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ORIGINAL ARTICLE

Dyslipidemia in Women with Polycystic Ovary Syndrome in Khammam District, Telangana, India

[1]Malidu Priyanka, [2]Madrol V Bhaskar, [3]Manchikanti Madhulatha, [4]Praveen K Kodumuri

ABSTRACT

Introduction: Polycystic ovary syndrome (PCOS) is one of the most common endocrine disorders of women in the reproductive age group, with a prevalence of 5 to 10% of the female population. Dyslipidemia, insulin resistance, and obesity are all potent cardiovascular risk factors that tend to cluster in women with PCOS. The Androgen Excess-PCOS Society consensus statement recommended a complete lipid profile, including low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein-cholesterol (HDL-C), non-HDL-cholesterol (non-HDL-C), and triglycerides (TGs) in all subjects with PCOS for cardiovascular risk prevention.

Aim: The purpose of this study is to evaluate lipid levels in subjects with PCOS and to correlate with obesity.

Materials and methods: Study group comprised 142 women with PCOS and 65 healthy non-PCOS subjects. Body mass index (BMI), waist circumference, and lipids were measured in PCOS subjects and age-matched non-PCOS subjects.

Statistical analysis: All values are expressed as mean ± standard deviation (SD). The results obtained are analyzed statistically using unpaired t-test to evaluate the significance of difference between the mean values.

Results: The mean BMI, waist circumference, serum cholesterol, TGs, LDL-C, and non-HDL-C values significantly increased, whereas serum HDL-C significantly decreased in PCOS subjects when compared with non-PCOS subjects, and serum lipids correlated with obesity.

Conclusion: Dyslipidemia was observed in the present study and serum lipid levels correlated with obesity in women with PCOS.

Keywords: Cardiovascular disease, Dyslipidemia, Non-high-density lipoprotein cholesterol, Polycystic ovary syndrome.

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[1,3,4]Associate Professor, [2]Professor

[1]Department of Biochemistry, Kannur Medical College, Kannur Kerala, India

[2]Department of Biochemistry, Nizam's Institute of Medical Sciences, Hyderabad, Telangana, India

[3]Department of Biochemistry, Mamata Medical College Khammam, Telangana, India

[4]Department of Physiology, Varun Arjun Medical College & Rohilkhand Hospital, Shahjahanpur, Uttar Pradesh, India

Corresponding Author: Praveen K Kodumuri, Associate Professor, Department of Physiology, Varun Arjun Medical College & Rohilkhand Hospital, Shahjahanpur, Uttar Pradesh India, Phone: +919030553866, e-mail: pkphysio@gmail.com

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INTRODUCTION

Polycystic ovary syndrome is one of the most common endocrine disorders of women in the reproductive age group, with a prevalence of 5 to 10% of the female population.[1] It is a heterogeneous condition characterized by hyperandrogenism, ovulatory dysfunction, and polycystic ovaries. The diagnosis of PCOS was based on Rotterdam criteria.[2] Moreover, PCOS is not only been recognized as an endocrine disorder but it is also highly associated with cardiometabolic risk factors, including obesity, insulin resistance, and dyslipidemia.[3] The AE-PCOS Society consensus statement recommended a complete lipid profile including LDL-C, non-HDL-C, HDL-C, and TGs in all patients with PCOS for cardiovascular risk prevention.[4]

Dyslipidemia is the most common metabolic abnormality in PCOS, with a prevalence of up to 70% by the National Cholesterol Education Program criteria.[5] Dyslipidemia includes an atherogenic lipid profile characterized by elevated TG, total cholesterol, LDL-C, and lowered HDL-C.[6]

Dyslipidemia is mainly the consequence of insulin resistance that impairs the ability of insulin to suppress lipolysis, thereby increasing mobilization of free fatty acids (FFAs) from adipose stores. Consequently, increased hepatic delivery of FFAs impairs insulin inhibition of hepatic very-low-density lipoprotein (VLDL) synthesis, causing altered catabolism of VLDL.[4] Additionally, the ability of insulin resistance to alter the expression of lipoprotein lipase and hepatic lipase may also contribute to this abnormal lipid pattern.[7] Excessive adipose tissue increases insulin resistance, and is likely to be found in obese patients with PCOS.

