Original Research Article

Reproductive Endocrinologic Pattern in Infertile Black Women with Polycystic Ovarian Syndrome

Running Title: ReproductiveEndocrinology inPCOS Infertile Women

Abstract

Background:Polycystic ovarian syndrome (PCOS) is avery common endocrine cause of infertility affecting about 10% of women of reproductive age. We evaluated the pattern of reproductive hormones in infertile Nigerian women with PCOS.

Methods:This was aprospective cross-sectional study at the Lagos State University Teaching Hospital over a 6-month period in which One hundred and fifty infertile women, with diagnosis of PCOS using the Rotterdam's criteria,had quantitative assessment of their reproductive hormones (Luteinizing Hormone (LH), Follicle Stimulating Hormone (FSH), Progesterone, Testosterone, Prolactin and Thyroid Stimulating Hormone (TSH)) determined, with relevant socio-demographic and clinical data noted in the study proforma. Student t-test, chi-square and correlation tests were used as appropriate to analyse the data with $p<0.05$ significance level.

Findings:The mean age of infertile women with PCOS was 26.50±4.4years; all the women had either oligomenorrhea (62%) or secondary amenorrhea (38%) and 56.5% were obese.While 37.7% of the women had abnormally elevated serum LH, 16.4% had high serum FSH, 39% had LH:FSH ratio> 2.5, 96% had low serum progesterone, 29% had high serum prolactin, 17.4% had high serum TSH values and 92% had features of polycystic ovaries on trans-vaginal ultrasound. Correlation of age and BMI with serum FSH, LH and prolactin values were weak and insignificant.

***Conclusion*:** PCOS is common among young Nigerian women presenting for infertility treatment; with dominant features of oligomenorrhea and polycystic ovaries. Hormonal abnormalities are common, varied and not associated with other clinical characteristics.

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Key Words:PCOS, Polycystic Ovarian Syndrome, Infertility, Rotterdam's Criteria, Hormonal Profile.

Introduction

Polycystic ovary syndrome (PCOS) is a common endocrinologic disorder in women that affects reproductive function [1]. It occurs in 5-10% of women of child bearing age and its exact cause is not known [2,3].The Rotterdam 2003 criteria require at least presence of two of the following three conditions for the diagnosis of PCOS: Oligo- or anovulation (menstrual irregularity), clinical or biochemical signs of hyperandrogenism, and polycystic ovaries on ultrasound [4].PCOS is a well-established medical condition that negatively affects reproduction, general health, sexual health, and quality of life [5].

Less is known about the influence of race on the PCOS phenotype [6].Emerging evidence suggeststhat ethnicity may be associated with PCOS phenotype due to varying genetic and environmental propensity to metabolic and hormonal abnormalities [7-9].In developed countries, although much has been clarified, on the pathogenesis, diagnosis, clinical manifestations, and treatment of PCOS, [5] adequate profiling of women with PCOS in developing countries and black African populations is relatively sparse.We, therefore, assessed the pattern of reproductive hormone levels in infertile Nigerian women with PCOS.

Materials and Methods

This was a prospective cross-sectional study of150 women,with PCOS who were being evaluated for infertility at the gynaecology clinic of the Lagos State University Teaching Hospital between January and June 2017. Consenting women aged 18-45years with history of primary or secondary infertility were recruited while women on ovulation induction medications, with co-existing ovarian tumours and on chemo- and/or radio- therapy were excluded from the study.

Each recruited participant completed a structured administered questionnaire to obtain socio-demographic data, sexual history, obstetrics history, medical history and menstrual history. The anthropometric measurements, weight and height of each subject were taken using a calibrated weighing scale (Medfield equipment and Scientific Ltd. England) and a meter height scale (Avery Co. Ltd, England).

The study participants were examined in a well-lit changing room, for facial, chest, abdominal, arms, thighs, back hair distribution to give the Ferriman and Gallwey score for hirsutism. Diagnosis of hirsutism was made if the score was greater or equal to 8.

