



ORIGINAL ARTICLE

Correlation Between Doppler Indices, Clinical and Laboratory Findings in Cases of Polycystic Ovarian Syndrome

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ABSTRACT

Background: Polycystic ovary syndrome (PCOS) is the most common cause of anovulatory infertility in more than 70% of cases. Because 16 to 25% of the normal population has polycystic appearing ovaries on ultrasound, the presence of polycystic ovaries was considered to be suggestive but not diagnostic of PCOS. This study aimed to compare Doppler hemodynamic in ovarian and uterine arteries of PCOS patient with a group of fertile women who have normal ovarian function. **Methods:** This prospective (case control study) was conducted in Ultrasound and Infertility Units in the Department of Obstetrics and Gynecology of Zagazig University Hospitals. The patients were classified into 3 groups: Group I (control): include (11 women) ovulatory normal fertile women with regular cycle; Group II (cases): include (11 women) non obese women diagnosed as pcos patients (according to Rotterdam criteria); and Group III (cases): include (11 women) obese women diagnosed as PCOS patients. **Results:** In our study, there was no statistically significant difference between the second (PCOS non obese women) and the third (PCOS obese women) groups regarding type of infertility (primary or secondary) and PCOs symptoms. **Conclusion:** Uterine artery and ovarian vessels Doppler indices can be correlated to overweight in cases with PCOS. Doppler examination may be useful for the evaluation of PCOS patients, in addition to conventional hormonal and biochemical parameters.

Keywords: Polycystic ovarian syndrome, infertility, Doppler.

INTRODUCTION

Polycystic ovarian syndrome (PCOS) is the common heterogenous endocrine disorder which affect 5-10% of fertile women at reproductive age, its etiology is still understood and it's the most common cause of anovulatory infertility^[1].

Women with PCOS have abnormalities in the metabolism of androgens and estrogen and in the control of androgen production. PCOS can result from abnormal function of the hypothalamic-pituitary-ovarian (HPO) axis^[2].

The clinical expression of this syndrome varies, but common includes menstrual cycle

disturbance, signs of androgen excess, insulin resistance, obesity, elevated serum LH level, dyslipidemia, increase risk of type II diabetes mellitus, cardiovascular events, and the women manifested by acne, obesity, hirsutism, baldness and have inability to conceive^[3].

Requires the existence of two of the following three criteria to make the diagnose of PCOS^[4].

- I- Oligo-ovulation and / or an ovulation.
- II- Clinical or biochemical signs of hyperandrogenism.
- III- PCOS on ultrasonography.

According to Rotterdam consensus definition, the polycystic ovaries are present when:

1. One or both ovaries has 12 or more follicles which measuring (2-9) mm in diameter
2. The ovarian volume exceeds 10 cm³ by scanning.

Only one ovary meeting either of these criteria is sufficient to establish the present of PCO^[5].

There are interesting debate regarding the actual role of transvaginal Doppler ultrasound for assessment of uterine and ovarian vascularities of PCOS, and most of researchers are agree that the patterns of blood flow of organ are directly associated with the function and morphology of relevant organ^[6].

The studies of color Doppler ultrasound in patients with PCOS shown that there is obvious increase in numbers of intraovarian stromal arteries and peak systolic blood flow velocity in PCOS women, compared to women with normal ovarian morphology. Although that the intraovarian vascularization are not seen before days 8-10 of 28 day cycle. So, from these changes in intrastromal ovarian vascularities we think that the ovarian stromal Doppler evaluation are helpful in explanation of pathophysiology of PCOS^[1]. So, in our study we will try to address this issue to evaluate the impact of PCOS changes on ovarian vascularity. The aim of study was to assess the ovarian and uterine blood flow in women with PCOS compared to normal ovulatory fertile women.

METHODS

This prospective study was carried out in the unit of Ultrasound and Infertility in department of Obstetrics and Gynecology in Zagazig university hospital during the period from September 2018 to June 2019. This study included 33 women.

The study was carried according to the Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans. Written informal consent was obtained from all subjects and the study was carried according to the research ethical committee of Faculty of Medicine, Zagazig University.

