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Ovarian blood flow pattern in lean and obese patients with polycystic ovary syndrome

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***Abstract*- Background**: Transvaginal color Doppler has opened up exciting new possibilities for the better understanding of the physiology and pathophysiology of ovarian blood flow, resulting in a number of completely new diagnostic parameters in polycystic ovary syndrome.

Objective: To determine whether obese patients with polycystic ovary syndrome show different ovarian blood flow pattern in comparison with lean patients.

Study design: Cross sectional study.

Setting: Department of Obstetrics and Gynecology Al-Elwiya Maternity Teaching Hospital, Baghdad-Iraq.

Patients Methods:

Eighty patients who are already diagnosed as having polycystic ovary syndrome were arranged in two groups according to their BMI; obese with BMI>30 Kg/m^2 and lean with BMI<25 Kg/m^2. Ovarian blood flow study by Doppler ultrasound including PI, RI and S/D ratio were measured and compared in both groups. Same, serum levels of LH, FSH and total testosterone were measured and compared.

Result: The PI index in obese and lean patients was (1.19+/-0.13, 1.02+/-0.21 respectively, p value=0.028), RI in obese and lean patients was (0.53 +/-0.07, 0.61 +/-0.06 respectively, p value=0.000) with statistically significant difference in these values between these two groups. While S/D ratio show no statistically significant difference.

LH levels in obese and non obese patients were (10.78-\+1.31, 8.18-\+1.16 respectively, P value=0.000). FSH levels in obese and non obese patients were (3.80-\+1.04, 3.06-/+0.67 respectively, P value 0.000). Testosterone levels in obese and non obese were (1.59-/+0.65, 1.02-/+0.37 respectively, P value 0.ooo).

Conclusion: Ovarian Doppler analysis showed an increase in blood flow in obese women with PCOS when compared to non obese PCOS women with significantly increased PI value and decreased RI value.

***Index Terms*-** polycystic ovary, ovarian blood flow

I. INTRODUCTION

Polycystic ovary syndrome is the most common endocrine disorder of reproductive-aged women and affect approximately 4 to 12 percent, it presents a heterogeneous collection of signs and symptoms that form a spectrum of disorders with reproductive, endocrine and metabolic dysfunction. Key features include menstrual cycle disturbance, hyperandrogenism, and obesity(1,2).

There are no certainties about the origin of PCOS (3). However, a genetic basis that is both multifactorial and polygenic is suspected, as there is a well-documented aggregation of the syndrome within families (4). Insulin resistance appears to contribute to hyperandrogenism and other gonadotropin abnormalities by reducing circulating SHBG levels, resulting in increased bioavailable (free) Testosterone Both insulin and LH stimulate androgen production by the ovarian theca cell . As a result affected ovaries secrete elevated levels of testosterone and androstenedione levels contributing to an increase in estrone levels through peripheral conversion by aromatase (5,6).

The ovaries of women with PCOS have prominent vessels in the stroma, whereas normal ovaries have scant or absent flow. Intraovarian vascular flow pattern is virtually seen only in women with PCOS. This flow pattern has similar characteristics to the flow pattern in women with ovarian neoplasms, with adnexal inflammatory disease, or with metabolically active ovaries. Different mechanisms may be responsible for the hemodynamic anomalies that are uniformly observed in patients who do not undergo the type of luteal conversion occurring in normally cycling women. The abnormal hemodynamic patterns seen in the ovaries of women with PCOS may be due to an abnormal timing of LH-dependent prostaglandin release (7). Bourne and associates have shown the existence of a direct correlation between LH levels, prostaglandin activity, and blood flow changes in the ovary. An alteration in the finely tuned timing for the release of specific prostaglandins is likely to interfere with ovulation in humans (8). intraovarian vessels normally are not visible before days 8 to 10 of the cycle, these vessels are seen between days 3 and 5 in patients with PCOS. Vascular flow is observed in 88% of ovaries of patients with PCOS compared to less than 50% of ovaries of normal cycling women on days 3 to 8 of the menstrual cycle. (9). Color flow Doppler imaging can be used to assess the amount and pattern of blood flow within the ovary, and indirectly indicates its functionality. This is particularly useful to characterize the presence of luteal tissue, in early developing tumors, or in luteinized cysts (10).

Aim of the study is to study ovarian blood flow Doppler indices criteria in both obese and lean PCOS patients.

