Relation of elevated androgen to lipid profile in patients with polycystic ovary syndrome

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Abstracts

Background: Polycystic ovary syndrome is considered to be the most prevalent endocrinopathy resulting from anovulation and affects 5-10% of women. Both insulin resistance and hyperandrogenemia predispose polycystic ovary syndrome patients to atherogenic lipid profile. It is not clear however what role hyperandrogenism has on the development of the metabolic syndrome.

Objective: To investigate the effect of elevated androgen level in patients with polycystic ovary syndrome on lipid profile.

Methods: Between October 2012 and October 2013, forty polycystic ovary syndrome patients and forty healthy controls were recruited into this cross sectional study where the following parameters were determined for PCOS patients and compared to healthy control: Serum Follicle stimulating hormone , Luteinizing hormone level and testosterone levels. Serum lipid profile (total cholesterol, triglyceride, high density lipoprotein and low density lipoprotein) were measured by spectrophotometry by enzymatic colorimetric method. Linear regression analysis was used to evaluate the association between the lipid parameters and the testosterone level.

Results: This study has showed that the luteinizing hormone (LH), Follicle stimulating hormone (FSH), and testosterone are significantly different between the two groups(8.4±1.16 vs. 7.02±1.8; *p*=0.002, 4.43±1.3 vs. 5.4±1.24; *p*=0.04, 2.104±1.161 vs. 0.82±0.32; *p*=0.001 respectively). Regarding lipid profile, Polycystic ovary syndrome patient display lower high density lipoproteins level (40.3143±7.5994 vs. 45.7272±11.348; p<0.001) and higher triglyceride level (168.6±34.6401 vs. 129.625±45.4125; p<0.001). In linear regression analysis total cholesterol was positively associated with testosterone level and High density lipoprotein cholesterol was negatively associated with testosterone level(regression coefficient = 0.313 for total cholesterol, r=0.409 for High density lipoprotein-cholesterol). No association was observed between Low density lipoprotein-cholesterol or triglyceride levels with testosterone level.

Conclusion: Our results suggest that the characteristic hyperandrogenemia in women with PCOS were associated with dyslipidemia.

Keyword: Polycystic ovary syndrome, lipid profile, androgen

Introduction

Polycystic ovary syndrome (PCOS) is one of the most common endocrine disorders in women of reproductive age and is the most frequent cause of hyperandrogenism and anovulation [1].

A PCOS diagnosis is considered a hyperandrogenic disorder of exclusion with an obvious etiology. In 2006, the androgen excess PCOS society recommended that PCOS to be defined by clinical and/or biochemical hyperandrogenism, with either oligo-anovulation and/or polycystic ovaries, excluding related disorder [2].

Women with androgen excess are at higher than normal risk for hyperlipidemia especially when accompanied by obesity [3].

There is evidence that insulin resistance, central obesity and hyper-androgenaemia have an adverse effect on lipid metabolism [4] and considered as risk factors for the development of hypertension and dyslipidemia, diabetes mellitus and coronary disease in PCOS [5].

The clustering of lipid risk factors identifies individuals at increased risk for coronary heart disease [6].

There is increasing evidence that patients with polycystic ovary syndrome (PCOS) have increased cardiovascular risk compared with age matched controls. It has been estimated that myocardial infarction is seven times more likely in patients with PCOS [7].Hypertriglyceridemia, increased levels of very low-density lipoprotein (VLDL) and LDL cholesterol, and decreased levels of HDL-cholesterol [8] predispose patients to vascular disease in the polycystic ovary syndrome [9].

Androgen excess is considered by some investigator to be the key feature of PCOS [2].

Objective of this study is to investigate the effect of elevated androgen level in patients with polycystic ovary syndrome on lipid profile

Patients and Methods:

A total of forty female with PCOS and mean age 31 years (25-37) were included in the study. They had not been prescribed any medication before enrollment and were diagnosed using Rotterdam criteria (the presence of two out of three criteria): oligo-ovulation or anovulation, clinical and/or biochemical signs of hyperandrogenism or polycystic ovaries, and exclusion of other etiologies [10]. They were presented to out - patients unit at Alramadi maternity teaching Hospital and to private clinic. This cross- sectional study was conducted over a period of thirteen months from the first of October 2012 to the end of October 2013. Forty healthy female patients matched for age (mean age 30 range 25-35 years) but without PCOS were included in the control group. Body mass index (BMI) was calculated as weight (kg)/height (m^2).

