	65.37 ± 3.47	55.2 ± 7.84	S
Body mass index	Mean ± SD	26.8 ± 1.53	22.2 ± 2.6	S
Waist circumference	Mean ± SD	88.08 ± 6.7	81.3 ± 4.46	S
Hip circumference	Mean ± SD	89.73 ± 8.75	85.47 ± 5.58	NS
Waist/hip ratio	Mean ± SD	0.99 ± 0.1	0.95 ± 0.5	NS

Table 3 Comparison of biochemical characteristics in cases and controls groups

		Group 1	Group 2	*P* value
LH	Mean ± SD	15.87 ± 7.5	5.75 ± 1.7	0.000
FSH	Mean ± SD	8.59 ± 2.8	7.79 ± 1.2	0.162
ESTRADIOL	Mean ± SD	37.73 ± 4.4	29.22 ± 4.4	0.000
TESTOSTERONE	Mean ± SD	44.52 ± 12.18	37.78 ± 11.06	0.029
DHEAS	Mean ± SD	197.66 ± 53.75	157.36 ± 46.35	0.003
FASTING INSULIN	Mean ± SD	15.99 ± 4.2	11.19 ± 2.72	0.000
FBS	Mean ± SD	89.03 ± 4.98	77.13 ± 6.47	0.000
HOMA IR	Mean ± SD	3.53 ± 1.01	2.14 ± 0.59	0.000
TSH	Mean ± SD	2.38 ± 0.84	2.34 ± 0.95	0.861
PROLACTIN	Mean ± SD	11.79 ± 3.40	11.40 ± 3.51	0.671

HOMA IR—fasting glucose (mg/dl) × fasting insulin (µU/ml)/405 [2]

Table 4 Comparison of two-dimensional ultrasonographic findings of cases and controls groups

		Group 1	Group 2	*P* value
Volume of left ovary	Mean ± SD	12.27 ± 4.1	6.90 ± 1.4	0.000
Volume of right ovary	Mean ± SD	12.238 ± 3.8	7.649 ± 1.7	0.000
Number of follicles (left ovary)	Mean ± SD	12.40 ± 2.9	5.33 ± 1.2	0.000
Number of follicles (right ovary)	Mean ± SD	12.97 ± 2.3	4.93 ± 1.1	0.000
Endometrial thickness	Mean ± SD	4.890 ± 1.4	4.947 ± 0.9	0.851

Table 5 Comparison of power Doppler indices in left and right ovaries of cases and controls groups

		Group 1	Group 2	*P* value
Difference VI (left–right)	Mean ± SD	1.51 ± 5.79	5.2 ± 0.86	0.361
Difference FI (left–right)	Mean ± SD	1.47 ± 5.99	2.88 ± 4.91	0.321
Difference VFI (left–right)	Mean ± SD	0.55 ± 2.12	0.45 ± 0.81	0.816

Table 6 Comparison of average of power Doppler indices of bilateral ovaries in cases and control groups

		Group 1	Group 2	*P* value
Average VI	Mean ± SD	7.26 ± 4.63	0.88 ± 0.51	0.000
Average FI	Mean ± SD	28.23 ± 4.69	16.61 ± 3.12	0.000
Average VFI	Mean ± SD	2.15 ± 1.48	0.16 ± 0.40	0.000

Table 8 Comparison of power Doppler indices in both the groups in subjects having LH/FSH > 1

		Group 1	Group 2	*P* value
VI	Mean ± SD	6.19 ± 4.82	0.37 ± 0.39	0.001
FI	Mean ± SD	26.18 ± 5.56	15.17 ± 4.44	0.008
VFI	Mean ± SD	1.67 ± 1.59	0.05 ± 0.05	0.001

For estimation level of association, unpaired t test was used. *P* value < 0.05 was taken as significant. Microsoft Excel 2013 was used to analyze the data.

