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Lipid Profile in Women with Polycystic Ovary Syndrome

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ABSTRACT

Background: Polycystic ovarian syndrome and obesity contribute to the metabolic problems that reproductive-age women experience.

Objective: This research aimed to examine the effect of abdominal obesity using BMI and the waist/hip ratio [WHR] on metabolic parameters in patients with polycystic ovary syndrome.

Patients and Methods: This prospective study was carried out on eighty [80] women, aged 20- 35 years-old attending the Gynecology Clinic of Zagazig and Al-Ahrar Educational Hospital. The selected cases were divided into four groups after taking a written or verbal consent to be included in the study: **Group I:** Twenty cases of obese PCOS, **Group II:** Twenty cases of non-obese PCOS, **Group III:** Twenty cases of obese non-PCOS and **Group IV:** Twenty cases of non-obese non- PCOS.

Results: Lipid profile in obese PCOS and non obese PCOS demonstrated statistically highly significant difference between both groups regarding serum total cholesterol, serum triglycerides and serum low density lipoprotein [LDL]. There was a statistically insignificant differences between both groups as regard serum very low density lipoprotein [VLDL].

Conclusions: This study showed that women with PCOS had atherogenic lipoprotein profile characterized by increased cholesterol, LDL and triglycerides especially in obese group, which might be a risk factor for developing cardiovascular complication.

Keywords: Lipid Profile, Polycystic Ovary Syndrome, Obesity.

INTRODUCTION

The new system also could avoid undesirable diagnosis and intervention. Classification of women with PCOS as below can prevent ambiguity in care and to some extent avoid follow-up:

- Asymptomatic form: individuals with PCO morphology only.
- Mild form: PCO morphology + anovulation.
- Classical form: hyperandogenicity + ovarian dysfunction (Anovulation and/or PCO).
- Metabolic form: a combination of mild and traditional types of obesity and/or resistance to insulin (abdominal obesity, insulin resistance, high waist/hip ratio, etc) [1].

The Polycystic Ovary Syndrome [PCOS] is the most common endocrine syndrome affecting women of reproductive age. The presence of persistent ovaries with several [2-8 mm] small cysts and hypervascularized androgen secreting stroma has long been recognized as synonymous with symptoms of excess androgen [hirsutism, alopecia, acne], obesity and menstrual cycle disturbance [oligomenorrhea or amenorrhea] [1]. In general, the European view is that the disease includes any of the above described signs, symptoms or endocrine disorders [high serum androgen and/or luteinizing hormone concentrations [LH] [2]. In North America, there is agreement that the disorder is denoted by the combination of hyperandrogenism and ovulatory dysfunction in the absence of non-classical adrenal hyperplasia without the need to assess the existence of polycystic ovaries by ultrasonic scanning [3].

Higher concentrations of circulating testosterone and lower concentrations of globulin binding sex hormones [SHBG] are common findings and hence the free androgen index [FAI] is often increased. Roles of hormonal derangements on lipoprotein defects remain unclear. However, both androgen and estrogens are known to have opposing effects on lipoprotein metabolism. These effects can be mediated by hepatic control of the lipoprotein metabolism, insulin sensitivity and body fat distribution [4].

In obese patients with PCOS, the lipoprotein profile is characterized by elevated plasma triglycerides and decreased lipoprotein cholesterol [HDL-C] concentrations, which mimic those seen in subjects with type 2 diabetes [5]. Low-density lipoprotein cholesterol [LDL-C] in PCOS is often only slightly elevated. Nevertheless, because LDL does not exist as homogeneous particles, a simple quantitative LDL concentration calculation may be misleading. Alternatively, LDL contains several particle subpopulations differing in lipid composition, density, size and atherogenic potential. Small and compact LDL particles [LDL-III] are known to be more atherogenic than larger LDL species [LDL-1 and LDL-II] and are associated with a higher prevalence of coronary heart disease [CHD] and type 2 diabetes in circulation [even in normal LDL-cholesterol concentration] [6]. Topics with PCOS currently lack information on LDL subfractions.

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Plasma triglyceride concentrations have a defining effect on the concentration of low, dense LDL in normal population [7].