Technique of Trans-vaginal Ultrasound

Each participant was asked to empty her urinary bladder and then taken into the examination room ensuring adequate privacy with a female chaperone in attendance. She was placed in a supine lithotomy position with both knees flexed on the examination couch with adequate exposure of the vulva. The examination area was sufficiently screened. All scans were performed in a systemic manner using the trans-vaginal 7.5 to 12 MHz Broad Band ultrasound curved-array transducer. A Mindray Real Time Ultrasound Scanner Model Z5 was used. Folded sheets or pads were placed under the participant's buttocks to elevate her pelvis above the examination couch to allow room for transducers manipulation. Ultrasound

coupling gel was applied into a latex male condom and used to completely cover the trans-vaginal probe. A different condom was used for each woman. After parting the labia, the probe covered with condom was then gently introduced into the participant's vagina advancing slowly toward the cervix. The transducer was then moved laterally to the adnexal area to properly visualize the ovaries. During the trans-vaginal ultrasound scanning, the ovaries could be brought into view by using one hand to compress the lower abdominal wall while the other hand manipulated the transducer. The trans-vaginal ultrasound image of the ovary in longitudinal plane appeared and was frozen for measurements**.** The ovaries were often identified by the presence of follicles, which appeared hypoechoic or anechoic. Once scanning was completed in the longitudinal plane, the probe was rotated 90 degrees counterclockwise so that the transducer was now in a transverse plane and frozen for measurements**.** After identification of the ovaries the size of the ovary was measured in three orthogonal planes, namely; longitudinal (length) transverse (thickness) and anteroposterior (width). On measuring the dimensions, inherent volume software in the machine automatically calculated the volume.The measurements were obtained from the frozen ultrasound images with electronic calipers. The total number of follicles in each ovary was counted. Follicles were counted on the frozen images of two non-overlapping planes in the longitudinal section of each ovary and summed up together. Measurements of the follicles were made in their maximum internal diameters and recorded in mm; their distributions were also noted as either peripherally or randomly.

The diagnosis of polycystic ovary (PCO) morphology was made if 10 or more follicles each measuring 2-8 mm in diameter were present and peripherally arranged in the ovaries (giving a string of pearl appearance) and/or ovarian volume was increased greater than 10mls [10]. A description of the distribution of the follicles was recorded by visual assessment of location of follicles as being scattered through the stroma or arranged peripherally in the classically

described “string of pearl” at the margin of the ovary. Stromal echogenicity was defined as normal or increased (echogenic) in comparism to the myometrium whose echogenicity is greater than normal ovarian stroma [10,11]. To reduce intra observer variability, the measurements were taken thrice and an average obtained. After the procedure, the probe was withdrawn gently and slowly, patient was cleaned up with tissue paper and politely asked to stand up and dress up.

The hirsutism scores using the Ferriman/ Gallwey scoring system, trans-vaginal sonographic ovarian findings (ovarian volume, follicular number, size, distribution and stromal echogenicity) for each woman were recorded in the study proforma for subsequent data analysis.

Statistical analysis

The data obtained from the questionnaires were coded, imputed into the computer and analyzed using SPSS 20.0 statistical software. Percentage and proportions were determined for categorical variables. Pearson’s Chi-square (test for association) was used to assess the significance of relationships between categorical variables. Students-t test and Pearson’s correlation was used to compare continuous variables. P–values less than 0.05 were considered to be statistically significant at a confidence level less than 95%. Ethical approval was obtained from the Health Ethics and Research Committee of the Lagos State University Teaching Hospital.

Results

A total of 150 women, who met the Rotterdam diagnostic criteria for PCOS, being evaluated for infertility were studied. The mean age of the women with PCOS in this study was 26.50years with the majority (76%) of age range 21 to 30years (Table 1). All the women had some degree of menstrual abnormalities with oligomenorrhea occurring in62.0% and amenorrhea in 38.0% (Table 1). More than half (56.5%) of the women were obese, 33.3% had hirsutism, 29.3% had acne and 92.0% had ultrasound findings of polycystic ovaries (Table 1).

