Evaluation of Some Biochemical Markers in Patient's with Polycystic Ovarian Syndrome

تقييم بعض الدالات البايوكيميائية لدى مريضات متلازمة تكيس المبيض

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Abstract

The present study aims to detect several biochemical markers associated with PCOS (Polycystic ovary syndrome) in Iraqi women comparing the results with control normal fertile women and also studying the effect of obesity on the same biochemical markers. Ninety eight women with PCOS, 51 non-obese [body mass index (BMI) less than 25 kg/m^2] and 47 obese (BMI >25 kg/m^2) were enrolled for the study. Each group of them was compared forty normal fertile women as control group matched for each in age and BMI. The first part of this study was devoted to the measurement of Body Mass Index (BMI) and Waist Hip Ratio (WHR), subdivided PCOS according to the body mass index, and measurement of fasting insulin, fasting glucose, Homeostatic Model Assessment (HOMA), HbA_{1c} and lipid profile. A significant differences was found in HbA_{1c} (P≤0.0001) VLDL (p≤0.0001), triglyceride (p≤0.05) and cholesterol (p≤0.05) between obeses and lean PCOS patients. Insulin serum level (P≤0.0001) was highly significantly increased in obeses PCOS patients as compared to obeses control, the serum insulin (P≤0.0001) also significantly increased in lean PCOS women when compared with lean control. There was a significant differences between HOMA (P≤0.05) in obeses PCOS patients than in the obese control group and between obese and lean women PCOS patients.

Key Words: PCOS, Obesity, Obese Patients.

الملخص

تهدف الدراسة الحالية إلى دراسة بعض المعلمات البيوكيميائية في متلازمة تكيس المبيض لدى النساء العراقيات ومقارنة النتائج مع مجموعة من النساء ذوات الإنجاب الطبيعي وكذلك دراسة تاثير السمنة على هذه البيوكيميائية: تضمنت الدراسة الحالية جمع 98 عينة من المصابات بمتلازمة تكيس المبيض51 مريضة نحيفة (محتوى الجسم من الكتلة اقل من 25 كغم/م^2) و 47 مريضة بدينة (محتوى الجسم من الكتلة أعلى من 25 كغم / م^2). كل مجموعة قورنت مع مجموعة من النساء ذوات إنجاب طبيعي كمجموعة سيطرة تطابق مجاميع المرضى بالعمر وبمحتوى الجسم من الكتلة (BMI) .الجزء الاول من هذه الدراسة تضمن قياس محتوى الجسم من الكتلة (BMI) و نسبة قياس الخصر الى الورك,مجموعة مريضات متلازمة تكيس المبيض قسمت الى مجاميع فرعية اعتمادا على محتوى الجسم من ألكتله وتم قياس الانسولين الصيامي ,الكلوكوز الصيامي, HOMA و الهيموغلوبين وشريط الدهون ,واظهرت النتائج ان هناك فرق معنوي في الهيموغلوبين فئة سي (P≤0.0001) ,معدل البروتين الدهني المنخفض جدا (p≤0.0001), والكلسريد الثلاثي (p≤0.05) الكولسترول (p≤0.05) بين مجاميع البدينات والنحيفات من مجموعة المريضات وان هناك فزق معنوي كبير في معدل الانسولين (P≤ 0.0001) في المريضات البدينات عند مقارنتها مع مجموعة السيطرة من النحيفات و هناك زيادة معنوية كبيرة في الانسولين المصلي (P≤ 0.0001)في النساء النحيفات المريضات عند مقارنتها مع مجموعة السيطرة من النحيفات وان هناك اختلاف معنوي ما بين HOMA (P≤0.05) في المريضات البدينات عنه في البدينات من مجموعة السيطرة وما بين النساء البدينات والنحيفات المريضات بالمتلازمة.

الكلمات المفتاحية: متلازمة تكيس المبيض, السمنة, مرضى السمنة

Introduction:

Polycystic ovary syndrome (PCOS) is a common hormonal disorder among women of reproductive age with a prevalence of 6.6–6.8%[1]. The name of the condition comes from the appearance of the ovaries in most, but not all, women with the disorder - enlarged and containing numerous small cysts located along the outer edge of each ovary (polycystic appearance) [2]. Other names for this syndrome include polycystic ovarian syndrome (also PCOS), polycystic ovary disease (PCOD), functional ovarian hyperandrogenism, Stein-Leventhal syndrome (original name, not used in modern literature), ovarian hyperthecosis and sclerocystic ovary syndrome [3].

