Lipid Parameters in Patients with Polycystic Ovary Syndrome

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Abstract
The purpose of our study was to investigate the lipid profile in patients with polycystic ovary syndrome (PCOS).

Methods: a retrospective review of the medical records of female patients addressing for a consultation in a private healthcare network in Cluj-Napoca between 2009 and 2011 was performed. Patients with complete lipid profile and without previous treatment were included in the PCOS group. PCOS was diagnosed using Rotterdam criteria for PCOS. Healthy female patients matched for age but without PCOS were included in the control group.

Results: Compared with healthy women, women with PCOS presented higher total cholesterol levels (mean difference = 27.5 mg/dl for total cholesterol, p = 0.004) and LDL-cholesterol (mean difference = 38.1 mg/dl, p < 0.001). HDL-cholesterol displayed lower levels in PCOS patients compared with healthy women (44.4±12.2 mg/dl vs. 50.5±12.2 mg/dl, p = 0.02). No difference was observed between groups in terms of triglycerides levels. In regression analysis both total cholesterol and LDL-cholesterol were positively associated only with the presence of PCOS (β = 0.30, p = 0.01 for total cholesterol, β = 0.44, p<0.001 for LDL-cholesterol). No association was observed between HDL-cholesterol levels and the presence of PCOS. Conclusion: The results of our study show that women with PCOS have altered lipid profile, with higher cholesterol levels (both total and LDL) and lower HDL cholesterol compared with healthy women. These lipid parameters were associated with the presence of PCOS and not with parameters describing body weight.

Keywords: Polycystic ovary syndrome; Dyslipidemia; Cholesterol.

Introduction
One of the most common disorders in women at childbearing age is polycystic ovary syndrome (PCOS), which is a complex disorder affecting not only hormones regulating the normal development of eggs in the ovaries but also other metabolic pathways [1]. PCOS is a very common condition affecting 4% to 18% of women [2,3] and it is associated with metabolic features and diabetes and cardiovascular disease risk factors including high levels of insulin or insulin resistance and non-alcoholic fatty liver disease.

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 [4-6]. Furthermore, since these patients are often hyperinsulinemic and insulin resistant, it would also be expected to be at increased risk for the dyslipidemia associated with insulin resistance [7]. A number of studies have shown that women with PCOS have lower high-density lipoprotein (HDL) and/or HDL2 levels, as well as higher triglyceride and low-density lipoprotein (LDL) levels than age-, sex-, and weight-matched control women [8,9].
Hypertriglyceridemia, increased levels of very low-density lipoprotein (VLDL) and LDL-cholesterol, and decreased levels of HDL-cholesterol [9] predispose patients to vascular disease in the polycystic ovary syndrome. Both insulin resistance and hyperandrogenemia contribute to this atherogenic lipid profile. Testosterone decreases lipoprotein lipase activity in abdominal fat cells, and insulin resistance impairs the ability of insulin to exert its antilipolytic effects [10].

Cardiovascular risk factors are usually present even in younger age and this suggests that the chronic disturbances in hormonal and metabolic status typical for the syndrome predispose the patients to development of early atherosclerosis and premature clinical presentation of cardiovascular disease [11].

Based on the above data, the aim of the study presented here was to compare the lipid parameters in patients with PCOS to those in healthy women and to investigate the relationship between lipid parameters, presence of PCOS, body mass index and waist circumference.

Material and Method

Study Design and Study Subjects

A retrospective review of the medical records of female patients addressing for a consultation in a private healthcare network in Cluj-Napoca between 2009 and 2011 were identified through retrospective review of the medical records and were included in PCOS group. Patients with complete lipid profile and without previous treatment for PCOS were included in the PCOS group. PCOS was 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 [12].

Healthy female patients matched for age but without PCOS were included in the control group. Body mass index (BMI) was calculated as weight (kg)/[height(m)]^2.

Biochemical Evaluation

Total cholesterol, HDL-cholesterol and triglycerides levels were collected from patients’ files. The blood samples were collected after an overnight fast. LDL-cholesterol was calculated using Friedewald formula: 
\[ \text{LDL (mg/dl)} = \text{total cholesterol (mg/dl)} - \text{HDL (mg/dl)} - (\text{triglycerides (mg/dl)/5}) \] [13].

Statistical analysis was carried out using SPSS-PC 13.0 (SPSS Inc., Chicago, IL, USA). Normal distribution of variables was tested with Kolmogorov-Smirnov test. Descriptive statistics are presented as mean ± standard deviation (SD) for normally-distributed variables. Student t-test was used to compare variables with normal distribution. Linear regression was used to evaluate the association between the lipid parameters, the presence of PCOS, BMI and waist circumference. For inclusion in the linear regression as independent variable, PCOS was recoded in a dummy variable: no diagnosis of PCOS = 0 and diagnosis of PCOS present = 1. The level of significance was set at 5% (p < 0.05) in all analyses.