In the study population, the median values of serum LH was 14.9mIU/ml, serum FSH was 6.0mIU/ml, serum prolactin was 13.7ng/dl, serum TSH was 2.1mIU/ml and serum testosterone was 1.9ng/ml (Table 2). Majority (62.3%) of the women had high serum LH values, 83.6% had normal serum FSH levels, 39% has a high LH:FSH ratio, 96% had low serum progesterone values and 29% had elevated serum prolactin levels (Table 3).

Clinical and endocrinologic values were similar in women with PCOS who had polycystic ovarieson ultrasonography when compared with women without polycystic ovaries (Table 4). Correlation of age and body mass index (BMI) with Hormonal values of FSH, LH and prolactin were weak and insignificant (Table 5).

Table 1: Socio-demographic and clinical characteristic of the women

Variable	Frequency (N = 150)	Percentage (%)
Age (in years)		
<20	9	6.0
21 – 30	114	76.0
31-40	27	18.0
Mean ± SD	*26.50±4.4*	
Range	*16-40*	
Education		
None	14	9.3
Primary	8	5.3
Secondary	33	22.0
Tertiary	95	63.4
Religion		
Christianity	106	70.7
Islam	44	29.3
Marital Status		
Single	62	41.3
Married	88	58.7
Menstrual symptoms		
Oligomenorrhea	93	62.0
Secondary amenorrhea	57	38.0
Body Mass Index		
Underweight	20	16.4
Normal	24	19.7
Overweight	9	7.4
Obese	69	56.5
Hirsutism		
Yes	50	33.3
No	100	66.7
Acne		
Yes	44	29.3
No	106	70.7
Ultrasound features		
PCOS	138	92.0
Non-PCOS	12	8.0

Table 2: Median Values of Hormonal Levels in Women with PCOS

Hormone	Median	IQR
LH(mIU/ml)	14.9	15.8
FSH(mIU/ml)	6.0	4.1
Prolactin (ng/dl)	13.7	12.0
TSH (mIU/ml)	2.1	2.8
Testosterone (ng/ml)	1.9	1.8

IQR – Inter quartile range, LH - Luteinizing hormone,
FSH -Follicular stimulating hormone, TSH – Thyroid Stimulating Hormone

Table 3: Distribution of hormonal levels in women with PCOS

Hormone	Serum Level	Frequency	%
LH	Normal = 0.5-10.9mIU/ml	55	37.7
	High≥ 11mIU/ml	91	62.3
FSH	Normal = 2.0-12mIU/ml	122	83.6
	High ≥ 12mIU/ml	24	16.4
LH / FSH ratio	Normal ratio ≤ 2.5	89	61.0
	High ratio > 2.5	57	39.0
Progesterone	Normal ≥ 20ng/ml	5	4
	Low < 20ng/ml	145	96
Testosterone	Normal = 15ng/ml-70ng/ml	120	95.2
	Low <15ng/ml	6	4.8
Prolactin	Normal level≤ 19ng/dl	103	71.0
	High level > 19.0ng/dl	42	29.0
TSH	Normal ≤ 6.2mIU/ml	90	82.6
	High > 6.2mIU/ml	19	17.4
LH - Luteinizing hormone, FSH -Follicular stimulating hormone, TSH – Thyroid Stimulating Hormone			

Table 4: Comparison of PCOS women with polycystic ovaries versus women without polycystic ovaries on ultrasound