The patients were classified into 3 groups:

Group I (control): include (11) ovulatory normal fertile women with regular cycle.

Group II (cases): include (11) non obese women (BMI \leq 25 kg/m²)

diagnosed as PCOS patients (according to Rotterdam criteria)

Group III (cases): include (11) obese women (BMI \geq 30kg/m²)

diagnosed as PCOS patients.

Inclusion criteria for each group:

First group:

Normal fertile women, regular menstrual cycle.

Normal BMI 18.5-25 kg/m²

Second group: -

BMI \leq 25 kg/m². Women with (existence of 2 out of 3 of Rotterdam criteria): oligo/or anovulation, hyperandrogenism, polycystic ovary by ultrasound. Documented polycystic ovary by transvaginal ultrasound with presence of 12 or more follicles in at least one ovary ranging between (2-9) mm, ovarian volume >10cm³, signs of menstrual irregularity and hyperandrogenism^[3].

Third group:

BM \geq 30 kg/m². Women with (existence of 2 out of 3 of Rotterdam criteria): oligo /or anovulation, hyperandrogenism, polycystic ovary by ultrasound. Documented PCOS by transvaginal ultrasound with presence of 12 or more follicles in at least one ovary ranging between (2-9 mm), ovarian volume >10cm³,

signs of menstrual irregularity and hyperandrogenism^[3]

Exclusion criteria for study population:

- 1- Any patient has hypertension, diabetes mellitus, autoimmune disease, cardiovascular disease, anemia, Cushing syndrome, thyroid disease, hyperprolactinemia or any condition that may affect circulatory system.
- 2- Women on drugs for induction of ovulation.
- 3- Androgen secreting tumor ovarian or adrenal.
- 4- Adult onset congenital adrenal hyperplasia.
- 5- Patient with follicular cyst > 20mm in early follicular phase.
- 6- History of tubal or ovarian surgery or pathology
- 7- All pregnant women
- 8- Women on Contraceptive pills

Operational design:

All patients were submitted to the following:

An informed written consent was taken from all patients. Detailed history including: age, parity, hirsutism, menstrual and obstetrics history. General, abdominal, and pelvic examination

Measurement of Body mass index (BMI) and classification as follow: -

Underweight	BMI <18.5kg/m ²
Normal weight	BMI 18.5-25 kg/m ²
Overweight	BMI 25-30 kg/m ²
Obese	BMI ≥ 30 kg/m ²
Morbid obesity	BMI >35 kg/m ²

Assessment of hirsutism by modified Ferriman Gallwey score: This scoring system evaluated 11 body areas, including the upper lip, chin, chest, upper back, lower back, upper arm, forearm, upper and lower abdomen, thighs and lower legs. Laboratory investigation in early follicular phase (cycle day 2 to 5) (basal examination): measurement of FSH, LH, RBS, testosterone, 21 α hydroxylase enzyme and DHEA-S. Transvaginal ultrasound examination with color and Spectral Doppler Study as follow:

Technique of Transvaginal Doppler ultrasound examination:

Doppler flow measurements of the uterine and intraovarian blood vessels were performed transvaginal. The bladder is Completely emptied to minimize the external effects on

blood flow. The patients were asked to undress, usually from the waist down, the lie down on a table with bent of the knees in a dorsal position. The probe was covered with a gloves or condom and gel then inserted into the vagina. The apparatus used was Voluson 730 pro V equipped with a 2.8-7.7 MHZ transvaginal transducer. Identical fixed preinstalled power Doppler ultrasound settings were used in all women. Introduce the probe into vagina, visualize the position of uterus and both ovaries, then used color Doppler mode to visualize the vascularization of uterus and ovaries. Then take mid sagittal plane, uterine dimension, endometrial thickness, parasagittal plane , then tilt lateral uterine wall, uterine artery was visualized laterally to the cervix at the level of internal os in a longitudinal plane .The pulsed Doppler sample volume was placed across the vessel with the angle between the ultrasound beam and the vessel close to zero. The different Doppler indices (PI- RI- S/D ratio) were obtained (fig. 1).