The study was conducted in accordance with the Declaration of Helsinki and approved by the Institutional Ethics Committee.

Results

The present analysis evaluates 43 women with PCOS (PCOS group) and 45 healthy patients, matched for age and sex (control group). The demographic features and biochemical results of patients with PCOS and healthy controls are displayed in Table 1.

There was no difference between groups in terms of body mass index (p = 0.60) or waist circumference (p = 0.06).

Compared with healthy women, women with PCOS presented higher total cholesterol levels.
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(mean difference = 27.5 mg/dl for total cholesterol, p = 0.004) and LDL-cholesterol (mean difference = 38.1 mg/dl, p < 0.001). HDL-cholesterol displayed lower levels in PCOS patients compared with healthy women (mean difference = 6.1mg/dl, p = 0.02). No difference was observed between groups in terms of triglycerides levels.

Linear regression was used to evaluate the relationship between the total cholesterol, LDL-cholesterol, HDL-cholesterol, BMI, waist circumference, and the presence of PCOS (table 2). In linear regression analysis both total cholesterol and LDL-cholesterol were positively associated only with the presence of PCOS (p = 0.01 for total cholesterol, p < 0.001 for LDL-cholesterol). No association was observed between HDL-cholesterol levels and the presence of PCOS. Additionally no association was observed between total cholesterol, LDL-cholesterol, or HDL-cholesterol and BMI or waist circumference (p > 0.05 in all cases). Different results displayed the analysis of triglycerides. A positive association was observed of this parameter with BMI and waist circumference (p < 0.05), while no association was observed with the presence of PCOS (p > 0.05).

Table 1. Anthropometrics and laboratory results of patients with PCOS and healthy controls

<table>
<thead>
<tr>
<th>Parameter</th>
<th>PCOS group (n=43)</th>
<th>Control group (n=45)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>31.9±9.0</td>
<td>31.3±7.3</td>
<td>0.76</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>32.9±8.8</td>
<td>32.2±5.1</td>
<td>0.60</td>
</tr>
<tr>
<td>Waist circumference (cm)</td>
<td>107.6±24.7</td>
<td>99.9±12.9</td>
<td>0.06</td>
</tr>
<tr>
<td>Total cholesterol (mg/dl)</td>
<td>199.3±49.2</td>
<td>171.9±35.9</td>
<td>0.004</td>
</tr>
<tr>
<td>HDL-cholesterol (mg/dl)</td>
<td>44.4±12.2</td>
<td>50.5±12.2</td>
<td>0.02</td>
</tr>
<tr>
<td>LDL-cholesterol (mg/dl)</td>
<td>133.7±44.9</td>
<td>95.6±31.6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Triglyceride (mg/dl)</td>
<td>105.8±61.2</td>
<td>128.6±82.2</td>
<td>0.15</td>
</tr>
</tbody>
</table>

Data are presented as mean ± SD (standard deviation);
PCOS - Polycystic ovary syndrome; BMI - body mass index;
HDL - high-density lipoprotein; LDL - low density lipoprotein

Table 2. Linear regression analysis for total cholesterol, LDL-cholesterol, HDL-cholesterol

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Regression coefficient</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total cholesterol</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>-0.15</td>
<td>0.66</td>
</tr>
<tr>
<td>Waist circumference (cm)</td>
<td>0.09</td>
<td>0.81</td>
</tr>
<tr>
<td>PCOS</td>
<td>0.30</td>
<td>0.01</td>
</tr>
<tr>
<td>LDL-cholesterol</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>-0.14</td>
<td>0.68</td>
</tr>
<tr>
<td>Waist circumference (cm)</td>
<td>0.06</td>
<td>0.87</td>
</tr>
<tr>
<td>PCOS</td>
<td>0.44</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>HDL-cholesterol</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>-0.16</td>
<td>0.65</td>
</tr>
<tr>
<td>Waist circumference (cm)</td>
<td>-0.10</td>
<td>0.77</td>
</tr>
<tr>
<td>PCOS</td>
<td>-0.22</td>
<td>0.06</td>
</tr>
<tr>
<td>Triglycerides</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>0.24</td>
<td>0.03</td>
</tr>
<tr>
<td>Waist circumference (cm)</td>
<td>0.22</td>
<td>0.04</td>
</tr>
<tr>
<td>PCOS</td>
<td>-0.16</td>
<td>0.15</td>
</tr>
</tbody>
</table>

BMI - body mass index; PCOS - Polycystic ovary syndrome; HDL - high-density lipoprotein; LDL - low density lipoprotein

Discussion

The main findings of the study presented here are the high levels of the total and LDL-cholesterol and low HDL-cholesterol observed in women with PCOS when compared with healthy women. Metabolic features associated with PCOS include increased risk factors for type 2 diabetes...
mellitus and cardiovascular disease (worsened lipid profile, high blood pressure, worsened blood vessel function) [14, 15] and an increase prevalence of the metabolic syndrome (a clustering of risk factors for cardiovascular disease), impaired glucose tolerance or prediabetes, type 2 diabetes and potentially cardiovascular disease [16].