Variables	PCO	Non-PCO		
	Median ± IQR	Median± IQR	z-test	p-value
Weight	72 ± 18	43.5± 54.2	1.673[z]	0.094
Height	1.61 ± 0.09	1.61± 13.9	-0.364[z]	0.715
BMI	42.5 ± 40.5	5.5±43.5	1.623[z]	0.104
LH	15.0 ± 15.7	7.3±1.1	1.313[z]	0.189
FSH	6.0± 5.0	5.2±3.0	0.186[z]	0.852
Prolactin	11.8± 11.8	23.4±16.7	-0.961[z]	0.336
TSH	2.3± 2.7	2.0±1.1	0.863[z]	0.388
Testosterone	1.9± 1.5	1.9±1.3	-0.094[z]	0.924
T3	5.3± 2.0	1.1± 0.0	1.451[z]	0.146
T4	10.5± 44.5	15.0± 0.0	-0.707[z]	0.479

z– test for non-parametric test applied, PCO-Polycystic ovary,LH - Luteinizing hormone, FSH -Follicular stimulating hormone, TSH – Thyroid Stimulating Hormone, T3-Triiodothronine, T4-Thyroxine.

Table 5: Correlation of age and BMI with hormonal values in women with PCOS

	Correlation coefficient	**p-value**
Age and FSH	0.127	0.127
Age and Prolactin	0.102	0.221
Age and LH	0.090	0.278
Age and LH/FSH ratio	0.082	0.162
BMI and FSH	-0.095	0.299
BMI and Prolactin	-0.057	0.533
BMI and LH	0.005	0.954
BMI and LH/FSH ratio	0.007	0.345
LH - Luteinizing hormone, FSH -Follicular stimulating hormone, TSH – Thyroid Stimulating Hormone, BMI-Body Mass Index		

Discussion

The mean age of the women with PCOS in this study was 26.5years with about three-fourth of them (76%) being within the age range 21 to 30years. This is similar to the mean age of 27years reported in women with PCOS by Igwegbe et al [3] in a study in Nnewi, south-eastern Nigeria but lower than the mean age of 30years and 31.5years,in women with PCOS, observed by Ugwu et al [12] in Enugu and Omokanye et al [13] in Ilorin, Nigeria respectively.PCOS is a condition in women within the reproductive age group and this explains all the mean ages in these studies being within this category.

None of the women had normal menstrual cycle length,with oligomenorrhea occurring more frequently(62%) than amenorrhea which was present in 38% of the women (Table 1). Of these women with PCOS in our study, we observed that more than half (56.5%) of the women were obese, 33.3% had hirsutism, 29.3% had acne and 92% had ultrasound findings of polycystic ovaries. The abnormal menstrual cycle length is very likely due to anovulation, a common finding in women with PCOS. Oriji et al [14] in Port Harcourt Nigeria noted that majority of women (65.5%) with PCOS in their study had normal cycle lengths, 27.5% had oligomenorrhea and 41.3% had acne. March et al in an Australian study also found that a lower proportion (23.8%) of women with PCOS were oligomenorrheic. This variation with our findings may be due to the small number of women with PCOS in the study by Oriji et al [14]and phenotypic differences with women in the Australian study [15].

Oriji et al however found that 92% of infertile women with PCOS had at least one polycystic ovary; this finding is in keeping with observations in our study [14].Reports, by Ugwu et al[12] in south east Nigeria, of oligomenorrhea in 72.6%, obesity in 51.6% and a LH/FSH ratio > 2 in 45.2% in women with PCOS are similar to findings of our study. We noted that 39.0% of women with PCOS had a LH/FSH ratio of > 2.5.

Median values of weight, height, body mass index (BMI) and serum LH, FSH, Prolactin, TSH, Testosterone, T3 and T4 were similar when women with PCOS with ultrasound features of polycystic ovaries were compared with women without ultrasound features of polycystic ovaries, but met the diagnostic criteria for PCOS. This probably suggests that the presence of the polycystic ovarian morphology typical of PCOS is not a mandatory pre-requisite for anovulation or infertility in women with PCOS. Neither age nor BMI correlated with serum values of LH, FSH and prolactin in women with PCOS.

Conclusion

In conclusion, PCOS is common among young Nigerian women presenting for infertility treatment; with dominant features being oligomenorrhea and polycystic ovaries. Reproductive hormonal abnormalities are common, varied and not associated with other clinical characteristics in these women.

COMPETING INTERESTS DISCLAIMER:

Authors have declared that no competing interests exist. The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

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