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Reproductive Features and Insulin Sensitivity in Cameroonian Women with Polycystic Ovary Syndrome Consulting for Infertility

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Abstract

Background: Polycystic ovary syndrome (PCOS), characterized by ovulatory dysfunction, polycystic ovary (PCO), hyperandrogenism and insulin resistance is the commonest endocrine disorder in women of reproductive age. It is an intriguing pathology that involves the perpetuation of a vicious circle with reproductive, endocrine and metabolic components. We aimed to assess the reproductive features and insulin sensitivity (IS) in infertile women with or without PCOS.

Materials and Methods: We carried out a cross-sectional analytic studyat the outpatient Obstetrics and Gynaecology Department of the YaoundeGyneco-obstetric and Pediatrics hospital, Cameroon from September 1st 2012 to March 31st 2013 giving total study duration of 07 months. Laboratory analyses were carried out at the National Obesity Centre (NOC) of the Yaounde Central hospital, Cameroon.

Results: Overall, 36 infertile females were enrolled, which included 15 diagnosed cases of PCOS according to Rotterdam consensus meeting of 2003 and 21 non PCOS subjects as control. PCOS women were younger than non PCOS women (28.8± 5.5 *vs.*35.0± 4.2 years; $p = 0.0004$). The majority of the women in the PCOS group were spaniomenorrheic (11/15), and ultrasonographic findings were typical of PCOS. Hirsutism score was higher in the PCOS group with a median of 9(7-13). Insulin sensitivity was impaired in two thirds of the study population, with 12 women found to be insulin resistant (6 PCOS, 6 non PCOS), 12 patients had intermediate insulin sensitivity (2 PCOS, 10 non PCOS) and 12 insulin sensitive (7 PCOS, 5 non PCOS). Apart from blood glucose levels (p=0.007), all other anthropometric and biological parameters were not significant. Spearman's correlation identified fasting plasma glucose and total cholesterol as factors associated with insulin sensitivity in females with PCOS. Impaired fasting glucose was observed in 13 patients with 08 from the PCOS group.

Conclusion: We conclude that young age, spaniomenorrhea and hirsutism are common findings in PCOS. Furthermore our findings suggest that PCOS may be more of a systemic metabolic disease than solely a purely gynecologic disorder as described hitherto. Despite normal fasting plasma glucose levels, a good proportion of these women have impaired insulin sensitivity and it is associated to the metabolic syndrome.

Keywords: Reproductive features; Insulin sensitivity; Impaired fasting blood sugar; Infertility; PCOS

Introduction

Polycystic ovary syndrome (PCOS), recognized as the commonest endocrinopathy in females of reproductive age [1,2], is characterized by hyperandrogenism, polycystic ovary (PCO), and ovulatory dysfunction. Recently, PCOS is now thought to be more complex than purely a reproductive disease. An increase in androgen synthesis, disrupted folliculogenesis, and insulin resistance lie at the core of the pathophysiology of PCOS [3-5]. An intriguing concept involves the perpetuation of a vicious

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Table 1: Baseline Characteristics of Study Population.

CHARACTERISTICS	NON PCOS (n=21)	PCOS (n=15)	P value
Number of subjects (n)	21	15	
Age (years)	35.0 ± 4.2	28.8 ±5.5	**0.0004**
BMI (Kg/m^2)	27.8 ± 5.3	26.7 ± 3.5	0.4753
SBP (mmHg)	122.7 ± 15.9	123.9± 13.9	0.8207
DBP (mmHg)	86.2 ± 10.3	85.9 ± 11.4	0.9335
Waist Circumference (cm)	92.1 ± 13.2	86.3 ±8,1	0.1437
Total Body Fat (kg)	26.2 ± 10.1	23.6 ± 6.4	0.3964
Percent Body Fat (%)	34.9 ± 7.3	32.6 ± 5.6	0.2926
Fat free mass (kg)	46.4 ± 4.1	47.8 ± 3.7	0.2954

BMI: Body mass Index, SBP: Systolic Blood Pressure, DBP: Diastolic Blood Pressure.

Table 2: Systolic and Diastolic Blood Pressure and PCOS status.

Tension	PCOS status			Fisher's exact *p* value
		PCOS negative (n=21)	PCOS positive (n=15)	
Systolic Blood Pressure	Normal	17	09	0.37
	Prehypertension	02	04	
	Hypertension	02	02	
Diastolic Blood Pressure	Normal	08	08	0.68
	Prehypertension	05	02	
	Hypertension	08	05	

circle with reproductive, metabolic, and endocrine components.

