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Research Article

INSULIN RESISTANCE IN WOMEN WITH POLYCYSTIC OVARY SYNDROME

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ABSTRACT

Polycystic ovary syndrome (PCOS) is reproductive disorder and metabolic syndrome. Prevalence of insulin resistance in women with PCOS is from 44 to 70%, but IR is not present in all PCOS women. The PCOS phenotypes identified with the Rotterdam criteria Hyperandrogenism + PCO with ovulatory cycles (phenotypes Type C), and anovulation and PCO without hyperandrogenism (Phenotypes Type D) have modest or absent evidence for insulin resistance. We study a group of women with menstrual disorder and impaired fertility in our clinic and the aim of study is to evaluate the correlation of insulin resistance with different phenotype of PCOS according to Rotterdam/NIH criteria.

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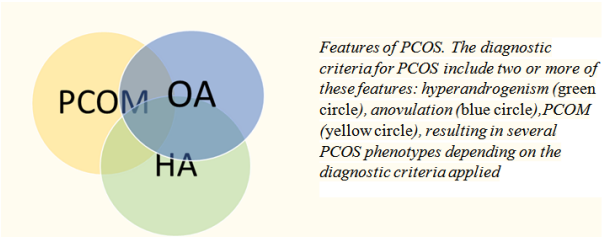
INTRODUCTION

The PCOS is characterize by Hyper androgenism, Chronic Anovulation, and Polycystic Ovary (PCO). There are several criteria for PCOS. The NICHD[(1)] consensus did not include the polycystic ovary morphology as criteria of PCOS. In 2003 in Rotterdam the polycystic ovary morphology (PCOM) on ultrasound examination was added to the NICHD diagnostic criteria[(2)]. The Rotterdam criteria[(3, 4)] for the diagnosis of PCOS required the presence of two of the following findings, after the exclusion of disorders of the pituitary, ovary, or adrenals that could present in a manner similar to PCOS: 1) Hyperandrogenism (clinical or biochemical); 2) Chronic Anovulation; and 3) PCOM. These criteria have extended the diagnosis to include two new groups of affected women: 1) PCOM and Hyperandrogenism without chronic anovulation; and 2) PCOM and Chronic Anovulation without Hyperandrogenism [(5,1)].



Features of PCOS. The diagnostic criteria for PCOS include two or more of these features: hyperandrogenism (green circle), anovulation (blue circle), PCOM (yellow circle), resulting in several PCOS phenotypes depending on the diagnostic criteria applied

In 2006, an expert panel of the AES recommended that hyperandrogenism be considered as an essential component of PCOS (5). These criteria require the combination of biochemical or clinical hyperandrogenism with chronic anovulation or PCOM [(6,5)]

Polycystic ovary syndrome (PCOS) is considered also as a metabolic disorder and the role of insulin is important in physiopathology of PCOS. Prevalence rates of insulin resistance have been reported from 44 to 70% [(7,8,9)], (10) but some women with PCOS have normal insulin sensitivity(11).

The phenotype C (HA + PCOM) and C (OA+ PCOM) are reported to have low or absence of IR.[(12,13)]. Different studies [(14,15)] had suggested that these subgroups differed metabolically from the group with classic PCOS. Women with ovulatory cycles and hyperandrogenemia (34) or PCO (89) had normal insulin sensitivity. Furthermore, ovarian morphology did not correlate with the severity of symptoms in PCOS (16,17). The Hyperandrogenic woman with PCOM but documented normal ovulation was recognized as a distinct phenotype of PCOS by both the Rotterdam criteria and the AES criteria (18,3,4).Women with this phenotype are often leaner than those with classic PCOS (19-22), and have milder metabolic abnormalities or may even be metabolically normal (19-22,23). There is general consensus that obese women with PCOS are insulin resistant (4)., but lean women with PCOS not always has insulin resistance (24,25) .

AIM OF STUDY

The aim of study is to evaluate the correlation of insulin resistance with different phenotype of PCOS according to Rotterdam/NIH criteria in women with menstrual disorder and impaired fertility.