Results

A total of 30 cases (PCOS women)—Group 1 and 30 controls (normal women)—Group 2 were taken. Women in the two groups were compared with respect to clinical characteristics, as shown in Table 2. Menstrual history, history of stress, height, weight, BMI and waist circumference had statistically significant difference in the two groups. However, age, history of weight gain, height, hip circumference and waist to hip ratio were not statistically significant in the two groups.

Clinical signs of hyperandrogenism like acne were present only in PCOS group in 46.7% cases; alopecia and acanthosis nigricans were present only in one PCOS women, while hirsutism was present in 20% of PCOS women.

Table 3 shows comparison of biochemical characteristics in cases and controls. LH, FSH, estradiol, testosterone, DHEAS, fasting insulin, fasting blood sugar, TSH and prolactin were measured on day 2 of the menstrual cycle. The mean of LH, estradiol, DHEAS, fasting insulin, fasting blood sugar and homeostatic model assessment-insulin resistance (HOMA IR) was found to be significantly higher in PCOS group than the control group, while the difference of FSH, testosterone, TSH and prolactin was not statistically significant.

Difference in volume of ovaries and number of follicles between the two groups was found to be statistically

Table 7 Comparison of power Doppler indices in cases and control group on the basis of age-wise distribution

		Group 1		Group 2		*P* value
Age (years)		16–25	26–35	16–25	26–35	
VI	Mean ± SD	6.76 ± 4.56	6.33 ± 4.97	0.53 ± 0.53	0.81 ± 0.86	0.001
FI	Mean ± SD	27.13 ± 6.81	27.46 ± 5.83	15.68 ± 4.10	14.15 ± 3.53	0.001
VFI	Mean ± SD	1.86 ± 1.28	1.86 ± 1.87	0.09 ± 0.09	0.13 ± 0.15	0.001

Table 9 Comparison of power Doppler indices in both the groups in subjects having HOMA IR > 2

		Group 1	Group 2	*P* value
VI	Mean ± SD	6.50 ± 4.74	0.63 ± 0.67	0.001
FI	Mean ± SD	27.32 ± 6.13	15.27 ± 3.96	0.001
VFI	Mean ± SD	1.86 ± 1.63	0.10 ± 0.11	0.001

significant. Volume of ovaries was higher in PCOS women. Also, number of follicles were more in PCOS women than normal women (Table 4).

The difference between left and right ovary of power Doppler indices was not statistically significant (Table 5).

So, average of bilateral ovaries was measured. There was statistically significant difference of VI, FI and VFI between normal and PCOS women. Values were higher in PCOS group (Table 6).

To consider age-related changes in ovarian vascularity, the subjects were classified in two groups, 16–25 and 26–35 years and power Doppler indices were compared between the two groups. VI, FI and VFI of PCOS women were higher than the normal women in both the age groups (Table 7).

Comparison of LH/FSH ratio and insulin resistance using HOMA IR with the ovarian vascularity was also done. Patients having increased LH/FSH ratio had significantly higher values of VI, FI and VFI (Table 8). Also, insulin-resistant subjects had significantly raised VI, FI and VFI (Table 9).

Discussion

The hypothesis in the present study was that 3D power Doppler ultrasonography provides the possibility of systemic analysis of volume, blood flow and vascularization of the whole ovary.

In this study, we used VOCAL-imaging program to compare 30 controls and 30 PCOS patients according to Rotterdam's criteria. The ovary was examined during early follicular phase and not during the late follicular phase when developing follicle of > 10 mm diameter is likely. In the present study, the ovary was examined on day 6 (early follicular phase).

The results were in accordance with those recently presented by Al-Rab et al. [3], El Behery et al. [4] and Elmashad et al. [5]. They used similar 3D power Doppler ultrasonography to compare VI, FI and VFI between normal and PCOS group. They discovered that polycystic ovaries have increased stromal blood flow and vascularity like in the present study.