More recently recognized findings include hyperinsulinemia and hyperlipidemia [6-8]. Evidence has it that hyperinsulinaemia may mediate the development of hyperandrogenemia, which in turn results in anovulation and infertility [9,10]. Infertility is a common complaint at gynaecological consultations in our context. To the best of our knowledge, no such study has been done in our setup. This study will therefore serve as a starting point for research in this syndrome.

Materials and Methods

This was a cross sectional analysis conducted in the at the Out-patient department of the Yaounde Gyneco-Obstetric and Pediatric Hospital, Cameroon from September 1,2012 to March 31, 2013 giving total study duration of 07 months. The study population included women who came in for infertility, aged between 15 and 49 years and who consented to partake in the study. We excluded patients who refused to take part in the study, those who were diabetic and those who were on insulin sensitizing drugs. Cases of PCOS was diagnosed using Rotterdam's criteria which stipulates the presence of a minimum of two of the following; oligoamenorrhoea, chronic an ovulation, clinical signs of hyperandrogeneamia (hirsutism, acné, alopecia) or laboratory evidence of hyperandrogeneamia (raised testosterone or and rostenedione levels) and polycystic ovaries on ultrasonography [11].

The variables measured included: age, body mass index (BMI), medical, gynaecologic, obstetrical and family past history and biological variables such as lipid profile, fasting glycaemia, fasting insulin levels, lipid profile, blood glucose levels, testosterone and androstenedione measured by the Jaffe method using a Roche-Hitachi Cobas C311® analyser at the National Obesity Centre (NOC) of the YaoundeCentral hospital, Cameroon.

Table 3: Reproductive profiles in the study population.

Characteristics	PCOS (n=15)	NON PCOS (n=21)	P value
Mean Menarche(Years)	13±1.7	14±1.6	0.0805
Type of Infertility			
Primary	10	8	0.0962
Secondary	5	13	
Menstrual Cycle			
Regular	4	17	0.0011
Spaniomenorrhea	11	4	
Obstetric History			
Gravidity[1]	0(2)	1(6)	
Parity[1]	0(1)	1(4)	
Abortions[1]	0(2)	0(3)	
Ferriman–Gallwey Score[2]	9 (7.13)	1 (0.3)	<0.0001

[1]: results expressed as medians (maximum values),
[2]: results expressed as medians (inter quartile range).

The sample size was determined using apre-estimate change in insulin sensitivity of 20% between the two groups. The mean insulin sensitivity, M, of a normal non HIV-infected, non-diabetic Cameroonian population is M= 14.3 ± 2.2 mg/kg/min [12]. Choosing α (two-sided) at 0.05, a statistical power of 80%, the minimum sample size was 10 subjects per group.

The data on the questionnaires were computed and validated using the Epi data software, version 3.5.1 and then exported to Microsoft Excel 2007 for further analysis.

Before carrying out this study, ethical approval was granted by the ethics committee of the Faculty of Medicine and Biomedical Sciences of the University of Yaounde I, Cameroon.

Results

During the study, 54 infertile females were recruited. Eighteen patients later withdrew from the study. Out of the remaining 36 who participated in the study, we had 15 cases of infertility associated with PCOS and 21 cases of infertility without PCOS.

In the study population the demographic and clinical characteristics were similar. The means of age, BMI and waist circumference (WC) 32.4 ± 5.6 years, 27.3 ± 4.7kg/m^2 and 89.7 ± 11.7cm respectively. Infertile females with PCOS were significantly younger than those without PCOS (28.8±5.5 vs 35.0±4.2 years; p = 0.0044), while the other baseline characteristics between both groups were statistically insignificant. The detailed socio-demographic characteristics between both groups are illustrated in Table 1. There systolic and diastolic blood pressure values between infertile females with PCOS and those without PCOS were similar (Table 2).

The reproductive profiles in study populations were also analysed. The average age at menarche was 14.0±1.6 years. Primary infertility was recorded in 18 patients and secondary infertility in 18 patients. Spaniomenorrhea was more frequent in females with PCOS than those without PCOS (p=0.0039). Clinical signs of hyperandrogenism were graded using the Ferriman-Gallwey score for hirsutism. These scores were relatively higher in the PCOS group. Details of these comparisons are elaborated in Table 3.

Table 4: Ultrasonographic findings in study population.

Pelvic Ultrasound	PCOS status			Fisher's exact *p value*
		PCOS negative	PCOS positive	
PCO	Negative	21/21	2/15	<0.0001
	Positive	0/21	13/15	
MYOMAS	Negative	17/21	13/15	1
	Positive	4/21	2/15	
NORMAL ECHOGRAPHY	Abnormal	3/21	8/15	0.03
	Normal	18/21	7/15	

Table 5: Linear regression analysis of predicators of KITT in women with the PCOS.