Studies showed that the operation of the enzyme hepatic lipase [HL] enriches the larger LDL particles when plasma triglyceride concentrations are elevated and thus makes them suitable for conversion to smaller species [8]. Increased HL activity has a strong association with up-regulating androgen activity and down-regulating estrogen activity. Nevertheless, the relationship between endogenous hyperandrogenemia and HL activity in women with PCOS was not reported to assess abnormalities in the LDL subfraction profiles [9].

In addition to dyslipidemia in PCOS, there are several causes, such as obesity, diabetes mellitus, cigarette smoking and genetic factors, which may exacerbate the atherogenic process and CHD. An important public health effort in recent decades has been exerted to delay the onset and reduce the progression of atherosclerosis. Because atherosclerosis is so closely linked to the accumulation of lipoprotein particles, one of the most effective strategies was to manage dyslipidemia, particularly in patients at high risk [10].

AIM OF THE WORK

The aim of this study was to assess the lipid profile in cases of PCOS, however the ultimate aim was to predict and detect dyslipidemia in this group of patients. So, it becomes possible to prevent or to delay the onset of atherosclerosis and CHD. This diagnosis of dyslipidemia in young women may have a major implications for long term health.

PATIENTS & METHODS

This prospective case control study was carried out on eighty [80] women aged 20- 35 years-old, attending the Gynecology Clinic of Zagazig and Al-Ahrar Educational Hospital. The selected cases were divided into four groups after taking a verbal consent to be included in the study:

Group I: Twenty cases of obese PCOS, **Group II:** Twenty cases of non-obese PCOS, **Group III:** Twenty cases of obese non-PCOS and **Group IV:** Twenty cases of non-obese non- PCOS.

The cases of PCOS were diagnosed clinically by presence of: 1. Signs and symptoms of hyperandrogenism [hirsutism and / or acne] and 2. Menstrual cycle disorders [perimenarcheal on set of oligomenorrhea and amenorrhoea]. Moreover, progestagen- withdrawal bleeding test was performed for every severe oligomenorrhoeic, and amenorrhoeic patients and was positive in all cases. Ultrasonic examinations were performed during the first 7 days of the menstrual cycle. The ovary was defined as being polycystic if there were > 10 subcapsular follicles each measuring 2-8 mm in diameter arranged around a dense stroma in one plane in one ovary. The main recent advance in the agreed definition of PCOS agreed with **Rotterdam ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group** [11].

Traditionally, there had been an on-going debate between gynecologists in Europe and North America about how best to define PCOS. In the UK and Europe, most physicians concluded that the existence of polycystic ovaries on ultrasound was important throughout their diagnosis and that PCOS was diagnosed if polycystic ultrasound ovaries were observed in conjunction with one or more of the clinical and LDL-III biochemical features of excess androgen and chronic anovulation. Confirmation of PCOS was performed through biochemical hormonal analysis including serum FSH, serum LH, free & total testosterone and progesterone level in day 3 to 5 of the cycle. Obesity was assessed when the body mass index was > 30 kg/ m2 of surface area according to World Health Organization 2017 [12].

Inclusion criteria of our study:

The women were in good health and had not used medications known to affect lipid, for at least 3 months. PCOS- women were not exposed to any adjuvant surgical treatment for PCOS previously.

Exclusion criteria:

Women with a history of glucose intolerance or non-insulin-dependent diabetes mellitus and women who were using any medications that affect insulin secretion or action, such as the oral contraceptive pill, at last 3 months before enrollment in the study were excluded. In addition, the possible involvement of endocrinological, abnormalities such as nonclassic 21- hydroxylase deficiency, congenital adrenal hyperplasia, hyper-prolactinemia or thyroid dysfunction were also excluded on the basis of normal serum 17α- hydroxyprogesterone, prolactin and thyroid hormone concentrations. None of the patients had features of Cushing's syndrome. The participants were not actively involved in any exercise program, and the majority of them had similar diets, lifestyles and daily exercise patterns.

For all cases, the following was carried out:

1. **Complete history taking ;** *Personal history:*

Name, address- age- occupation, martial state and special habits of medical importance.

- Present History:
- Regularity of cycle.
- Vaginal discharge.
- Chronic pelvic diseases
- Manifestation of androgen excess [hirsutism, acne].
- Galactorrhea

- Past History:
- Of operations especially previous wedge resection or ovarian drilling by laparoscopy.
- Of disease e.g. D.M. –hypertension, cardiac, thyroid disease.
- Family History:
- Menstrual History:

2. General Examination:

- Weight by kg and height [cm]
- Body mass index [BMI]: BMI is calculated as weight in kilograms divided by the square of height in meters [kg/m^2 > 30] **[12].**
- Waist hip ratio [WHR]. Waist-hip ratio included waist circumference at the narrowest point of the tarso, hips at the widest point [normal 0.65-0.75] abnormal if WHR > 0.9.