In healthy women with normal body weight and preserved insulin sensitivity, the adipocytes release small amounts of free fatty acids (FFAs) and have a normal activity of the lipoprotein lipase (LPL) [17]. In women with obesity, there is an increased production of FFA and decreased activity of LPL as a result of the prominent insulin resistance. In these conditions, the high androgen levels additionally worsen the disturbances in the lipid metabolism [17]. It is thought that approximately 70% of the patients with PCOS have disturbances in serum lipid levels [18]. Even after weight adjustment, the lipid abnormalities persist [11]. Our results support these findings. In the study presented here the levels of total cholesterol, HDL-cholesterol and LDL-cholesterol were associated with the presence of PCOS and not with the BMI or waist circumference. But this association was not observed for triglycerides levels.

Dyslipidemia is common in PCOS compared to weight matched controls [8, 14, 19], with higher triglycerides and lower density lipoprotein cholesterol [1]. The dyslipidaemia occurs independently of BMI [20], however there is a synergistic deleterious effect of obesity and insulin resistance in PCOS analogous to that seen in type 2 diabetes. This could explain the association observed in our study between the triglycerides levels and the variables that usually describe obesity, such as BMI and waist circumference. The causes of dyslipidaemia in PCOS are again 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 [21].

As with studies of insulin action, studies of lipid metabolism in PCOS have been confounded by differences in body weight and ethnicity between patient and control groups.

The study of Cupisti et al. evaluated differences among the 8 most frequent phenotypes of PCOS women with regard to metabolic changes, in terms of markers of lipid profile (LDL, HDL, cholesterol, and triglycerides). Only HDL was significantly lower in women with hyperandrogenemia, hirsutism, and oligomenorrhea than in controls and in comparison with women with oligomenorrhea and polycystic ovaries [22]. In our study the women with PCOS displayed significantly higher total cholesterol and LDL-cholesterol levels and lower HDL cholesterol levels when compared with control group (p<0.05 for all). 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].

The women with PCO also have higher free testosterone, triglyceride, and C-peptide levels and lower LDL levels than the women with normal ovaries, suggesting that they have both the endocrine and the metabolic derangements of PCOS [24]. 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 nonobese group of women and were more closely related to androgens than fasting insulin [25]. They also demonstrate an increase in LDL particle number and a borderline decrease in LDL size and suggest that androgens may play a more significant role in pathogenesis of lipid abnormalities in PCOS [25]. The mechanism by which hyperandrogenism may contribute to development of lipid abnormalities in PCOS is not clear. 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 [26-29].

Current evidence suggests that following a healthy lifestyle reduces body weight and abdominal fat, reduces testosterone and improves both hair growth, and improves insulin resistance. There was no evidence that a healthy lifestyle improved cholesterol or glucose levels in women with PCOS [30].

Some investigators have found that LDL and HDL changes in PCOS can be accounted for by obesity and that only modest increases in total triglyceride levels appear secondary to PCOS-related insulin resistance [31, 32]. A case control study does suggest that there are lipid abnormalities in PCOS after statistical adjustments for obesity [9]. However, Legro and colleagues [33] found atherogenic alterations in lipoprotein levels in normal Hispanic women that did not differ further in
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Hispanic PCOS women. Thus, there appear to be important additional genetic and environmental factors influencing lipid metabolism in PCOS.

Conclusions

The results of our study show that women with PCOS have altered lipid profile, with higher cholesterol levels (both total and LDL) and lower HDL-cholesterol compared with healthy women. Furthermore, these lipid parameters were associated with the presence of PCOS and not with parameters describing body weight. The evaluation of the lipid profile should be compulsory for the global cardiovascular risk assessment in women with PCOS.

Ethical Issues

The study was conducted in accordance with the Declaration of Helsinki and approved by the Institutional Ethics Committee.

Conflict of Interest

The author declares that he has no conflict of interest.

References


23. Fruzzetti F, Pertini D, Lazzarini V, Partini D, Genazzani AR. Adolescent girls with polycystic ovary syndrome showing different phenotypes have a different metabolic profile associated with increasing androgen levels. Fertil Steril 2009;92:626-34.