Predictors	Spearman Rho coefficient (r)	*P value*
Age	-0.009	0.97
Waist circumference (cm)	-0.04	0.9
Body mass index (Kg/m2)	0.20	0.5
Systolic blood pressure (mmHg)	-0.02	0.95
Diastolic blood pressure (mmHg)	0.14	0.6
Body mass (kg)	0.21	0.4
% body fat	0.06	0.8
Fat mass (Kg)	0.12	0.67
Lean body mass(kg)	0.33	0.23
Fasting plasma glucose (mg/dL)	0.86	**<0.0001**

BMI: Body mass Index, SBP: Systolic Blood Pressure, DBP: Diastolic Blood Pressure.

There was a significant difference between polycystic ovary found on ultrasound examination and the PCOS status (P< 0.0001). The presence or absence of myomas, normal and abnormal ultrasound findings did not have any statistically significant differences as far as PCOS or no PCOS were concerned (Table 4).

There were 12 insulin resistant subjects (6 PCOS, 6 non PCOS), 12 intermediate insulin sensitivity (2 PCOS, 10 non PCOS) and 12 insulin sensitive subjects (5 PCOS, 7 non PCOS). Comparisons between these subgroups were carried out. In order to identify the factors associated with insulin sensitivity in women with PCOS, linear regression analysis was carried out using the Spearman's correlation. Significant differences were observed with fasting plasma glucose (P values <0.05), as depicted in Table 5.

Discussion

Mean anthropometric variables in our study include WC 89.7 ±11.6cm, BMI 27.3± 4.6kg/m^2 and age 32.4±5.6 years. Age in our study was significant with the younger population being those with PCOS. The same observation was made in Cotonou by Denakpo and collaborators who found that PCOS patients were the younger population with an age range of 26 to 35 years [13]. BMI categories in our study found 36% lean subjects, 39% overweight and 25% were obese. These values though not statistically significant, were similar to those found in Ghana which were significant [14]. Obesity had only a marginal impact on our results.

In our study, 13 women had menstrual irregularity with spaniomenorrhea from the PCOS group (p= 0.002). Clinical hyperandrogenism, mainly hirsutism was more frequent in the PCOS group when compared to non PCOS group (p<0.0001). This concords with many consensus which define PCOS as pathology associated with menstrual irregularities and hyperandrogenism [15]. Ultrasound evidence of polycystic ovaries was seen in 13/15 of women. The majority of patients in the PCOS group consulted for primary infertility, while the majority in the non PCOS group consulted for secondary infertility. Pembe and collaborators [16] had similar findings. Denakpoand collaborators in Cotonou [13] found spaniomenorrhea, hirsutism and polycystic ovaries as signs with highest frequency in the PCOS population.

Our study showed that 6 out of 15 PCOS patients were insulin resistant, 2 had intermediate insulin sensitivity and 7 were insulin sensitive. These findings are different from those obtained in Egypt where 58% of the study population were insulin resistant compared to 42% noninsulin resistant [17]. The prevalence rate of insulin resistant in females with PCOS varies across studies. Some authors advocate that insulin resistance is always present in these females [18] whereas others estimated the prevalence rate of insulin resistance to vary between 40% to 70% [19]. These results vary due to the diagnostic methods used [12,20,21]. Interestingly, the same number of insulin resistant (IR) subjects were found in non PCOS women. This reiterates the role played by factors other than obesity in the regulation of insulin resistance. These findings corroborate with those of the Insulin Resistance and Atherosclerosis Study in black adults who demonstrated evidence of insulin resistance when compared with white adults of a similar body weight [22]. Likewise, a study conducted on US black women showed that there were more insulin resistant despite a lower amount of visceral fat [23]. This difference in prevalence of IR could be explained by fact that the pathogenesis of IR involves the interplay of both genetic (often polygenic in nature) and environmental factors [24]. Nonetheless, several other factors have been implicated in the aetiology of IR, namely prenatal factors, ethnicity, diet, puberty, and sedentary lifestyles.

We acknowledge some limitations to this study; the control group was limited to women seeking treatment for infertility. This may have caused bias in the selection of the represented population.

Conclusion

We conclude therefore that PCOS is a common finding in our population of infertile women and that young age, spaniomenorrhea and hirsutism are also common clinical findings in PCOS in our population. Overall, our findings suggest that PCOS may be more of a systemic metabolic disease than solely a purely gynecologic disorder as previously described in the literature. Despite normal fasting plasma glucose levels, a good proportion of these women have impaired insulin sensitivity and it is associated to the metabolic syndrome. The clinical characteristics of PCOS and the metabolic features should always be considered when treating such patients.

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