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MATERIAL AND METHOD

The subjects were selected from the database of the gynecological clinic in Tirana. Women attended the clinic mainly due to oligomenorrhea or impaired fertility. All women fulfilling the diagnostic criteria of PCOS according to the Rotterdam/NIH consensus were included in the study. PCOM was assessed in all the subjects, Oligo-Anovulation was defined as prolongedmenstrual interval more than 35 days or 8 or less cycles in a year; Hyperandrogenism was assessed from clinical (hirsutism with modified Gerry Ferryman score; and acne) and hormonal changes. We have excludedthe cases with other entity that can cause menstrual disorders or hirsutism.

We have used the Rotterdam/NIH criteria to select the cases with PCOS and to determine the phenotypes as A, B, C, D .
In all women with PCOS we have evaluate the insulin resistance by the HOMA, (Homeostatic Model Assessment = fasting glucose/insulin ratio), and quantitative insulin sensitivity check index. The samples are divided in three subgroups based on HOMA IR: < 3%, 3-6.5% and > 6.5%.
IR was studied in relevance with PCOS phenotypes categories (A,B,C,D), metabolic state and sexual hormones.

STATISTICAL

Data were entered into a computer using SPSS for analysis. Continuous data were assessed for normal distribution using the Shapiro–Wilk test. All continuous data were not found to be normally distributed and were compared between the four phenotype groups of PCOS using Kruskal–Wallis. Dichotomous variables were compared with a two-tailed Chi-square or Fischer exact test where appropriate. P-value>0.05 was considered statistically significant.

RESULTS

A total of 122 women aged from 25 to 40 years old, fulfilling the diagnostic criteria of PCOS according to the Rotterdam/NIH consensus were recruited in the study. Mean age was 30 ± 4.4 years old. Mean weight 74.68 ± 9.8 kg.

The distribution of the PCOS women according to the phenotype A, B, C, D was respectively:43 (35.2%) A, 0% B, 9 (7.4%) Cand (70) 57.4% D(tab 1).

Tab. 1 PCOS phenotypes distribution in 122 women

	n	%
Phenotype A (HA + OA + PCOM)	43	35.2
Phenotype B (HA + OA)	0	0
Phenotype C (HA + PCOM)	9	7.4
Phenotype D (OA +PCOM)	70	57.4

The mean BMI of women with PCOS was 28±3.2 kg/m2, varying from a minimum of 22 kg/m2 to a maximum of 42 kg/m2. 19.7% were obese,75% of women were overweight and only 5.3% of the population with normal weight.

We have observed the changes of distribution of the phenotypes when the population was stratified based on BMI and normal weight patient was 100% phenotype D, overweight was predominantly phenotype A (40,4%) and less phenotype C, obese women was 100% phenotype A. (Tab.2)

Tab 2 PCOS phenotypes distribution according body weight

	Normal weight	Over weight	Obese	P value
	%	%	%	
Phenotype A (HA + OA + PCOM)	0	40.4	66.7	0,075
Phenotype B (HA + OA)	0	0	0	
Phenotype C (HA + PCOM)	0	10.5	0	
Phenotype D (OA +PCOM)	100	49.1	33.3	

HOMA -IR was calculated in 122 women. The mean value HOMA-IR was 5.8 ± 2.1 with a range varying from 2.5 to 12.5. According HOMA-IR divided in three subgroups (HOMA IR: < 3%, 3-6.5% and > 6.5%) we had the following distribution of Phenotypes of PCOS (tab.3)

Tab 3. PCOS phenotypes distribution according insulin resistance

	HOMA < 3	**HOMA 3 – 6.5**	**HOMA > 6.5**	**P value**
	%	%	%	
Phenotype A (HA + OA + PCOM)	14.3	41.2	29.8	0,045
Phenotype B (HA + OA)	0	0	0	
Phenotype C (HA + PCOM)	28.6	8.8	2.1	
Phenotype D (OA +PCOM)	57.1	50	68.1	

In group of women with moderated HOMA (<3) the Phenotype A is less present (14.3%), and in the group with HOMA moderate Hight (>3-6.5) and very High (> 6.5), translated high insulin resistance,phenotype C (with only hirsutism) is lesspresented (.8.8 %, 2.1%)
In the table 4 is represented HOMA-IR correlationwith other variables as weight, HbA1C, total cholesterol, LDL, HDL and Triglycerides. We found a statistically significant correlation with weight, HbA1c and lipidic profiles.