Hyperandrogenemia is additional modifier of dyslipidemia in women with PCOS. Androgen levels were associated with TG levels in some studies and low HDL in other studies.[8] The pathogenesis of dyslipidemia in PCOS remains controversial due to the clustering of interrelated risk factors involved in PCOS. Hyperandrogenemia, hyperinsulinemia, and obesity are intimately interrelated, and each of these factors has independent and synergistic effects on dyslipidemia, so the exact cause

and pathophysiology of dyslipidemia in PCOS are still unknown.[9]

The non-HDL-C concept was recommended as secondary target by Third National Cholesterol Education Programme-Adult Treatment Panel (NCEP-ATP-III).[10] The non-HDL-C estimation provides information on atherogenic particles, including intermediate density lipoprotein, VLDL, LDL, and lipoprotein (a). The importance of non-HDL-C over LDL-C as measurement of vascular event risk was emphasized in some clinical trials.[11] The cutoff points for lipids in Indians according to NCEP criteria are: LDL (<100 mg/dL), non-HDL-C (<130 mg/dL), and total cholesterol level (<170 mg/dL). The non-HDL-C is more important than LDL when the TG is <150 mg/dL.[12]

Dyslipidemia was found to be common in women with PCOS. It is recommended that all women with PCOS should be screened for dyslipidemia, including LDL-C and non-HDL-C determinations, for effective cardiovascular risk prevention.[13] The purpose of this study is to evaluate lipid levels in the PCOS cases compared with non-PCOS controls.

MATERIALS AND METHODS

The present study was carried out in Department of Biochemistry, Mamata Medical College and General Hospital, Khammam, Telangana, India. The study was approved by Human Ethical Committee. Informed consent was obtained from the subjects selected. A total of 142 PCOS cases were selected from the outpatient and inpatient Departments of Obstetrics and Gynecology Unit of Mamata General Hospital, and hospitals in Khammam town, Telangana, India; 65 healthy non-PCOS controls were included in the study. Controls included were volunteers from relatives of the patients, staff, and students.

Body weight, height, and waist circumference were measured and BMI was calculated as weight (kg) divided by height in square meter (m^2). Waist circumference is a measure of abdominal or centralized obesity, and is taken approximately midpoint between the lower margin of last palpable rib and top of iliac crest.

The PCOS cases were categorized into normal (BMI < 23), overweight (BMI = 23–25), and obese (BMI ≥ 25) as per Ministry of Health guidelines. Patients were divided into two groups based on the BMI: subgroup 1 consisting of patients with normal BMI (<23) and subgroup 2 consisting of patients with increased BMI (≥23; overweight and obese). Based on waist circumference, PCOS were categorized into two groups: Normal cases (waist < 80) and obese cases (waist ≥ 80). Controls were also subcategorized based on BMI and waist.

After overnight fast (12 hours), 5 mL of blood was collected from the subjects as well as controls by venipuncture. After collection of blood sample, the blood was allowed to clot (for 45 minutes) and serum was separated by centrifugation at 2500 rpm for 20 minutes. Total cholesterol was measured using cholesterol oxidase/peroxidase method. Triglycerides were measured using glycerol phosphate oxidase/peroxidase method; HDL-C by phospho-tungstate precipitation method. The non-HDL-C is obtained from the difference between total cholesterol concentration and HDL-C concentration. The LDL-C was calculated using Friedewald's formula.

Study Design

The present clinical study was a cross-sectional comparative study.

Inclusion Criteria

All the patients in the age group of 20 to 35 diagnosed for PCOS using Rotterdam criteria were included. Subjects with normal kidney function were also included.

Exclusion Criteria

The subjects having diabetes mellitus, hypertension, coronary heart disease, and endocrine disorders were excluded. Alcoholics, smokers, pregnant women, subjects on vitamin supplementation, and subjects with altered kidney function (random urinary protein >16 mg/dL, serum creatinine >1.1 mg/dL) are also excluded from the study.

Statistical Analysis

All values were expressed as mean ± SD. The results obtained were analyzed statistically using the unpaired t-test to evaluate the significance of differences between the mean values.

RESULTS

Serum cholesterol, TG, LDL-C, and non HDL-C levels were higher, and HDL-C levels were lower in PCOS patients when compared with non-PCOS controls. The mean BMI and waist circumference were also increased in PCOS cases when compared with controls (Table 1).