Polycystic ovary syndrome also causes female infertility. In addition to poor conception rates, pregnancy loss rates are high (30–50%) during the first trimester with PCOS. Polycystic ovary syndrome is also characterized among other things by oligoamenorrhea and may account for more than 75% of cases with an oluvatory infertility [4].

Worldwide, PCOS affects 6–10% of women according to 1990 NIH criteria [14,15] or 6.6–6.8% [1], and even more individuals according to the broader Rotterdam criteria [5], which makes it one of the most common human disorders and the single most common endocrinopathy in women of reproductive age. Several types of women have an increased risk of PCOS, including those with clinical hyperandrogenism (namely, hirsutism, acne or alopecia), menstrual dysfunction, PCO, hyperinsulinemia from adiposity-dependent insulin resistance and a family history of PCOS[6].

Many symptoms are associated with PCOS. All, some or only one of the following symptoms may be present, to varying degrees of severity, in women who suffer from PCOS. First: Hyperandrogenism**:** Hyper and rogenism may be present clinically as hirsutism, acne, and/or male pattern alopecia. Hirsutism is the most common endocrine and metabolism disorder due to androgen excess affecting approximately 10% of women in US [7]. It is defined as the presence of hair in androgen-dependent sites. This is to be distinguished from hypertrichosis that involves a more uniform, whole body distribution of fine hair [8], menstrual abnormalities[9], acanthosis nigricans [10], cystic ovaries [11], enlarged ovaries [12], early pregnancy loss [13]. Studies have shown a clear relationship between the raised serum LH level often found in women with PCOS and early pregnancy loss [15]. Prevalence of obesity increased worldwide [16]. Obesity impairs human reproduction by reducing pregnancy chances and increasing miscarriage rates and obstetric complications for both mother and fetus, leading to reduced live birth rates. This effect seems to occur in all types of conception [17]. Obesity may impair human reproduction through different ways such as altered secretion of pulsatile gonadotropin-releasing hormone (GnRH), reduced sex hormone binding globulin (SHBG) leading to an alteration of androgen and estrogen delivery to target tissues, insulin resistance and hyperandrogenism[18].

Aim of study

The present study aims to detect several biochemical markers associated with PCOS(Polycystic ovary syndrome) in Iraqi women comparing the results with control normal fertile women and also studying the effect of obesity on the same biochemical markers**.**

Materials and Methods:

This study was carried out in Kamal AL-Samaraee Hospital- Baghdad during the period from July 2011 to December 2011.The study groups include ninety eight (98) PCOS women with age range of 20-35 years .These women were distributed in four groups: group (A) forty seven obese with PCOS (BMI $\geq$ 25 kg m^2) ; group(B) fifty one lean with PCOS (BMI $\leq$ 25 kg m^2); and in addition 40 healthy normally menstruating women (20) obese normally menstruating; and 20 lean control group D**.**

The controls were selected among subjects who were healthy in terms of regular cycle, normal hormonal assay, non-diabetic, non-hypertensive, no other endocrine disorders and were free of acute illness or infection at time of sampling. Patients and control groups were subdivided into subgroups according to fertility status and prevalence of some symptom such as depression, hirsutism and acne.

Ten milliters of Blood samples were collected from each patient and control by venipuncture after an overnight fast from each healthy control women on 2-5 day window of the early follicular phase. From each patient and control. The blood sample was divided into three aliquots; 2,1 and 7ml. The first aliquot was dispensed in tube containing ethylene diaminetetracetic acid (EDTA) (1.5 mg/ml). This blood was processed in less than three hours and was used for HbA_{1c} estimation, while the second aliquot was used in the estimation of plasma glucose and lipid profile level. The third aliquot was dispensed in a plain tube and left for around an hour to clot at room temperature (22°C). Then, it was centrifuged at 3000 rpm for 10 minutes to collect serum. The serum was divided into aliquots (250µl) in Eppendorff tubes and stored in the freezer (-20ºC) until use.

Serum level of insulin, Plasma level of glucose Glycosylated haemoglobin (HbA_{1c}) and Lipid profile (VLDL.C,LDL.C,HDL.C&triglyceride)were measured for all studied groups .Insulin resistance index was calculated as HOMA test for each patient and control [19]. .