Then turn probe 90⁰, moving up tilt uterine fundus. Then lateral bent to seen the adnexa , Intraovarian blood flow was then evaluated in pulsed Doppler mode by examining vessels in the ovarian stroma (looking for any small artery in the ovarian stroma not close to the surface of the ovary or located near the follicular wall) and in the wall of the leading follicle . No correction was made for the angle of insonation of the Doppler beam (fig. 2). For each examination the mean value of three consecutive waveforms was obtained on both sides.

Statistical analysis

Data were collected, tabulated and analyzed by SPSS 20, software for Windows. The level of significance was < 0.05.

RESULTS

[Table 1], showed that there was Statistically significant difference in ovarian artery S/D between early and late follicular phase. But regarding other variables, there was no Statistically significant difference between early and late follicular phase in the 1st group. [Table 2], showed that there was statistically

significant difference in ovarian artery RI, S/D and uterine artery S/D between early and late follicular phase. But regarding other variables, there was no Statistically significant difference between early and late follicular phase in the 2nd group. [Table 3], showed that there was Statistically significant difference in ovarian artery S/D and uterine artery S/D between early and late follicular phase. But regarding other variables, there was no Statistically significant difference between early and late follicular phase in the 3rd group. [Table 4], showed that there was no statistically significant correlation between BMI level and any variable in the 1st group. [Table 5], showed that there was statistically significant positive correlation between BMI with LH, LH/FSH and RBS (increase BMI is associated with increased LH, LH/FSH and RBS levels). And there was

statistically significant negative correlation between BMI with Uterine artery PI, ovarian artery PI and RI (increase BMI is associated with decreased Uterine artery PI, ovarian artery PI and RI levels). But regarding other variables, there was no statistically significant correlation with BMI in the 2nd group. [Table 6], showed there was statistically significant positive correlation between BMI with LH, LH/FSH, RBS and right ovarian volume (increase BMI is associated with increased LH, LH/FSH, right ovarian volume and RBS levels). And there was statistically significant negative correlation between BMI with ovarian artery PI and RI (increase BMI is associated with decreased ovarian artery PI and RI levels). But regarding other variables, there was no statistically significant correlation with BMI in the 3rd group.

Table 1. Demographic data of the studied groups: -

Variable	Group I mean ± SD (Range) No(11)	Group II mean ± SD (Range) No (11)	Group III mean ± SD (Range) No (11)	F-test	p-value	LSD
Age	32±6.6 (22-40)	29.1±4.8 (20-36)	32.2±7.1 (20-40)	0.8	0.4	0.2 0.9 0.3
BMI	23±5.6 (19-39)	19.3±2.1 (16-23)	29.7 ±5.2 (25-37)	16.9	0.001**	0.02*(1) 0.001** 0.001**

* Statistically significant difference ($P \leq 0.05$)

** Statistically highly significant difference ($P \leq 0.001$)

F test : One way ANOVA test

LSD : Least significant Difference.

Table 2. Comparison between the three studied groups regarding Laboratory findings: -

Variable	Group I mean \pm SD (Range) No (11)	Group II mean \pm SD (Range) No (11)	Group III mean \pm SD (Range) No (11)	test	p-value	LSD
LH (mU/ml)	5.4 \pm 2.9 (1.3-6.8)	9.4 \pm 1.9 (6.6-13.6)	15.6 \pm 1.3 (10-17.6)	K 22.8	0.001**	0.001**(1) 0.001**(2) 0.02*(3)
FSH (mU/ml)	6.4 \pm 1.6 (5.1-10.9)	7.1 \pm 0.7 (5-10)	8.0 \pm 0.64 (5-12.5)	F 2.6	0.1	0.05(1) 0.09(2) 0.7(3)
LH/FSH	0.69 \pm 0.42 (0.0-1.2)	1.9 \pm 0.27 (1.2-3.1)	2.08 \pm 0.16 (1.6-3.8)	K 37.6	0.001**	0.001**(1) 0.001**(2) 0.06(3)
RBS (mg/dl)	92.9 \pm 17.4 (75-124)	106.1 \pm 21.7 (70-133)	126.7 \pm 31.3 (80-200)	F 5.4	0.01*	0.04*(1) 0.003*(2) 0.05(3)

K; Kruskal- Wallis test.

