Chapter 4

Metabolic Disorders Associated with Biological Insulin Resistance in Congolese Woman with Polycystic Ovary Syndrome (PCOS)

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Abstract

We aimed to identify metabolic disorders associated with insulin resistance (IR) in Congolese women affected by polycystic ovary syndrome (PCOS). Fifty-four PCOS women and 40 controls from three hospitals of Kinshasa were enrolled to our case-control study. Blood samples were collected, and concentrations of high-density lipoprotein (HDL) and low-density lipoprotein (LDL) cholesterol, triglycerides (TG), fasting insulin, and glucose levels were measured. IR under basal conditions was evaluated with homeostasis model assessment (HOMA-IR). Dyslipidemia was observed in 37.5 controls and 55.6% PCOS women ($p < 0.05$). The two main lipoproteins concerned were HDL and LDL; nevertheless, the difference in LDL levels between PCOS and controls was not significant. Higher TG (>150 mg/dl) was not found in the two groups, whereas TG levels in PCOS patients were significantly higher than in controls ($p < 0.05$). Impaired glucose tolerance (IGT) and metabolic syndrome were observed, respectively, in 1.9% of PCOS patients. Insulin resistance is associated with metabolic disorders in Congolese woman with PCOS. Dyslipidemia (55.6%), mainly due to low HDL levels, is the most common metabolic disorder. Impaired glucose tolerance and metabolic syndrome represent a small proportion.

Keywords: PCOS, dyslipidemia, insulin resistance, Congolese women, HOMA-IR

1. Introduction

Polycystic ovary syndrome (PCOS) characterized by androgen excess with or without clinical evidence of hyperandrogenism is one of the most common endocrine dysfunctions that affects 5–10% of women of reproductive age [1, 2]. Literature data revealed that PCOS is associated

with several metabolic complications, including insulin resistance (IR) with compensatory hyperinsulinemia, impaired glucose tolerance, dyslipidemia, and metabolic syndrome (MS) [2–4].

PCOS women with dyslipidemia show lower HDL and higher TG, without change in LDL [5, 6].

Apridonidze et al. [7] observed that 68% of women had low HDL and 35% higher triglycerides. Another American multicentric study showed lower HDL in 66% of cases and higher TG in 32% of cases [8].

Metabolic syndrome is found in the third part of PCOS women [6, 8–11]. It appears in women with obesity or overweight, suggesting a "knock effect" of the gain of weight, probably in genetically predetermined women [5]. It has been found, respectively, in 43% of PCOS women by Apridonidze et al. [7] and 33.4% by Ehrmann et al. [8].

Likewise, race and age affect the prevalence of IR and metabolic disorders. Therefore, measures used to estimate these features in PCOS patients might take into account these factors.

Currently, few data are available on the prevalence and metabolic disorders of PCOS in African women. Therefore, the present study aimed to determine the frequency and metabolic features associated with IR in Congolese women affected by PCOS using a case-control study.

2. Patients and methods

The present study was carried out from February 2006 to February 2007 in three hospitals of Kinshasa. Fifty-four women with PCOS were recruited while a group of 40 healthy, age matched female subjects were used as controls. Women were all black, African, and from a Congolese ethnic group. Presence of PCOS was defined according to the Rotterdam 2003 consensus [1] by the presence of at least two of the following three features: (1) clinical and/or biochemical signs of hyperandrogenism; (2) oligomenorrhea, that is, menstrual cycles > 45 days or less eight cycles/year and/or anovulation; and (3) presence of polycystic ovaries. Clinical hyperandrogenism was defined by the Ferriman-Gallwey score (F-G score) as > 8. None of these PCOS patients had used hormonal preparation for at least 2 months preceding the study. Control women came from the same ethnic group; they were non-hirsute, without personal or family history of hirsutism and/or endocrine disorders, and free of any treatment. They had regular menstrual cycles, and none of them satisfied any of the PCOS criteria of the Rotterdam 2003 consensus.

PCOS and controls were excluded if they were prepubertal, premenopausal, or pregnant.