Statistical Methods

The data were processed with the software package SPSS (statistical package for social sciences) Vesrsion.18 and Microsoft Excel XP version. Descriptive analysis was used to show the mean and standard deviation of variables. ANOVA test was used to show the differences between variables of differentiated groups. Correlation analysis was used to test the linear relationship between parameters. The significance of differences between mean values were estimated by Student T-Test. The probability $P \leq 0.05$ = significant, $P \geq 0.05$ = non-significant.

Results and Discussion

General Description of the Studied Groups

The obeses PCOS patients showed no differences in BMI in comparison with obeses control (30.44±3.11 vs. 30.03±3.02 kg/m^2), also in lean patient and control the BMI was identical(23.16±1.63 vs. 23.18±1.13kg/m^2) . In contrast, the W-H ratio showed a slightly increased mean in the obeses patients with PCOS and the controls with (0.89 vs. 0.86). Also in the lean groups patients and controls there was no significant differences between them, but there was highly significant ($p \leq 0.0001$) differences between obeses and lean groups, Table(1).

The mean age (mean±SD) of obeses and lean polycystic ovarian syndrome patients were (28.11±4.99, and 27.50±4.24 respectively) ranging from 20 to 35 years while that of obeses and lean control were (27.50±4.24, 28.25±3.89 respectively) ranging from 20 to 37 years with no significant differences between these groups ($p \leq 0.05$).

Table(1): The age, BMI and WHR distribution of study groups

Mean±SD (Range)	Obeses patients	Obeses control	Lean patients	Lean control	P using ANOVA
Age (year)	28.11±4.99 (20-35)	26.61±4.60 (20-35)	27.50±4.24 (20-35)	28.25±3.89 (20-37)	0.141
BMI (Kg/m2)	30.44±3.11 (25.90-35.73)	30.03±3.02 (25.43-35.60)	23.16±1.63 (18.70-24.80)	23.18±1.13 (20.75-24.66)	0.0001*
WHR	0.89±0.05 (0.82-0.98)	0.86±0.04 (0.80-0.95)	0.81±0.04 (0.73-0.89)	0.78±0.02 (0.74-0.82)	0.0001*

*Significant using Students-t-test for two independent means at 0.05 level of significance

The Fertility status is shown in Table (2). The primary infertility is 63.8% and 58.8% in obeses PCOS and lean patients, respectively .Whereas, the percentage of secondary infertility were 36.2% and 41.2% respectively with no significant differences between these groups.

Table (2): The fertility status in patient groups

Fertility status	Obeses patients		Lean patients	
	No	%	No	%
Duration of disease (month)	39.57±19.04 (12-120)		30.63±15.89 (12-60)	
P value		0.013*		
Primary infertility	30	63.8	30	58.8
Secondary infertility	17	36.2	21	41.2
P value		0.611		

Patients with polycystic ovarian syndrome suffer from symptoms such as depression, acne and hirsutism in varying degrees, as shown in the Table(3)

Table (3):Observed Symptoms among patients

		Obeses patients		Lean patients	
		No	%	No	%
Acne	Yes	15	31.9	27	52.9
	No	32	68.1	24	47.1
	P value		0.036*		
Depression	Yes	10	21.3	12	23.5
	No	37	78.7	39	76.5
	P value		0.789		
Hirsutism	Yes	37	78.7	25	49.0
	No	10	21.3	26	51.0
	P value		0.002*		

As shown in Table (4) Patients with polycystic ovarian syndrome suffer from irregularity of the menstrual cycle which usually either amenorrhea or oligomenorrhoea. In the present study, 57.4% from obese PCOS patients were having amenorrhea and the rest suffer from oligomenorrhoea in the lean patient were oligomenorrhoea was present in 64.7% and the rest were having amenorrhea (P 0.028).

Table (4) : Groups of PCOS women according their menstrual cycle

		Obeses patients		Lean patients	
		No	%	No	%
Menstrual cycle	Amenorrhea	27	57.4	18	35.3
	Oligomenorrhoea	20	42.6	33	64.7
	P value		0.028*		

*Significant using Pearson Chi-square test at 0.05 level of significance

The means of systolic/diastolic blood pressure was (126.38/82.34mmHg) in obese PCOS patient and in the lean patients was (122.94/80.2 mmHg), with no significant differences between obese as compared to lean patient groups. The mean systolic/diastolic blood pressure was (122/80 mmHg) in obese and in the lean control was 122/ 79.5 mmHg Table (5).