II. Patients and Methods

The study was approved by the Obstetrics and Gynecology committee of the Iraqi Board for medical specialization and the hospital administration.This study included 80 women aged 19 _34 years, they were already diagnosed as having polycystic ovary syndrome and further diagnosis confirmation done according to Rotterdam criteria, and were selected while attending the Gynecology and Infertility clinic at Al-Elwiya Maternity Teaching Hospital over a period of six month ,from 1st of March 2015 to the end of August 2015. Verbal consent obtained from the patients after explanation to them the aim of the study.

The study protocol included a questionnaire form designed to include age, detailed history of menstrual cycle, fertility status, hair growth and distribution, weight, height, acne, endocrine abnormalities and ultrasound and hormonal findings.

Clinical examination was concentrated on weight, height and hair distribution. Hirsutism was assessed according to the Ferriman-Gallwey score (FGS), and body mass index (BMI) was computed according to the ratio of weight divided by the height squared (kg/m^2).

According to BMI the patients were arranged into two groups:

A) Obese patient with PCOS, BMI more than $30kg/m^2$.

B) Lean patient with PCOS, BMI equal or less than $25kg/m^2$.

Those whom BMI was more than $25kg/m^2$ and less than $30kg/m^2$ were excluded from the study because they were classified as overweight.

Medical diseases were also excluded according to detailed history, clinical examination i.e. blood pressure measurement and investigations i.e. blood sugar and renal function tests.

Hormonal assay including: luteinizing hormone (LH), follicle stimulating hormone (FSH), total testosterone (total T) was performed during 2nd and 3rd day of the cycle while transvaginal ultra-sonographic and color Doppler analysis for the ovarian stromal artery were performed soon after menses and after bladder evacuation.

Ultrasound examinations were performed using a 6.5MHz vaginal transducer (Philips, HD, 11XE) equipped with color Doppler. Doppler flow measurements of the ovarian stromal vessels were performed tranvaginally at the same setting. All the patients were studied between 8.00 and 11.00 AM. For ovarian stromal blood vessels measurements color signals were sought in the ovarian stroma at the maximum distance from the surface of the ovary. Blood vessels located near the wall of a follicle were not measured. Whereas several blood vessels were detected inside the ovarian stroma, only the vessel with the lowest downstream impedance was selected for Doppler measurements. Resistance index (RI) and pulsatility index (PI) were electronically calculated according to the following formula: PI = (S_D)/mean, RI = (S - D)/S, where S is the peak shifted Doppler frequency, D is the minimum Doppler shifted frequency and 'mean' is the mean maximum Doppler shifted frequency over the cardiac cycle. Four waveforms were recorded from each artery examined on both sides, and the average measurements from these four waveforms were included in the calculations. Ultrasound and color Doppler analyses were performed by the same persons (the researcher and specialist sonography). The data obtained from Doppler ultrasound and hormonal assay were collected and arranged in tables for statistical analysis

III. Data Analysis

A. Descriptive statistics; by applying tables, percentages, mean and SD.

B. Analytical statistics: t test for continuous variable test and chi square test for categorical variable used for data analysis.

C. Statistical level of significant: p-value of less than 0.05 considered statistically significant.

Results:

The results of this study were based on the analysis of the data of 80 women diagnosed with polycystic ovary. The study sample was classified into two groups, obese (n=40) and non obese (n=40) depending on their BMI. The mean age of obese group was 25.38 years (±3.48) versus 25.78 years (±3.95). Regarding BMI, the mean (±SD) values of obese and non-obese were 33.13 (2.28) and 22.35 (1.81) respectively.

The status of their menstrual cycle and presence of hirsutism are presented in table 2.

Table 1: Frequencies and percentages of hirsutism and menstrual regularity of the study sample.

Variable	No	%
Menstrual status	9	11.25
Regular	71	88.75
Irregular		
Hirsutism	69	86.25
Present	11	13.75
Absent		

The levels of hormones, LH, FSH, and testosterone, are presented in Table3.

Table 2: Mean, SD and levels of LH, FSH, and testosterone of the study sample.

Hormone	Mean	SD	Min	Max
LH	9.48	1.78	5.9	13
FSH	3.43	0.96	2	6
Testosterone	1.30	0.59	0.6	2.5

The sample PI index, Resist Index and SD ratio are shown in table 4.

Table 3: Levels of PI, RI and SD ratio for the study sample.