- Vital signs:

a-Head and neck.
b- Breast examination.
c-Chest examination.
d- Lower limbs examination.
e-Abdominal examination

3. Local examination:

4. Blood sampling for biochemical evaluation of:

Patient have to be fasting for 12-14 hr with no fatty meal the night before.

- Total cholesterol
- Triglycerides
- High density lipoprotein [HDL]
- Low density lipoprotein [LDL]
- Very low density lipoprotein [VL DL]

Blood samples were obtained by venipuncture to perform lipid assays at 08.00-09.00 am within the first 7 days of menstrual cycle. The biochemical analytical samples were checked automatically. Women in control had regular menses every 24 to 35 days and had no history of hypertension, a personal diabetes history or a first-degree diabetes relative. Enzymatic Calorimetric Tests determined total serum cholesterol, triglyceride, VLDL and LDL **[1].**

Total Cholesterol: Was determined using human kit for in vitro human diagnosis [Gesellschaft für Biochemica and Diagnostica mbH, Max-Planck-Ring 21- D- 65205 Wiesbaden-Germany]. The cholesterol esters present in plasma were hydrolyzed to free cholesterol and fatty acids by the cholesterol esterase enzyme. The oxygen-free cholesterol is then oxidized to cholesterone and hydrogen peroxide by cholesterol oxidase, which reacted to a colored complex in the presence of peroxidase enzyme with phenol and 4-amino-phenazone. The intensity of the form color was measured spectrophotometrically at 505 nm.

Ethical approval:

The study was approved by the Ethics Board of Zagazig University and an informed written consent was taken from each participant in the study.approval number:4170.

Statistical analysis

Recorded data were analyzed using the statistical package for social sciences, version 20.0 (SPSS Inc., Chicago, Illinois, USA). Quantitative data were expressed as mean ± standard deviation (SD). Qualitative data were expressed as frequency and percentage.

RESULTS

Table [1]: Laboratory hormonal data of non-obese PCOS cases and the control groups

	Non Obese PCOS [20]	Non Obese Control [20]	t	p
Serum testosterone [ng/ml]	1.3 ± 0.04	1.23 ± 0.03	1.65	>0.05
Serum Follicular stimulating hormone [iu/L]	6.9 ± 1.8	7.1 ± 2.3	1.43	>0.05
Serum Luteinizing hormone [iu/L]	8.2 ± 2.30	7.9 ± 2.2	1.79	>0.05

Table [1] included the laboratory diagnosis of non-obese PCOS in control groups that showed statistically non-significant difference between both groups regarding serum testosterone, serum FSH and serum LH.

Table [2]: Laboratory hormonal data of obese PCOS cases and the control groups

	Obese PCOS [20]	Obese Control [20]	t	p
Serum testosterone [ng/ml]	1.3 ± 0.04	1.23 ± 0.03	1.65	>0.05
Serum Follicular stimulating hormone [iu/L]	6.81 ± 1.91	7.1 ± 2.3	1.53	>0.05
Serum Luteinizing hormone [iu/L]	8.1 ±1.1	7.9 ±2.2	1.05	>0.05

Table [2] included the laboratory diagnosis of obese PCOS compared to control cases that showed statistically non significant difference of both groups regarding serum testosterone, serum FSH and serum LH.

Table [3]: Lipid profile in non- obese women groups [PCOS and the control groups]

	Non obese PCOS n= 20	Non obese Control n=20	t	p
Total cholesterol [mg/ dL]	**209.91 ± 15.28**	180.35 ±7.7	7.73	<0.001
Triglycerides [mg/ dL]	135.2 ± 11.3	110.3 ± 9.1	7.68	<0.001
High Density lipoprotein [mg/dL]	35.3 ± 3.75	34.2 ± 2.31	1.16	>0.05
Low density lipoprotein [mg/ dL]	106.71 ± 9.3	101.3 ± 11.2	1.66	>0.05
Very Low density lipoprotein [mg/ dL]	27.04 ± 1.5	22.06 ±9.4	1.5	>0.05

Table [3] showed that total cholesterol and triglycerides in non-obese PCOS were significantly increased compared to non-obese control, while there was statistically non-significant difference between both groups regarding HDL, LDL and VLDL.

