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RESEARCH ARTICLE

LEVELS OF FSH, LH, SHBG, TOTAL TESTOSTERONE, AND LH/FSH RATIO IN SUDANESE PATIENTS WITH POLYCYSTIC OVARY SYNDROMEIN RELATION TO BODY MASS INDEX

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ABSTRACT

Objectives: to examine the role of PCOS in alteration of FSH, LH, Total testosterone, LH/FSH ratio as well as correlating the outcome to obesity.
Methods: One Hundred female patients with PCOS based on Rotterdam 2003 criteria. Together with fifty healthy volunteer females included as controls. Serum levels of follicle stimulating hormone (FSH), luteinizing hormone (LH), sex hormone binding globulin (SHBG) and total testosterone were tested in the two group. On top of that, we calculated LH/FSH ratio in all attendants. Body Mass Index (BMI) evaluated to be a part of the correlation. The resulted data were organized in tables and subjected for statistical analysis.
Results: A significant increase was found in LH and total testosterone as well as significant decrease in SHBG in PCOS females compared to controls. Serum FSH was insignificantly increased in PCOS women. LH/FSH ratio was significantly high in non-obese patients when compared with obese patients and control.
Conclusions: Hyperandrogenism is intrinsic to PCOS. At the same time, LH/FSH ratio was increased in non-obese PCOS patients.

INTRODUCTION

Polycystic Ovary Syndrome (PCOS) is a frequent endocrine condition, which affects 2.2% to 26% of female of reproductive age (March *et al*., 2010). The etiology PCOS is unknown. Even though, PCOS could be the result of ovarian abnormalities that interact with one or more different congenital and perhaps environmental factors to result in dysregulation of steroidogenesis (Ehrmann *et al*., 1995). The primary biochemical finding in PCOS is hyperandrogenism (Dunaif and Thomas, 2001). On top of that, females with PCOS repeatedly present with weight problems and show a higher chance of developing metabolic syndrome (Dunaif and Thomas, 2001, Elting *et al*., 2001). Elevated androgens in PCOS were thought to result from increased androgen generation in ovaries as well as adrenals (Franks, 1995), moreover ovarian thecal cells produce only about 25-30% (Piltonen *et al*., 2002). On the other hand, there is clues for a substantial contribution of peripheral steroid genesis to androgen synthesis in PCOS (Fassnacht *et al*., 2003) as well as the ability of human adipose tissue to synthesize androgens (Quinkler *et al*., 2004). Obesity has been documented as a frequent finding in PCOS (Cascella *et al*., 2008) especially central obesity, since the majority of PCOS individuals exhibited an intermediate or android kind of fat distribution (Kirchengast and Huber, 2001). Moreover, body fat ratio, upper-half body fat ratio and upper-half/lower-half body fat ratio were remarkably increased in PCOS females compared to controls (Douchi *et al*., 1995). Likewise, visceral fat amount was significantly higher in PCOS patients as opposed to controls (Cascella *et al*., 2008). Furthermore, patients with PCOS had a higher trunk to extremity fat ratio (T/E fat) when compared with control (Puder *et al*., 2005). Interestingly, serum androgens are correlated with body mass index (BMI) not just in PCOS, but also in females with simple obesity (Taponen *et al*., 2003). When compared to weight-matched healthy women, those with PCOS have a similar quantity of total fat, but a higher amount of central abdominal fat (Carmina *et al*., 2007). Many researches have assessed body fat distribution in women with PCOS, yet it remains disagreeable whether the adiposity-related tendency to PCOS indicates an overall adiposity, as shown by the body mass index, or is more closely attributed to the local buildup of visceral/abdominal lipid, resulting in abnormalities of body fat distribution (Holte *et al*., 1995, Goodarzi *et al*., 2005). Founded on these considerations, the present study was conducted to assess the role of PCOS in modification of FSH, LH, and Total testosterone as well as relating the results to obesity.