After verbal consent, the following parameters were determined for PCOS patients and healthy control: Serum FSH, LH level, and testosterone were performed on the third day of normal or progestin induced

withdrawal bleeding using Mini VIDAS system. Serum lipid profile (total cholesterol, triglyceride, high density lipoprotein cholesterol and low density lipoprotein) were measured by spectrophotometry by enzymatic colorimetric method by using commercially available kit (biomaghreb). Serum low density lipoprotein was determined according to the following Friedewald equation: LDL=total cholesterol – (HDL+VLDL) where VLDL=$\frac{TG}{5}$

The statistical analysis was conducted using t - test (2 tailed) and the level of significance was taken as $p<0.01$. Linear regression was used to evaluate the association between the different lipid parameters and the testosterone level.

Results

The basic demographic data of the PCOS patients are shown in **table 1**. The majority of patients were oligomenorrhoic (67.5%) and 70% of total number of PCOS were nullipara, 18(45%) of PCOS patients had hirsutism and only 8(20%) complain of acne. Biochemical, endocrinological results, and BMI in patients with PCOS and control subjects are presented in **table 2**. There was no difference between groups in term of body mass index ($p = 0.2497$).Compared with healthy women, women with PCOS presented higher triglycerides levels (mean difference =46.829 mg/dl $p<0.001$). HDL-cholesterol showed lower levels in PCOS patients compared with healthy women (mean difference = 4.8857mg/dl, $p< 0.001$).No difference was observed between groups in terms of total cholesterol and LDL levels (**Figure 1**). Linear regression was used to evaluate the relationship between the total cholesterol, LDL cholesterol, HDL-cholesterol, triglyceride, and androgen level. In linear regression analysis total cholesterol was positively associated with testosterone level and HDL-cholesterol was negatively associated with testosterone level($r = 0.313$ for total cholesterol, $r=0.409$ for HDL-cholesterol). No association was observed between LDL-cholesterol or triglyceride levels with testosterone level**(table 3)**.

Table (1): Basic Demographic Data of PCOS patients

Characteristics	N (%)
Regularity of cycle	
Oligomenorrhoea	27(67.5)
Amenorrhoea	3(7.5)
Regular cycle	10(25)
BMI	
>25kg/m2	26(65)
<25kg/m2	14(35)
Hirsutism	
Non-hirsute	22(55)
Hirsute	18(45)
Acne	8(20)
Nulliparity	28(70)

Table (2): The biochemical, BMI and endocrinological results of PCOS patients & control.

Parameter	PCOS (n=40)	Control (n=40)	P value
BMI	31.004±2.4232	31.2±2.7988	0.2497
LH	8.4±1.16	7.02±1.8	0.002
FSH	4.34±1.3	5.4±1.24	0.04
Testosterone	2.104±1.161	0.82±0.32	0.001
Cholesterol	168.4324±36.84	176.454±27.724	0.142
Triglyceride	168.6±34.6401	129.625±45.4125	<0.001*
HDL	40.3143±7.5994	45.7272±11.348	<0.001*
LDL	99.8±32.75	91.1364±14.0112	0.062

Table (3): Correlation of Testosterone level with lipids parameters

	LDL	HDL	Cholesterol	Triglyceride
r	0.105	0.409	0.313	0.189

r- regression coefficient; HDL- high density lipoprotein
LDL=low density lipoprotein