Tab 4. HOMA-IR correlation with metabolic variables

	r	p
Age	0.65	0.577
Weight	0.388	0.001
HbA1C	0.84	< 0.001
Total Cholesterol	0.54	0.002
LDL	0.363	0.044
HDL	- 0.555	0.001
Triglycerides	0.587	0.001

Our results regarding the association of insulin resistance with PCOS characteristic OA, HA, sexual and reproduction hormone are illustrated on table 5, 6, 7. We found that PCOS women with HOMA IR > 6.5 have 100 % OA, and the % of patient with no OA is higher in the group with HOMA < 3 (P. value 0.044). The same trend is observed for Hyperandrogenism with no statistical significance (P value 0.184), and value of HOMA correlate only with LH (p.0.024).

Tab. 5 Oligo/anovulation related to insulin resistance

	HOMA < 3	**HOMA 3 – 6.5**	HOMA > 6.5	P value
	%	%	%	
No oligo/anovulation	33.3	11.9	0	0.044
With oligo/anovulation	66.7	88.1	100%	

Tab 6. Hyperandrogenism related to insulin resistance

	HOMA < 3	HOMA 3 – 6.5	HOMA > 6.5	P value
	%	%	%	
No HA	33.3	40.5	61.3	0.184
With HA	66.7	59.5	38.7	

Tab. 7 HOMA correlation with hormonal

	r	p
FSH	0.343	0.112
LH	0.263	0.024

LH/FSH	0.126	0.283
Testosterone	- 0.198	0.086
Estradiol	-0.703	0.135

DISCUSSION

In our group study of 122 women diagnosticated with PCOS, most of them with problem of infertility, the prevalence was higher in group D with OA + PCOM followed by the group C with Hirsutism and PCOM and the less the group A. This phenotype distribution has been reported by some other author. Obesity is a common feature of the PCOS. In our study the mean BMI of women with PCOS was 28±3.2 kg/m2, varying from a minimum of 22 kg/m2 to a maximum of 42 kg/m2. 19.7% were obese, 75% of women were overweight and only 5.3% of the population with normal weight. In United States the prevalence of obesity is 80% (26,27), and outside U.S it goes 50% (26). In Europe 25 % of obese and overweight women had PCOS. (28).

Besides this we have observed the changes of distribution of the PCOS phenotypes. When the population was stratified based on BMI normal weight patient was 100% phenotype D (OA+PCOM), overweight patients were predominantly phenotype A (40, 4%) and less phenotype C, obese was 100% phenotype A. This finding can go in the same lines with studies that have demonstrated that this ovulatory form (D) is often present in leaner than in classic PCOS (19,20,21).

In group of women with moderated HOMA (<3) the Phenotype A is less present (14.3%), and in the group with moderate and very high HOMA (>3-6.5; > 6.5), translated as high insulin resistance, phenotype C (with only hirsutism and PCOS) is less presented (.8.8 %, 2.1%). With this data we can conclude that higher insulin resistance is associated with the classic form of PCOS and the phenotype with only hirsutism and PCOS is not influenced by insulin resistance. It is generally accepted that this phenotype, classified by Rotterdam as C phenotype, with hyperandrogenism and normal ovulation represent a transitional, intermediate stage between normality and the classic anovulatory form of PCOS. Women with this phenotype are often leaner than those with classic PCOS (19,21). In addition, they have milder metabolic abnormalities or may even be metabolically normal (11, 21,29). This PCOS group may potentially convert to classic PCOS under the influence of environmental factors like weight gain (30). These data are supported by the fact that PCOS women in our study with HOMA IR > 6.5 have 100 % OA, and the % of patient with no OA is higher in the group with HOMA < 3 (P. value 0.044).
We found a statistically significant correlation of IR with weight, HbA1c and lipidic profiles and LH value but not in other hormones.

None of the author have conflict of interest.

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