Table [4]: Lipid profile in obese women groups [PCOS and non PCOS]

	Obese PCOS [n=20]	Obese non PCOS [n=20]	t	p
Total cholesterol [mg/ dL]	**293.88 ± 13.91**	195.93 ± 14.9	21.49	<0.001
Triglycerides [mg/ dL]	166.94 ±18.1	129.85 ±13.3	7.38	<0.001
High Density lipoprotein [mg/dL]	28.31 ± 7.31	28.61 ± 2.1	0.22	>0.05
Low density lipoprotein [mg/ dL]	**149.93 ± 10.1**	138.9 ± 10.8	3.34	<0.01
Very Low density lipoprotein [mg/ dL]	33.38 ± 6.1	25.97 ± 2.3	1.64	>0.05

Table [4] showed that serum total cholesterol, serum triglycerides and serum low density lipoprotein were highly significantly increased in obese PCOS compared to obese non PCOS group. There was statistically insignificant differences between both groups as regard serum high density lipoprotein [HDL] and very low density lipoprotein [VLDL].

Table [5]: Lipid profile in obese PCOS and non-obese PCOS women [Mean ± S.D.]

	Obese PCOS [n = 20]	Non-obese PCOS [n=20]	t	P
Total cholesterol mg/dl	293.88 ± 13.91	209.91 ± 15.28	18.17	<0.001
Triglycerides mg/dl	166.94 ± 18.1	135.2 ± 11.3	6.65	< 0.001
HDL mg/dl	28.31 ± 7.31	35.3 ± 3.75	5.98	> 0.05
LDL mg/dl	149.93 ± 10.1	106.71 ± 9.3	16.03	< 0.001
VLDL mg/dl	33.38 ± 6.1	27.04 ± 11.5	1.43	> 0.05

Table [5] showed that serum total cholesterol, serum triglycerides and serum low density lipoprotein [LDL] were significantly increased in obese PCOS compared to non-obese PCOS group. While, there was statistically insignificant difference between both groups as regards serum very low density lipoprotein [VLDL].

DISCUSSION

We found non-significant differences in TC, TG, LDL cholesterol, HDL cholesterol, VLDL cholesterol, TC/HDL cholesterol, and LDL cholesterol/HDL cholesterol among patients with PCOS and control subjects. Nevertheless, lower HDL cholesterol and apoA-I were observed in patients with PCOS with higher TG, TC and LDL cholesterol in PCOS observed higher mean TC/HDL cholesterol and LDL cholesterol / HDL cholesterol compared to controls. **Goldstein *et al.* [3].**

In our study low HDL [< 50 mg/dL] was observed as a dyslipidemia variable in cases. This is similar to findings in the South Indian population where low HDL has been seen in 93.3 percent of cases with PCOS. The cause of dyslipidemia in PCOS may be hyperinsulinemia and hyperandrogenemia. This allowed adipocytes to undergo increased lipolysis caused by catecholamine and release free fatty acids into the circulation. Increased free liver fatty acids cause VLDL secretion, leading to hypertriglyceridemia. Hypertriglyceridemia leads through the reverse cholesterol transfer pathway to reduced HDL cholesterol and elevated LDL cholesterol levels. The further androgenic priming of adipocytes in early life

predisposes PCOS-associated dyslipidemia . **Cinar *et al.* [1].**

In this study, the clinical characteristics of non-obese women with PCOS and control were similar in both groups and the difference was statistically insignificant [P > 0.05] illustrating the need for U/S and biochemical markers for diagnosis of PCOS, especially in non-obese women. This result is in agreement with **Goldstein *et al.* [3].**

Diagnosis of the metabolic portion of PCOS is documented by U/S and biochemical tests. Whereas, the U/S and biochemical markers of PCOS [serum testosterone, serum FSH, serum LH] in our sample were statistically non-significant in PCOS compared to the population. This agree with most PCOS studies [3].