Table 1: Mean ± SD and p-values of various biochemical parameters in PCOS cases (n = 142) and non-PCOS controls (n = 65)

Parameter	*Total controls*	*Total cases*	*p-value*
BMI (kg/m^2)	24.14 ± 5.20	24.31 ± 4.42	0.8153
Waist (cm)	79.95 ± 9.90	82.07 ± 9.47	0.1430
Cholesterol (mg/dL)	161.0 ± 32.40	190.6 ± 35.51	<0.0001*
TG (mg/dL)	115.7 ± 33.36	149.0 ± 48.32	<0.0001*
HDL-C (mg/dL)	42.0 ± 3.80	37.96 ± 4.26	<0.0001*
LDL-C (mg/dL	96.15 ± 30.08	123.2 ± 34.68	<0.0001*
Non HDL-C (mg/dL)	119.03 ± 31.55	152.77 ± 36.43	<0.0001*

*Statistically significant

Table 2: Mean ± SD of normal controls (n = 32) and normal cases (BMI < 23; n = 61); overweight controls (n = 13) and overweight cases (n = 26) (BMI 23–25); obese controls (n = 20) and obese cases (n = 55) (BMI ≥ 25)

Parameter	*Normal controls vs normal cases*	*Overweight controls vs overweight cases*	*Obese controls vs obese cases*
Cholesterol (mg/dL)	150.1 ± 24.56 *vs* 172.3 ± 25.59*	185.5 ± 32.36 *vs* 190.3 ± 28.69 NS	167.5 ± 38.85 *vs* 210.9 ± 37.25*
TG (mg/dL)	99.75 ± 31.07 *vs* 138.51 ± 38.96*	123.4 ± 11.73 *vs* 149.4 ± 33.13*	132.0 ± 30.52 *vs* 160.3 ± 60.39*
HDL-C (mg/dL)	43.15 ± 3.79 *vs* 38.90 ± 5.06*	43.00 ± 4.26 *vs* 38.06 ± 3.31*	40.30 ± 3.52 *vs* 36.45 ± 3.1671*
LDL-C (mg/dL)	88.15 ± 24.35 *vs* 106.81 ± 23.74*	117.2 ± 32.05 *vs* 121.4 ± 28.21 NS	100.8 ± 36.87 *vs* 142.3 ± 38.36*
Non-HDL-C (mg/dL)	106.93 ± 24.33 *vs* 159.26 ± 25.83*	143.46 ± 31.21 *vs* 151.31 ± 29.08*	127.15 ± 37.62 *vs* 174.45 ± 37.07*

NS: Not significant; *Statistically significant

Table 3: Subgroup 1: normal BMI (BMI < 23; n = 61) *vs* subgroup 2: increased BMI (overweight + obese) (BMI ≥ 23; n = 81) (mean ± SD)

Parameter	*Subgroup 1 (BMI < 23)*	*Subgroup 2 (BMI ≥ 23)*	*p-value*
BMI (kg/m^2)	20.44 ± 1.87	27.22 ± 3.44	<0.0001*
Cholesterol (mg/dL)	172.3 ± 25.59	204.3 ± 35.88	<0.0001*
TG (mg/dL)	138.5 ± 38.97	156.8 ± 53.21	0.0250*
HDL-C (mg/dL)	38.90 ± 5.06	37.26 ± 3.40	0.0225*
LDL-C (mg/dL)	106.8 ± 23.74	135.6 ± 36.58	<0.0001*
Non-HDL-C (mg/dL)	159.26 ± 25.83	167.02 ± 36.18	<0.0001*

*Statistically significant

Table 4: Normal cases (<80; n = 58) and obese cases (≥80; n = 84) (mean ± SD)

Parameter	*Normal cases Waist < 80*	*Obese cases Waist ≥ 80*	*p-value*
Waist (cm)	73.2414 ± 6.0533	88.1667 ± 5.9492	<0.0001*
Cholesterol (mg/dL)	175.4 ± 31.9650	201.0 ± 34.2297	<0.0001*
TG (mg/dL)	139.4 ± 40.0463	155.6 ± 52.5055	0.0489*
HDL (mg/dL)	39.4655 ± 4.7544	36.9286 ± 3.5628	0.0004*
LDL (mg/dL)	109.3 ± 30.5226	132.8 ± 34.2924	<0.0001*
Non-HDL-C (mg/dL)	135.98 ± 31.71	164.06 ± 34.67	<0.0001*

*Statistically significant

Based on BMI

An increase in mean serum cholesterol, TG, LDL-C, non-HDL-C and decrease in mean HDL-C was observed in normal, overweight, and obese cases when compared with their respective controls. The increase was not significant in the overweight category for cholesterol and LDL-C (Table 2).

When the PCOS cases were divided into two subgroups based on BMI, subgroup 1 with normal BMI (<23) and subgroup 2 with increased BMI (≥23), serum cholesterol, TGs, LDL-C, and non-HDL-C were increased with increase in BMI, whereas HDL-C decreased with increase in BMI (Table 3).

Based on Waist

Based on waist, cases were divided into two subgroups. There was significant difference in the mean values in all the parameters (Table 4).