LSD : Least significant Difference

F test : one way ANOVA test

* Statistically significant difference ($P \leq 0.05$)

** Statistically highly significant difference ($P \leq 0.001$)

Table 3. Comparing ovarian volume (ml) at early follicular phase between the three studied groups: -

Variable	Group I mean \pm SD (Range) No(11)	Group II mean \pm SD (Range) No (11)	Group III mean \pm SD (Range) No (11)	K test	p-value	LSD
Right	6.6 \pm 3.5 (2-10)	10.7 \pm 5.3 (6.1-15.5)	13.3 \pm 1.7 (10.1-16.3)	9.1	0.001**	0.001**(1) 0.001**(2) 0.6(3)
Left	4.9 \pm 2.3 (2-8)	10.9 \pm 8.9 (5.2-15.9)	12.2 \pm 1.8 (11.1-16.2)	9.2	0.001**	0.001**(1) 0.001**(2) 0.7(3)
Mean ovarian volume	5.75 \pm 2.9 (2.8-8.6)	10.8 \pm 7.1 (3.7-17.9)	12.65 \pm 1.75 (10.9-14.4)	9.15	0.001**	0.001**(1) 0.001**(2) 0.65(3)

K; Kruskal- Wallis test.

LSD : Least significant Difference

** Statistically highly significant difference ($P \leq 0.001$)

Table 4. Comparing uterine artery (mean value) Doppler findings at early follicular phase between the three studied groups: -

Variable	Group I mean \pm SD (Range) No (11)	Group II mean \pm SD (Range) No (11)	Group III mean \pm SD (Range) No (11)	K Test	p-value	LSD
uterine artery PI	2.62 \pm 0.78 (0.59-3.9)	2.89 \pm 1.2 (1.5-4.4)	2.37 \pm 0.8 (1.3-3.5)	5.07	0.03*	0.7(1) 0.06(2) 0.005*(3)
uterine artery RI	1.08 \pm 1.01 (0.5-2.0)	0.91 \pm 0.17 (0.3-0.91)	0.78 \pm 0.15 (0.5-1.1)	2.9	0.07	0.07 (1) 0.8(2) 0.06(3)
uterine artery S/D	7.7 \pm 3.1 (1.8-12.9)	3.2 \pm 2.4 (1.9-10.1)	2.8 \pm 2.5 (1.43-10.61)	4.1	0.03*	0.02*(1) 0.03*(2) 0.29(3)

K; Kruskal- Wallis test.

LSD: least significant difference

* Statistically significant difference ($P \leq 0.05$)**Table 5.** Comparing uterine artery (mean value) Doppler findings at late follicular phase between the three studied groups: -

Variable	Group I mean \pm SD (Range) No(11)	Group II mean \pm SD (Range) No (11)	Group III mean \pm SD (Range) No (11)	K test	p-value	LSD
uterine artery PI	2.52 \pm 0.5 (1.8-3.1)	2.63 \pm 1.3 (1.3-4.1)	2.02 \pm 1.09 (0.9-3.09)	8.8	0.003*	0.06(1) 0.07(2) 0.004* (3)
uterine artery RI	1.08 \pm 1.01 (0.5-1.8)	0.90 \pm 0.18 (0.3-0.93)	0.73 \pm 0.03 (0.5-1.4)	1.3	0.2	0.13 (1) 0.19(2) 0.8(3)
uterine artery S/D	7.3 \pm 2.8 (2.1-9.7)	5.2 \pm 1.5 (1.8-7.6)	5.6 \pm 2.9 (1.79-9.8)	6.2	0.05*	0.04*(1) 0.03*(2) 0.8(3)

K; Kruskal- Wallis test.