The present study showed a significant ($P \leq 0.05$) increase in the duration of infertility in obese patients as compared to lean patients (39.57 vs. 30.63 month)

Table(5): The clinical characteristic of all studied groups

Mean±SD (Range)	Obese patients	Obese control	Lean patients	Lean control	P using ANOVA
Systolic (mmHg)	126.38±12.41 (110-160)	122.00±6.16 (110-140)	122.94±6.72 (110-140)	122.00±4.10 (120-130)	0.108
Diastolic (mmHg)	82.34±8.65 (60-100)	80.00±3.24 (70-90)	80.20±5.10 (70-90)	79.50±3.94 (70-90)	0.215
Duration of infertility (month)	39.57±19.04 (12-120)	-- --	30.63±15.89 (12-60)	-- --	0.013*

Fasting serum insulin ,fasting serum glucose, HOMA and HbA1c in PCOS patients sub-group and control sub-group women were summarized in Table (6).

Table (6):Insulin and biochemical markers in PCOS patients compared to control

Mean±SD (Range)	Obese patients	Lean patients	Obese control	Lean control	P using ANOVA
Insulin (MU/ml)	26.12±13.43 (5.56-79.00)	24.96±10.29 (12.08-77.00)	14.55±3.36 (8.26-21.28)	12.60±4.83 (5.08-25.64)	0.0001*
HOMA	5.57±3.16 (1.26-19.51)	4.90±1.76 (1.76-13.31)	3.08±0.73 (1.65-4.41)	2.53±1.05 (1.17-5.38)	0.0001*
FBG (mmol/L)	4.79±0.82 (3.06-7.06)	4.50±0.74 (3.11-6.50)	4.76±0.37 (4.00-5.44)	4.51±0.53 (3.28-5.33)	0.145
HbA1c%	6.17±1.16 (3.70-9.00)	5.45±0.60 (4.40-6.80)	4.88±0.60 (4.10-6.20)	4.94±0.75 (3.50-6.50)	0.0001*

*P≤ 0.05 = significant, P≥ 0.05 = non-significant

The mean of insulin serum level was highly significantly increased in obese PCOS patients (26.12±13.43µIU/ml) as compared to obese controls(14.55±3.36 µIU/ml) , the mean serum insulin also

significantly increased in lean PCOS women (24.96±10.29) when compared with lean control (12.60±4.83)(P≤ 0.0001).

There was a significant difference (P≤0.001) between HOMA mean values (5.57±3.16) in obese PCOS patients than in the obese control group (3.08± 0.73). There was a significant difference (P≤0.05) in HOMA between obese and lean women PCOS patients .

There was no significant difference (p≥0.05) in plasma glucose between PCOS patients and control group or between obese and lean PCOS patients or obese or lean control.

A high level of HbA_{1c} (6.17±1.16) was observed in obese PCOS cases while in lean PCOS women (5.45±0.60), but HbA_{1c} mean a relatively low in obese and lean control (4.88±0.60, 4.94±0.75) when compared to patients group and the difference was highly significant (P≤0.0001).

The association between hyperinsulinemia and PCOS was first noted by Burghen *et al*..(1980) who found a significant positive correlation between insulin and PCOS among women[20].

The mean serum level of fasting insulin was significantly elevated in the obese PCOS patients when compared to that found in the obese control group, and also in lean PCOS patient when compared to lean control.

There was no significant difference in blood glucose between PCOS patients groups and control groups or between both PCOS patients groups and also between control groups, this finding is in agreement with other study[21].

In the current study, the mean of HbA_{1c} % level showed a statistically significant increase in PCOS obese women when compared to PCOS non-obese women. In addition, significantly higher mean of HbA1c % were detected in both the same previous groups [PCOS (obese & non-obese)] when compared to the control women (obese & non-obese) respectively.

The clinical utility of HbA1c for diagnosing impaired glucose tolerance and type 2 diabetes in PCOS in daily practice is low. Long-term prospective studies are needed to determine whether HbA1c is superior to glucose levels as a cardiovascular risk marker in patients with PCOS [22].