All women were subjected to a physical examination including evaluation of blood pressure, weight, abdominal, and hip circumference. Parametric measures included evaluation of body mass index (BMI) and waist-to-hip ratio (WHR). The waist circumference (WC) was defined as the smallest measurement between the iliac crest and lateral costal margin and the hip circumference, as the largest measurement over the buttocks. BMI was defined as body weight in

kilograms divided by body height in meters squared (kg/m^2). Overweight was defined as BMI ≥ 25 kg/m^2, and obesity was defined as BMI ≥ 30 kg/m^2, while WHR > 0.85 indicated visceral type of obesity.

2.1. Biochemistry

Capillary glucose was measured using a glucometer (Glucocard, Menarini, Italy). Serum insulin was performed by ELISA using the Mercodia Insulin Elisa kit. We also measured in serum HDL and LDL cholesterol and triglycerides by colometric enzymatic method.

Dyslipidemia was defined by one or more abnormal lipidic fractions using as normal values for LDL ≤ 160, HDL ≥ 50, and triglycerides < 150 mg/dl.

Impaired glucose tolerance (IGT) was defined as fasting hyperglycemia between 110 and 126 mg/dl.

Metabolic syndrome was defined according to Rotterdam 2003 consensus [1] by at least three of the following criteria:

- Abdominal circumference > 88 cm
- Triglycerides ≥ 150 mg/dl
- HDL cholesterol < 50 mg/dl
- Blood pressure ≥ 130/≥ 85 mmHg
- Fasting glucose > 110–126 and/or 2-h of glucose > 140–199 mg/dl

2.2. Statistical analysis

Data were analyzed with commercial software (SPSS version 13.0 for Windows). The Chi-square test, Fisher's exact test, and *t*-test were used to make comparison of quantitative variables and qualitative variables between study groups and sub-groups, according to each case. A p value < 0.05 was considered statistically significant.

3. Results

Table 1 shows the clinical features of PCOS patients and controls. The mean age and BMI were similar in both groups. There was a significant difference for menarche age between the two groups ($p < 0.05$) as well as for the Ferriman & Gallwey (F-G) score ($p < 0.001$), HDL, and TG ($p < 0.05$).

As shown in **Table 2**, dyslipidemia was found among 37.5% of controls and 55.6% of PCOS patients. HDL and LDL were the two lipidic fractions concerned. Lower HDL was the main abnormality observed ($p < 0.001$).

Higher TG (≥ 150 mg/dl) was not found although there was a significant difference between PCOS group and controls (**Table 1**).

Parameters	PCOS (n = 54)	Controls (n = 40)	P
Age	24.54 ± 5.2	23.98 ± 6.3	NS
Menarche age	13.77 ± 1.6	12.62 ± 1.6	<0.05
Ferriman-Gallwey Score	9.46 ± 6.1	3.38 ± 2.4	<0.001
Systolic blood pressure (mmHg)	110.57 ± 13.36	107.25 ± 9.3	NS
Diastolic blood pressure (mmHg)	71.70 ± 12.36	70.50 ± 9.0	NS
BMI	22.0 ± 4.39	22.0 ± 3.32	NS
WC (cm)	76.85 ± 10.9	75.82 ± 8.3	NS
WHR	0.80 ± 0.06	0.77 ± 0.05	NS
Glucose (mg/dl)	78.83 ± 12.7	76.42 ± 10.5	NS
Insulin (μU/L)	13.06 ± 9.1	5.83 ± 3.6	<0.001
HOMA-IR (mol × μU/l^2)	2.62 ± 2.1	1.08 ± 0.67	<0.001
HDL-cholesterol (mg/dl)	49.07 ± 13.72	57.65 ± 16.55	<0.05
LDL-cholesterol (mg/dl)	106.8 ± 31.6	111.10 ± 24.5	NS
Triglycerides (mg/dl)	57.12 ± 21.6	48.52 ± 12.87	<0.05

Table 1. Clinical and biochemical features of the study subjects.