But in the study by Lam et al. [6], Chinese women with PCOS had no significant differences in the 3D indices of ovarian vascularity and blood flow compared to the control group. Lam et al. recruited 40 Chinese women with PCOS from the assisted reproductive technology unit and the gynecology clinic as the study group and 40 subfertile Chinese women without PCOS who were undergoing intrauterine insemination treatment and/or ovulation induction for infertility due to male factors or to unexplained infertility as the control group. The reasons for this contradiction between Lam et al. and this study might be that different control groups were used in these two studies. We selected normal healthy volunteers with regular cycles and normal ovaries while Lam et al. chose subfertile women. Moreover, ovarian characteristics might be influenced by ethnicity also.

Our results suggest that in general the blood flow in polycystic ovaries was more than the normal ovaries in early follicular phase.

Three-dimensional power Doppler ultrasonography offers us a new tool to assess size of target organ, to quantify tissue blood perfusion, which may expand our knowledge concerning physiology of the organs. Although the implication of this finding in ovulation induction treatment is unknown, it may help to explain the excessive response often seen in women with PCOS when they are administered gonadotrophins [7]. The presence of an increased stromal Doppler signal in the PCOS group [8], compared with women with normal ovaries, supports the notion that PCOS is a primary disorder of the ovary.

Conclusion

The detection of an increased total ovarian Doppler signal by 3D power Doppler ultrasonography may be a possible new marker in the diagnosis of PCOS. Our results suggest that blood flow in ovaries of polycystic patients was more than in ovaries of normal women in early follicular phase. PCOS patients are more sensitive to the stimulation of gonadotrophins and are at higher risk of ovarian hyperstimulation syndrome. Increased ovarian blood flow in PCOS patient may lead to a greater dose of gonadotrophins to the granulosa cells of the developing follicles. Therefore, the assessment of the ovarian blood flow should be incorporated in the management of PCOS women undergoing ovulation induction or ovarian stimulation in order to reduce the associated risk of ovarian hyperstimulation syndrome.

We believe that 3D power Doppler ultrasound may provide substantial assistance to the management of PCOS

and is worthy of further research. However, further studies with larger sample size are definitely needed in this area.

Compliance with Ethical Standards

Conflict of Interest The authors declared that there was no conflict of interest.

Ethical Approval Research protocol was approved by the institutional ethics committee.

Informed Consent Informed consent was obtained from all subjects for being included in the study.

References

1. Legro RS, Arslanian SA, Ehrmann DA, et al. Diagnosis and treatment of polycystic ovary syndrome: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab. 2013;98(12):4565–92.
2. Gianchandani RY, Saberi S, Patil P, et al. Prevalence and determinants of glycemic abnormalities in cardiac surgery patients without a history of diabetes: a prospective study. Front Endocrinol. 2015;6:125.
3. Al-Rab MT, Mohammed AB, Mo'men MH, et al. Three-dimensional power Doppler indices of ovarian stromal blood flow and serum vascular endothelial growth factor after laparoscopic ovarian drilling in women with polycystic ovary syndrome. Middle East Fertil Soc J. 2015;20(3):138–43.
4. El Behery MM, Diab AE, Mowafy H, et al. Effect of laparoscopic ovarian drilling on vascular endothelial growth factor and ovarian stromal blood flow using 3-dimensional power Doppler. Int J Gynecol Obstet. 2011;112(2):119–21.
5. Elmashad AI. Impact of laparoscopic ovarian drilling on anti-Müllerian hormone levels and ovarian stromal blood flow using three-dimensional power Doppler in women with anovulatory polycystic ovary syndrome. Fertil Steril. 2011;95(7):2342–6.
6. Lam P, Raine-Fenning N, Cheung L, et al. Three-dimensional ultrasound features of the polycystic ovary in Chinese women. Ultrasound Obstet Gynecol. 2009;34(2):196–200.
7. Dumont A, Robin G, Catteau-Jonard S, et al. Role of Anti-Müllerian Hormone in pathophysiology, diagnosis and treatment of polycystic ovary syndrome: a review. Reprod Biol Endocrinol. 2015;13(1):1.
8. Senaldi L, Gopi RP, Milla S, et al. Is ultrasound useful in the diagnosis of adolescents with polycystic ovary syndrome? J Pediatr Endocrinol Metab. 2015;28(5–6):605–12.