The HOMA is a method for assessing ß-cell function and IR from fasting glucose and insulin or C-peptide concentrations. The relationship between glucose and insulin in the basal state reflects the balance between hepatic glucose output and insulin secretion, which is maintained by a feedback loop between the liver and ß-cells [23]. Decreases in ß-cell function were modelled by changing the ß-cell response to plasma glucose concentrations .Insulin sensitivity was modelled by proportionately decreasing the effect of plasma insulin concentrations at both the liver and the periphery[22].Some investigators had recommended calculating an index of IR from glucose and insulin levels [e.g. HOMA] [24]. HOMA was considered as valid method to assess insulin sensitivity in epidemiological studies [25].

The present study show that significantly higher HOMA mean were detected in both the same previous groups [PCOS (obese & non-obese)] when compared to the control women (obese & non-obese) respectively, Table (1), such finding is in agreement with other study [26].

The IR vastly reduces the number of insulin receptor sites on the membrane of the cells and glucose remains in the blood stream, causing elevated levels of blood glucose, which are sent to the liver. Once there, the glucose is converted into fat and stored via the blood stream throughout the body[27]. This process can lead to weight gain and obesity, the key factors in creating PCOS. The second way by which IR causes PCOS, is raising insulin levels in the blood stream. Unhealthy lifestyles and genetic conditions cause the pancreas to overproduce insulin. The cell is, in turn, overwhelmed by this excess insulin and protects itself by reducing the number of its insulin receptor sites. This process leaves too few sites for insulin to carry out its normal function, which attaches itself to the cell membrane, acting as a key in a lock allowing glucose to pass through the cell membrane, and converted into energy. The reduced number of receptor sites in insulin resistant people causes an excess of insulin "rejected" by the cell to free-float in the blood stream, creating unbalanced hormone levels in PCOS sufferers [28]

Total serum cholesterol levels were significantly (p≤0.001 related for all four groups) higher in obese PCOS patients when compared with controls (189.43±20.24 mg/dl) Vs.(184.10±7.99 mg/dl) respectively. In lean patients, total serum cholesterol (180.45±13.69 mg/dl) significantly higher

(p≤0.05) when compared to lean control (173.20±12.61mg/dl),as well as, there was a significant difference between two patient groups (p≤0.05),as shown in Table (7).

Triglyceride was found to be significantly higher (p≤0.0001) in obese patients with means of (144.45±20.07 mg/dl) compared to obese control with a mean of (118.70±17.41 mg/dl) as well as in lean patients when compared to lean control (126.65±22.51 vs. 109.55±19.42 , P≥0.05) , as shown in Table (7).

The mean serum level of HDL-cholesterol slightly decrease in the obese PCOS patients (58.15±10.91 mg/dl) when compared to that found in the obese control group (58.35±13.24 mg/dl) while in lean patients (57.24±8.11 mg/dl) there was significantly decrease[P≤0.001] in the mean of HDL when

Table (7): Lipid profile in PCOS groups compared t0 control

Mean±SD (Range)	Obese patients	Lean patients	Obese control	Lean control	P using ANOVA
S.cholesrol (mg/dl)	189.43±20.24 (156-256)	180.45±13.69 (117 -213)	184.10±7.99 (168-201)	173.20±12.61 (148-188)	0.001*
Triglycerid (mg/dl)	144.45±20.07 (113-198)	126.65±22.51 (78-177)	118.70±17.41 (89-156)	109.55±19.42 (79-142)	0.0001*
HDL (mg/dl)	58.15±10.91 (35-89)	57.24±8.11 (32 -78)	58.35±13.24 (31-77)	65.25±9.17 (52-83)	0.026*
LDL (mg/dl)	102.39±22.63 (57.20-179.80)	97.89±16.46 (28.40-126.60)	102.01±15.80 (73.20-132.80)	86.04±12.84 (63.20-102.60)	0.009*
VLDL (mg/dl)	29.00±3.95 (22.60-39.60)	25.53±4.71 (15.60-35.40)	23.17±4.34 (12.20-31.20)	22.94±4.11 (15.80-29.60)	0.0001*

***P≤ 0.05 = significant, P≥ 0.05 = non-significant**

compared to lean control (65.25±9.17 mg/dl)as shown in Table (7) shows also a significant (p≤0.05) difference between four study groups (using ANOVA test).

LDL-cholesterol levels were significantly (p≤0.01) higher in lean PCOS patients when compared with lean controls (97.89±16.46 mg/dl) vs. (86.04±12.84mg/dl) for lean PCOS patients and controls respectively while in obese PCOS patient(102.39±22.63 mg/dl) no significant difference (P≥0.05) when compared to obese control (102.01±15.80 mg/dl).