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MATERIALS AND METHODS

This a cross-sectional study carried out in Khartoum state, Sudan; between June 2013 and December 2014. The study included 100 female patients suffering from polycystic ovary syndrome (PCOS). The age of involved patients was 22 - 44 years (32.610 ± 5.696 years). Control group was consisted of 50 healthy volunteer females, whose mean ages were matched (30.140 ± 5.198 years). Patients diagnosed according to Rotterdam 2003 criteria (group, 2004). Informed consent was obtained from each participant. Pre-prepared questionnaire including data concerning patients and their PCOS information (such as age, family history, type of treatment, and BMI) was used following the protocol of the ethical committee of Omdurman Islamic University. Venous blood sample (10 ml) was obtained at 8:00-10:00 AM on day 2 of menstrual cycle from antecubital vein from patients and controls by standard venipuncture technique without venous stasis in serum separator tube (SST). Serum was separated after 20 minutes and then stored at -20°C till the time of analysis. Serum levels of follicle stimulating hormone (FSH), luteinizing hormone (LH), sex hormone binding globulin (SHBG) and total testosterone were analyzed with each sample. The hormones estimations were performed with ELISA. Testosterone, FSH and LH were analyzed as described by (Ganie *et al*., 2014). SHBG was measured by commercial immunoassays (Immulyte, Los Angeles, CA, USA) as described by Ly *et al* (Ly and Handelsman, 2005). Within the Division of Medical Laboratory, VRC Center, Khartoum, two levels of control material and analyses were performed by according to the manufacturer.

Methods of body mass index (BMI) estimation

The BMI calculates a value indicative of the fat content of the body by dividing the body weight by the square of body height. Following the method adopted by Ly *et al*. (2005), the BMI categories as follow:

Underweight is less than 18.5, normal weight is 18.5 - 24.9, overweight is 25 - 29.9, and obese is 30 or higher. Statistical analyses: All data was analyzed using the Statistical Package for Social Sciences (SPSS) software computer program version 11.0 (SPSS, Chicago, IL). Data were expressed as mean ± standard deviation (SD) following analyzes using student t-test, which was performed for comparison between control and patient groups. A value of $P < 0.05$ was considered significant.

RESULTS

As in Table 1, the mean age of PCOS females was matched with control females showing insignificant changes (P>0.05). The present study revealed a significant rise in LH and total testosterone and significant reduction in SHBG in PCOS females when compared to controls. Serum FSH registered insignificant rising in PCOS females. In Table 2, the PCOS females were classified according to BMI into two groups: obese and non-obese patients. All parameters showed insignificant alteration between these two groups (P>0.05), except LH/FSH ratio which was significantly higher in non-obese patients when compared with obese patients as well as control as shown in Table 3 that compared the result of LH: FSH in the three groups.

Table 1. Comparison of results between PCOS and control group

	PCOS patients	Control	P value
No.	50	50	
AGE(years)	32.61 ± 5.7	30.14 ± 5.2	P>0.05
FSH (mIU/mL)	5.78 ± 1.77	2.7 ± 1.41	P>0.05
LH (mIU/mL)	7.87 ± 2.03	2.75 ± 1.53	P<0.05
LH/FSH ratio	1.68± 1.26	1.33 ± 1.10	P>0.05
T. Testosterone(ng/dL)	71.63 ± 24.87	38.17 ± 14.34	P<0.001
SHBG (nmol/l)	29.85±5.72	50.72 ±5.51	P<0.001

Table 2. Comparison of results between obese and non-obese patients

	Non-obese PCOS	Obese PCOS	P value
No.	50	50	
AGE(years)	32.52±6.1	32.7±5.33	P>0.05
FSH (mIU/mL)	4.47 ±1.29	7.08±1.09	P>0.05
LH (mIU/mL)	9.3±1.43	6.44±1.45	P>0.05
LH/FSH ratio	2.42 ± 1.42	0.93 ± 0.27	P<0.001
T. Testosterone(ng/dL)	71.49 ±22.52	71.75±27.25	P>0.05
SHBG (nmol/l)	27.14±4.63	32.56 ±5.45	P>0.05