In our study in PCOS patients, total cholesterol and triglycerides were significantly higher in non-obese women compared to patient controls. Such results are consistent with the analysis by **Pagotto *et al.* [14]** where serum total cholesterol and serum triglycerides were elevated in non-obese PCOS compared to control group whereas plasma, HDL, LDL and VLDL were not statistically significantly different in both groups. In addition, **Cinar *et al.* [1]** showed a statistically significantly increase of total cholesterol and LDL in non-obese PCOS compared to control, while there was no statistically significant difference between trigylcerides and serum HDL.

In obese women, we observed in this analysis that total cholesterol, triglycerides and LDL were higher in the PCOS group compared to the non-PCO group and this disparity was statistically significant [P < 0.01] in LDL and extremely statistically significant regarding total cholesterol and triglycerides [P < 0.001]. while there was no statistically significant difference between HDL and VLDL groups. These results are in agreement with results of **Khomami *et al.* [10].** Besides, **Jones *et al.* [15]** showed increased cholesterol, triglycerides and decreased HDL in obese PCOS females compared to non-obese and control group. Also, **Jayasekara *et al.* [16]** showed that in PCOS, there were statistically significant increases in serum cholesterol, LDL and triglycerides relative to the matched control group, while serum HDL was lower in PCOS than control group. Their study showed that obese PCOS serum cholesterol and LDL increased statistically significantly compared to obese regulation. The increase in triglycerides in obese PCOS was not statistically significant in the analysis of **Goldstein *et al.* [3],** while lipid profile in PCOS group showed a statistically significant increase in VLDL [P < 0.01] and triglycerides [P < 0.05] compared to control. The increase in cholesterol was statistically non-significant [P > 0.05], whereas HDL and LDL were lower.

Women with PCOS may have an underlying metabolic pathological condition associated with long-term risk of coronary heart disease [such as insulin resistance or elevated levels of insulin], which is a major health issue. Many patients with PCOS that bear a significant risk factor for coronary heart disease can therefore be overlooked by relying on minimal classification criteria [8]. **Yang *et al.* [17]** Evaluated 143 women under the age of 40 who underwent coronary angiography for testing chest pain or valvular disease over a 2-year span. When the ovaries of these women were examined by transvaginal ultrasound, 42 per cent had polycystic ovaries. Females with polycystic ovaries had more severe coronary artery disease than women with normal ovaries. The prevalence of polycystic-appearing ovaries in patients with coronary heart disease was reported twice in a general population of women [9].

There was a statistically significant correlation between high serum total cholesterol and low HDL with polycystic ovary syndrome in our research but this relationship was not true for triglycerides and high LDL. Mean serum lipid levels also were not significantly different in control groups and in cases. Note that, when the findings were divided on the basis of the body mass index, significant differences were found in the average serum triglycerides in BMI > 30, as well as in total serum cholesterol in BMI < 25 and BMI < 30 patients. In all of these subjects, the case group had higher levels than the control group. Several studies have tested the dyslipidemia in females with polycystic ovary syndrome. Though different studies tend to report conflicting results in their study population due to factors such as race, genetics, diet, lifestyle and differences in economics.

Slowinska-Srzednicka *et al.* [18] showed that the role of insulin in lipid abnormalities was observed in hyperandrogenic women with PCOS when 27 women with PCOS were compared to 22 weight stratified [obese and nonobese] eumenorrheic control subjects. Women with PCOS showed significantly lower HDL concentrations and a marginal correlation between BMI and HDL serum levels.

Finally, our study showed a significant increase in the serum level of total cholesterol compared to the control subjects and a marginal correlation between the BMI and the total serum cholesterol rates. Also, the current study showed a more atherogenic lipid profile for females with PCOS. There has been a significant increase in total serum cholesterol, LDL-C and triacylglycerol, while a significant reduction in female PCOS HDL-C levels compared to control.

For patients with PCOS the significant increase in cholesterol indicated the presence of key improvements in lipid metabolism. The substantial increase in triacylglycerol could be attributed to triacylglycerol accumulation due to increased lipogenesis, decreased clearance or reduced oxidation of fatty acids.

CONCLUSION & RECOMMENDATIONS

From this study, we concluded that:

This study showed that women with PCOS had atherogenic lipoprotein profile characterized by increased cholesterol, LDL and triglycerides especially in obese group which may be a risk factor for developing cardiovascular complication later on.

The following recommendations should be considered:

1. Follow-up program for PCOS patients is essential to prevent coronary heart disease hazard.
2. Further prospective studies on a greater number of patients and longer duration are needed to document these findings in PCOS patients.

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