There was a significant (p≤0.001) difference in mean VLDL-cholesterol in obese PCOS patients (29.00±3.95 mg/dl) than in the obese control group (23.17±4.34 mg/dl) and there was a significant difference between lean PCOS patient (25.53±4.71 mg/dl) when compared with lean control (22.94±4.11mg/dl) and also between both patient sub-groups (p≤0.0001).

Total serum cholesterol levels were significantly higher in obese PCOS patients when compared with lean patients, as well as in obese control when compare to lean control ,as shown in Table (7). In addition, the mean serum TG level showed a statistically significant increase in PCOS obese women when compared to PCOS non-obese women. In addition, significantly higher mean serum TG levels were detected in both the same previous groups [PCOS (obese & non-obese)] when compared to the control women (obese & non-obese) respectively, Table (7).

Research has revealed metabolic stigmata in premenopausal women with PCOS, such as hypertriglyceridemia, hyperinsulinemia and insulin resistance [29]. Maida and Luma reported that women who are clinically and biochemically defined as PCOS(both normal weight and overweight groups) found to have higher levels of triglyceride and cholesterol, LDL, VLDL and atherogenic index were found to be significantly, and lower level of HDL[30].

The mean serum level of HDL-cholesterol was significantly decreased in the lean PCOS patients when compared to that found in the lean control group as shown in Table (7) LDL-cholesterol levels were significantly higher in lean PCOS patients when compared with lean controls as shown in Table (7) this table shows also a significant difference in mean VLDL-cholesterol in obese PCOS patients than in the obese control group, as well as, a significant difference between lean PCOS women and lean control.

Hyper androgenism in women results in higher mean serum TG and VLDL cholesterol levels, but lower HDL cholesterol levels [30].

Stojkovic suggest that obesity affects lipid metabolism in PCOS subject, especially by reducing HDL cholesterol levels, suggesting a reduced capacity for cholesterol removal from tissues with diminished antiatherogenic potential. PCOS per se, affects only triglyceride levels [31].

Robinson reported that atherogenic lipid profile abnormalities may be found in one-third of women with PCOS who have a normal lipid pattern. Future prospective studies are needed to test to which extent such atherogenic forms of dyslipidaemia may contribute to the increased cardiovascular risk in young women with PCOS [32].

Most studies of dyslipidemia and PCOS have reported on cholesterol levels and triglycerides (TGs). The lipid profile that is found in women with PCOS consists of elevated TG levels, together with low levels of high-density lipoprotein-cholesterol (HDL-C) [33].

These changes are consistent with the lipid profile that is typically found in association with insulin resistance. The effects of insulin resistance on lipid metabolism are well known. Increased secretion of very low-density lipoprotein (VLDL) particles by the liver results in elevated plasma TG concentrations. Subsequently, TGs are exchanged for cholesteryl ester (CE) by the activity of CE transfer protein. This process results in TG-enriched high-density lipoprotein (HDL) particles that are catabolized more rapidly, and CE-enriched VLDL particles that are converted into small dense low-density lipoprotein (LDL) particles [34]. As a consequence, insulin resistance contributes to decreased plasma levels of HDL-C and apolipoprotein (apo) A-I, and higher levels of apoB. [35].

In addition to insulin resistance, lipid metabolism in women with PCOS may also be affected by ovarian and/or adrenal secretion of sex steroids. The effects of sex steroids on lipid metabolism are complex and involve the actions of both androgens and estrogens. Hyper androgenism has been associated with increased hepatic lipase (HL) activity. This enzyme, which has a role in the catabolism of HDL particles, exhibits strong sexual dimorphism, with exogenous androgens up-regulating and estrogens down-regulating its activity [36]. A study of 17 female-to-male transsexuals who were exposed to treatment with exogenous testosterone (T) showed a significant increase in HL activity in association[37].

Endogenous estrogens may affect LDL metabolism through up-regulation of the LDL receptor, resulting in enhanced hepatic clearance of LDL particles from plasma [38].

Olivier and his team studied that a more atherogenic lipid profile, in particular related to HDL metabolism, was found in women with PCOS. Thehypothesis that both obesity and hyperandrogenism contribute to these changes. Furthermore, there was evidence for an additional influence of PCOS on lipid metabolism that was independent of obesity. The results of this study may indicate increased risk for cardiovascular disease in women with PCOS. However, this hypothesis still remains to be proven in prospective long-term follow-up studies of women with PCOS [36].

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