Parameters	PCOS (n = 54)	Controls (n = 40)
HDL-c (mg/dl)		
<50	27 (50%)	14 (35%)
≥50	27 (50%)	25 (65%)
LDL-c (mg/dl)		
<160	49 (90.7%)	39 (97.5%)
≥160	5 (9.3%)	1 (2.5%)
TG (mg/dl)		
<150	54 (100%)	40 (100%)
≥150	0 (0%)	0 (0%)
Dyslipidemia		
Present	30 (55.6%)	15 (37.5%)
Absent	24 (44.4%)	25 (62.5%)

Table 2. Prevalence of dyslipidemia.

Among PCOS women, dyslipidemia varied significantly by waist-to-hip ratio, HDL, and TG.

PCOS patients identified as having dyslipidemia were compared with those without dyslipidemia. Overall, PCOS patients with dyslipidemia had the same age and LDL level but lower HDL and higher TG level. In addition, they had greater android body fat distribution. There was no difference in the HOMA-IR index, although patients with dyslipidemia showed higher level of this parameter (**Table 3**).

Impaired glucose tolerance as well as metabolic syndrome was observed in only one PCOS women.

Parameters	PCOS with dyslipidemia (n = 30)	PCOS without dyslipidemia (n = 24)	P
WHR	0.81 ± 0.05	0.78 ± 0.06	<0.05
HDL-c	40.70 ± 10.09	59.53 ± 9.98	<0.001
LDL-c	111.63 ± 34.5	100.76 ± 27.2	NS
TG	63.6 ± 23.4	49.02 ± 16.1	<0.05
HOMA-IR	2.8 ± 2.3	2.4 ± 1.7	NS

Table 3. Variations of dyslipidemia among PCOS subjects.

4. Discussion

In our knowledge, this is the first study that describes lipid and lipoprotein profile and metabolic disorders associated to IR in Congolese women with PCOS.

We determined lipids and lipoprotein levels which were in the normal range. Our results are in accordance with previous African studies which had found lower levels of lipid and lipoprotein in African people compared to values reported in Caucasians [12–16, 22]. This difference could be explained by the low-fat and high-carbohydrate African diet. Indeed, nutritional transition is in process in Kinshasa. Although few people have modified their diet, eating more and more refined sugar and animal fat and less vegetable, the diet in people from Kinshasa remains poor in fat and wealthy in carbohydrates.

We observed in our study among PCOS women lower HDL and higher TG without change in LDL and this is consistent with other previous reports [7, 8, 17]. This inverse relation between HDL and TG is commonly found in insulin resistance and hyperinsulinemia.

We failed to observe a significant association between metabolic syndrome and biological insulin resistance as reported by several authors [5, 7, 8, 18, 19], possibly owing to the TG level ≥ 150 mg/dl in the metabolic syndrome's definition that we used. In addition, the small number of obeses in our PCOS group could also explain this observation. Previous studies

have reported greater proportion of obesity and overweight subjects. Indeed, the prevalence of metabolic syndrome increases with the rise of BMI [9, 10, 18, 20]. Overall, 30–50% of obesity or overweight can be found in women with PCOS. In the USA, more than 30% of adults are obese [5, 21]. In our study, only 3.7% of PCOS women were obese.

We observed the so-called TG paradox that has been described in Sub-Saharan African populations: normal triglycerides levels in the presence of IR [22].

The generally accepted cut-off point of TG level (≥ 150 mg/dl) could underestimate dyslipidemia and metabolic syndrome in African people due to lower lipid and lipoprotein levels reported in several African studies [12–16, 22]. It is, therefore, important to describe African lipid and lipoprotein profile and to propose another definition of metabolic syndrome, either in PCOS and in other patients. These findings may allow to discover existing metabolic syndrome in most of the PCOS patients from our study that could not be determined using international lipid and lipoprotein levels and the Rotterdam 2003 metabolic syndrome definition.

There were inherent limitations associated with this study: one of them was the limited number of patients. However, given the paucity of data available on PCOS in African women, our data, even though collected among a limited number of patients, confirm the need for further knowledge in endocrine and metabolic diseases in developing countries.

5. Conclusion

It is concluded that insulin resistance is associated with metabolic disorders in Congolese woman with PCOS. Dyslipidemia (55.6%), mainly due to low HDL levels, is the most common metabolic disorder. Impaired glucose tolerance and metabolic syndrome represent a small proportion.

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