Variable	Mean	SD	Minimum	Maximum
PI	1.06	0.32	0.34	2.35
RI	0.57	0.08	0.3	0.85
SD Ratio	2.6	0.74	1.4	6.8

The comparison of menstrual status and presence of hirsutism in both groups reveals no statistical significance as shown in table 6. There were no statistically significant differences regarding the percentages of both variables as classified into obese and non-obese.

Table 4: Frequencies and percentages of regularity of menses and presence of hirsutism in obese and non-obese patients.

Variable	Obese		Non Obese		P Value
	No	%	No	%	
Menes Regular	2	22.2	7	77.8	0.077
Irregular	38	53.5	33	46.5	
Hirsutism Present	34	49.3	35	50.7	0.745
Absent	6	54.5	5	45.5	

The levels LH, FSH, Testosterone hormones in the two groups were statistically different. Obese women showed the highest levels in all above hormones as shown in table 5.

Table 5: LH, FSH, Testosterone hormones levels in obese and non obese patients.

Hormone	Groups	Mean	SD	P Value
LH	Obese	10.78	1.31	0.000
	Non Obese	8.18	1.16	
FSH	Obese	3.80	1.04	0.000
	Non Obese	3.06	0.67	
Testosterone	Obese	1.59	0.65	0.000
	Non Obese	1.02	0.37	

The PI index and resistance index have showed a statistically significant difference between both groups. The PI index level was higher among obese group while resistance index level was higher among non-obese group. The SD ratio have showed no statistically significant difference between the groups as shown in table 6.

Table 6: The PI, RI and SD ratio among obese and non-obese patients.

Parameter	Groups	Mean	SD	P Value
PI Index	Obese	1.19	0.13	0.028
	Non Obese	1.02	0.21	
Resist Index	Obese	0.53	0.07	0.000
	Non Obese	0.61	0.06	
SD Ratio	Obese	2.74	0.59	0.337
	Non Obese	2.58	0.87	

IV. Discussion

Menstrual disturbance is the common complaint in women suffering PCOS, 88.75% of them have this problem. This is also reported by **Carmina E, Lobo RA** who recorded that 60%-85% of PCOS patient suffered from gross menstrual dysfunction (11). Hirsutism is the second major compliant in 86.26%, similar figure obtained by **Miguel Dolz, Newton G. Osborne** (7).

Regarding mean serum LH, it was 9.48 IU/L and mean serum FSH was 3.43 IU/L in PCOS patients. This differs from what was reported by **Bostanci, et al**, who found that mean serum LH 11.64 IU/L, and FSH 5.52IU/L (12). Mean serum total testosterone in this study was 1.30nmol/l, while **Bostanci, et al**, reported that total serum testosterone is 0.92 ± 0.62nmol/l (13). Levels of serum LH, FSH and Testosterone hormones in the two groups were statistically different. Highest levels were seen in obese group, this differs from what was reported by **Battaglia. C. et al**, who found that there was no significant difference between obese and non obese regarding these hormones (14). While **Miguel Dolz, et al**, found that LH level in non-obese was much higher than obese with PCOS, and found no significant difference in FSH between them (7).

The main statistical difference obtained from the study was between ovarian artery PI and RI values. The PI index level was higher among obese group while resistance index level was higher among non-obese group. The SD ratio showed no statistically difference between the groups. In contrast to our study, **Miguel Dolz, et al** reported that no statistically significant ultrasonographic or Doppler flow differences were found between obese and non obese PCOS patient (7). **Battaglia. C. et al**, also reported that there is no significant differences in ovarian vascularization were observed between lean and obese patient with PCOS (14).

Bostanci, et al compared Serum hormone levels and ultrasonographic and color Doppler analysis between 20 patients with PCOS and 20 healthy women with ultrasonographic evidence of polycystic and found that there was significant difference between uterine artery pulsatility index (PI), uterine artery resistance index (RI), ovarian stromal artery PI and ovarian stromal artery RI measurements of PCOS and healthy women with ultrasonographic evidence of polycystic groups (P values respectively; $P < 0.01$, $P < 0.05$, $P < 0.01$, $P < 0.01$) and concluded that In patients with PCOS uterine artery PI and RI values are higher than women with ultrasonographic evidence of polycystic while ovarian artery PI and RI values were lower (13).

V. Conclusion

Ovarian artery Doppler analysis show increase in blood flow in obese women with PCOS when compared to non obese PCOS women with significantly increased in PI value and decrease in RI value.

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