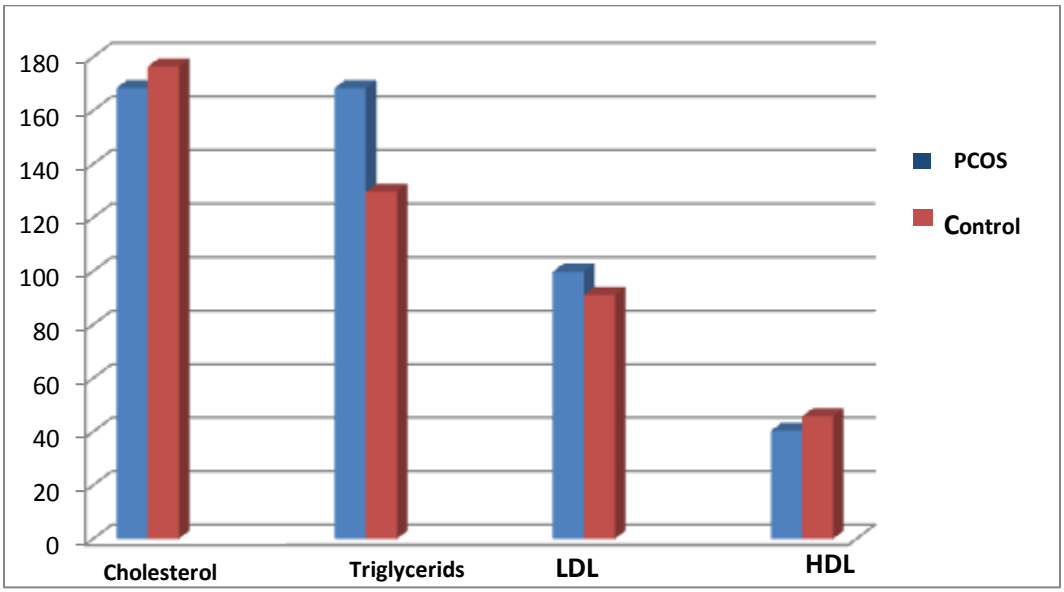

Figure (1) lipid profile in PCOS patients and controls

HDL- high density lipoprotein

LDL=low density lipoprotein

Discussion:

Long term health consequences of PCOS are still inconclusive and currently under investigation. Women with PCOS are at an increasing risk for the development of various metabolic derangements including glucose intolerance or overt type 2 diabetes mellitus, dyslipidemia, and hypertension. [11]. Women suffering from PCOS are considered to be at high risk for dyslipidemia due to elevated androgen levels and frequent association of this syndrome with obesity [12].

In the present study, dyslipidemia has been found in PCOS patient compared to the control which is in agree withRobinson *et al* [13]. Jayrasree R [14]. Gambineri *et al* [15] studies who documented altered lipid profile in PCOS women, in Jayrasree study for example; there were increased in TG and LDL level and decrease HDL level which is similar to this study.

The causes of dyslipidaemia in PCOS are multifactorial. Insulin resistance appears to have a pivotal role mediated in part by stimulation of lipolysis and altered expression of lipoprotein lipase and hepatic lipase [3]. Both this study and Macut D[16] study found increased TG and decrease in HDL level in PCOS patients compared to BMI matched healthy control but

Holte J [17] implicates obesity, not PCOS per se for altered lipid profile when he found thatthe lipoprotein lipid profile was not significantly more abnormal in obese women with PCOS than in their weight-matched controls.

Other studies implicate obesity as cause of abnormal lipid profile as in Stojkovic M *et al* [18] study when lean PCOS patient were compared with lean control and obese PCOS were compared with obese control and reach result that suggest that obesity affect lipid metabolism in PCOS subject, especially by reducing HDL cholesterol and PCOS per se affect only triglyceride level. Similarly Godinjak *et al* [19] concluded that patients with PCOS with BMI <25 were significantly different

from these with BMI >25 in value of triglyceride. The level of triglyceride can be a contributory factor for adiposity in PCOS women [20].

The results of present study are in agree with Cristian-Ioan[12] study where both studies concluded that women with PCOS have altered lipid profile, with higher cholesterol levels and lower HDL (in Cristian-Ioan study) and lower HDL cholesterol and higher TG in this study compared with healthy women. These lipid parameters were associated with the presence of PCOS and not with parameters describing body weight.

In this study, total cholesterol was positively associated with testosterone level and HDL-cholesterol was negatively associated with testosterone level but in Pirwany IR [21]serum testosterone concentration was not associated either in univariate or multivariate analysis with any of the measured lipid in the women with PCOS.

The mechanism by which hyperandrogenism may contribute to development of lipid abnormalities in PCOS is not clear [22]. Hyperandrogenism may lead to the abnormalities in lipoprotein profile by working directly at the liver, or it may alter body composition by favoring central adiposity [22].

In the current study PCOS patients showed high testosterone level compared to control andthere was a linear relationship between testosterone levels and HDL and testosterone and total cholesterol. In a study performed in 2009, Fruzzetti *et al* concluded that hyperandrogenemia is a risk factor for dyslipidemia, which was altered only in the phenotypes with elevated androgen levels [23]. A study conducted by Sidhwani *et al* demonstrated that independent of body weight, PCOS was associated with changes in lipoprotein profile that increases risk for cardiovascular disease. These changes were present in a mostly non-obese group of women and were more closely related to androgens than fasting insulin levels [24].

Conclusion: Our results suggest that the characteristic hyperandrogenemia in women with PCOS were associated with dyslipidemia.

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