When comparison was made between subgroups based on waist, significant increase of mean serum cholesterol, TGs, LDL-C, non-HDL-C and significant decrease in HDL-C were observed in normal and obese cases compared with respective controls (Table 5).

When the lipid levels were observed in the PCOS cases, the following patterns were noted (Table 6).

DISCUSSION

Lipid abnormalities are important risk factors for coronary artery disease and stroke. Women with PCOS are frequently found to have atherogenic lipid abnormalities that may reflect insulin resistance, genetics, ethnicity, obesity, and lifestyle factors. There are several studies reporting higher total cholesterol, LDL-C,[14] TGs,[15] and lower HDL-C levels among women with PCOS compared with control women.[16] This may be due to an earlier onset of hormonal disturbances, obesity, and intra-abdominal fat distribution among PCOS women.

In our study, lipid levels were compared among PCOS cases and controls as well as in subgroups based on BMI and waist circumference. Dyslipidemia was observed in 116 cases (142) with a prevalence of 81.6%. We observed

Table 5: Comparison based on waist: normal controls, normal cases (<80), obese controls, and obese cases (≥80) (mean ± SD)

Parameter	*Normal controls*	*Normal cases*	*Obese controls*	*Obese cases*
Waist (cm)	72.85 ± 4.678	73.24 ± 6.05	87.74 ± 8.075	88.16 ± 5.94
Cholesterol (mg/dL)	151.6 ± 22.94	175.4 ± 31.9*	171.4 ± 38.05	200.9 ± 34.22*
TG (mg/dL)	102.1 ± 28.61	139.4 ± 40.05*	130.6 ± 32.14	155.6 ± 52.50*
HDL-C (mg/dL)	42.62 ± 3.593	39.46 ± 4.75*	41.32 ± 3.97	36.92 ± 3.56*
LDL-C (mg/dL)	89.03 ± 20.92	109.33 ± 30.52*	103.97 ± 36.45	132.83 ± 34.29*
Non-HDL-C (mg/dL)	108.94 ± 22.45	135.98 ± 31.71*	130.09 ± 37.48	164.06 ± 34.67*

*Statistically significant

Table 6: Percentage distribution pattern of lipids in total PCOS cases according to modified NCEP criteria for Indians

Parameter	Values (>NCEP) criteria	PCOS cases (n = 142)	PCOS %
Cholesterol	>170	102	71.83
TG	>150	68	47.88
HDL-C	<45	103	72.53
LDL-C	>100	108	76
Non-HDL-C	>130	104	73.23

significant increase in mean levels of serum total cholesterol, TGs, LDL-C, non-HDL-C, and significant decrease in mean HDL-C in PCOS cases when compared with their respective controls. The increase was more pronounced with increase in BMI and waist. Higher levels were observed in obese cases when compared with normal cases and controls.

Obesity is associated with various risk factors for atherosclerosis, such as hypertension, insulin resistance, dyslipidemia, and increased platelet activation. Excess adiposity and insulin resistance contribute to dyslipidemia.[17] They increase the delivery of esterified fatty acids to the liver, and this combined with other mechanisms leads to preferential production of small, dense LDL and decrease in HDL size.[18] Hyperinsulinemia and hyperandrogenemia cause adipocytes to undergo increased catecholamine-induced lipolysis and release of FFAs into the circulation. Increased FFAs in the liver stimulate secretion of VLDL, which ultimately leads to hypertriglyceridemia.[19]

We have observed significant increase in non-HDL-C levels in PCOS compared with controls. The non-HDL-C estimation provides clue about presence of atherogenic particles which has gained attention as secondary target by NCEP-ATP III guidelines.[10] It can be beneficial as it is a calculated parameter without additional expense.[20] Non-HDL-C is reliable even in nonfasting state.[21,22] These results imply risk of future cardiovascular disease in women with PCOS. When non-HDL-C is considered as secondary target for treatment, more subjects will be included for treatment strategy, which can be beneficial in preventing cardiovascular risk in PCOS subjects.

CONCLUSION

Our study has demonstrated increased lipid concentrations in women with PCOS. The increase is more pronounced with increase in BMI and waist. This evidence supports that women with PCOS should undergo comprehensive evaluation for recognized cardiovascular risk factors emphasizing more on lipids, including non-HDL-C based on Indian reference values, and receives appropriate treatment based on these findings.

Epidemiological studies are needed to assess the risk of long-term health consequences and to identify the subgroups among PCOS women which need to be targeted for better intervention and prevention. The results of our study emphasize the need for initiating lifestyle measures in the overweight category itself to reduce obesity and dyslipidemia. This will supplement PCOS treatment and can help in minimizing future cardiovascular risk.

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