Table 3. Comparison of LH/FSH ratio between obese, non-obese patients and control

	Non-obese PCOS	Obese PCOS	Control
No.	50	50	50
LH/FSH ratio	2.42 ± 1.42[a b]	0.93 ± 0.27[c]	1.33 ± 1.10

a: Significant variation when compared to obese PCOS
b: Significant variation when compared to control
c: Insignificant variation when compared to control

DISCUSSION

PCOS is among the commonest endocrine diseases affecting females, even though its etiology is inadequately recognized (Kirchengast and Huber, 2001). In the current study, all PCOS women turned up to have significantly high T. testosterone (P<0.001), significantly high LH (P<0.05) and also significantly low SHBG (P<0.001) levels matched against controls, independently of the BMI. Aside from that, FSH showed insignificant difference between the two groups (P>0.05) as well as LH: FSH ratio. (Nestler *et al*., 1991) reported that levels of serum SHBG, which regulates the bioavailability of androgens to target tissues, are decreased with high levels of androgens. This study indicated that regardless of weight, PCOS patients (lean as well as obese) were essentially hyperandrogenic and were low in SHBG. Also, the result was in line with other studies (Dunaif and Thomas, 2001, Holte *et al*., 1994) with regard to hyperandrogenism in PCOS, and with report of (Martinez-Garcia *et al*., 2012) which stated that the level of SHBG is reduced in patients with PCOS.

LH/FSH ratio result was insignificantly different between PCOS patients and controls, although (Lewandowski *et al*., 2011) stated that females with PCOS have an increased rate of hypothalamic GnRH pulses, and this results in a rise in the LH/FSH ratio. According to (Chun, 2014), increased LH relative to FSH has long been recognized in PCOS. On the other hand, it was not included in the diagnostic criteria. In accordance with this, there was insignificant variation (p>0.05)

in LH/FSH ratio between the two groups. Conversely, that was not the situation when comparing obese and non-obese patients. According to BMI, the PCOS women in this study were classified as obese and non-obese. There were insignificant differences ($p>0.05$) in hormonal levels between non-obese and obese patients with PCOS except in LH/LSH ratio, despite that (Grulet *et al*., 1993) reported the presence of hyperandrogenism in obese compared to non-obese women with PCOS.

Result of high LH/FSH ratio in lean females with PCOS may negatively answer the question raised by (Alnakash, 2007) "does higher BMI inevitably imply a higher LH/FSH ratio". In addition, the Rotterdam group (2004) necessitated further studies in non-obese women with PCOS. Our study could be one of the studies responding to this recommendation. According to (Banaszewska *et al*., 2003), LH/FSH ratio is not a typical feature of all PCOS women. Additionally, (Cho *et al*., 2006) stated that the measurement of the LH/FSH ratio has limited value in the diagnosis of PCOS. However, the finding, in our study, of higher LH/FSH ratio in non-obese patients with PCOS when comparing it to obese patients as well as controls, could be explained by higher visceral fat amount in lean patients (difference of ratio between controls and obese patients with PCOS was insignificant). As emphasized by (Shuster *et al*., 2012), BMI is unable to make a distinction between subcutaneous and visceral fat compartments. (Svendsen *et al*., 2008) declared that the correlation between PCOS and low insulin sensitivity index (ISI) in lean females with PCOS could partly be explained by higher visceral/subcutaneous fat ratio. We expected this could be the case in our study regarding LH/FSH ratio. The result of this study highlights the statement of (Lord *et al*., 2006) that the most prominent factor correlating with metabolic disorders in women with PCOS is visceral fat, as compared with subcutaneous one, since accumulation of visceral fat causes insulin resistance. In conclusion, hyperandrogenism is inherent to PCOS, irrespective of whether the subject is lean or obese. In addition, LH/FSH ratio is high in non-obese PCOS patients which suggests the involvement of visceral fat in the pathogenesis of PCOS.

More studies should be carried to reveal the entire role of visceral fat in PCOS.

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