LSD: least significant difference

* Statistically significant difference ($P \leq 0.05$)

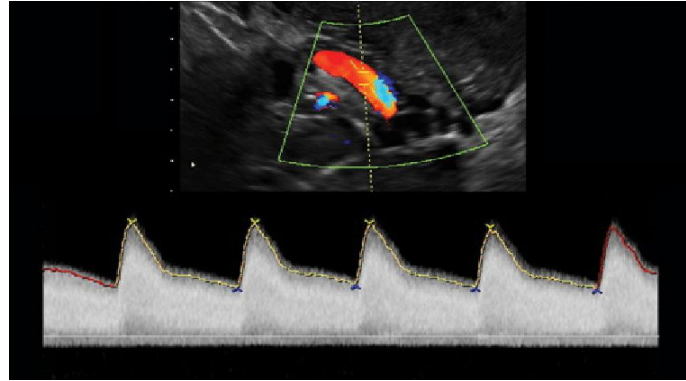


Fig 1. Uterine artery location

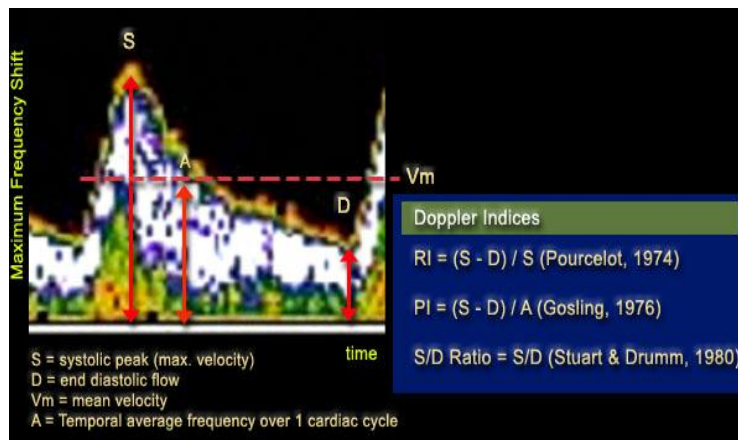


Figure 2. Doppler indices

DISCUSSION

Regarding uterine arteries RI there was statistically insignificant difference between the three studied groups in early and late follicular phase. This result was agreed with **Fetouh and Mohamed**.^[7] which found that there was statistically insignificant difference between cases PCOS and controls in uterine artery RI, but in contrast with a study by **Farshchian et al.**^[8] were the uterine artery RI on both sides significantly lower in PCOS patients than the healthy women.

And there was statistically insignificant difference between the cases (3rd, 2nd group) and control (1st group) regarding uterine arteries S/D ratio in early and late follicular phase, this agreement with **Fetouh and Mohamed**.^[7] which found that there was

statistically insignificant difference between cases PCOS and controls in uterine arteries S/D ratio, but in contrast with a study by **Ozkan**,^[9] which demonstrated that increased uterine arteries S/D ratio in cases than controls. These different finding in our study about uterine indices may be due to the relatively the small number of patients included in this study.

The results of doppler sonography in a study by **Mala et al.**^[10] which was performed on 25 PCOS patients and 25 healthy women showed the uterine artery RI was significantly higher in PCOS group than the control group, and ovarian artery RI was significantly lower. Moreover, vascularization of ovarian stromal arteries was significantly higher in PCOS patients than the healthy women.

According to the **Bostancia et al.**^[11] study, the results of color Doppler study of uterus and ovaries on 20 PCOS patients and 20 healthy women showed that there were considerable differences in the uterine artery and ovarian stromal artery RIs between the PCOS patients and healthy women. They found that the uterine artery RI was higher and ovarian stromal artery RI was lower in the PCOS patients than in the control group.

Our results are in agreement with **Allen et al.**^[12] which examined the ovary during early follicular phase and not during the late follicular phase when developing follicle of >10mm diameter, where suggest that general the blood flow in polycystic ovaries was more than the normal ovaries in early follicular phase.

CONCLUSION

Uterine artery and ovarian vessels Doppler indices can be correlated to overweight in cases with PCOS. Doppler examination may be useful for the evaluation of PCOS patients, in addition to conventional hormonal and biochemical parameters.

Conflict of Interest: Nothing to declare.

Financial Disclosures: Nothing to declare.

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