Insulin Resistance and Lipid Accumulation Product in Corelation to Body Mass Index in Women with Polycystic Ovary Syndrome

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Introduction: Women with Polycystic Ovary Syndrome (PCOS) are at increased risk for cardiovascular morbidity and metabolic disorders including: dyslipidaemia, hypertension, insulin resistance, gestational diabetes, type 2 diabetes, systemic inflammation and endothelial dysfunction. The prevalence of obesity and insulin resistance in women with PCOS is significantly higher compared to the general population. Lipid accumulation product (LAP) is considered a reliable indicator of risk for cardiovascular disease in women with PCOS (2). LAP was first tested in the general population in 2003 (3). Two easily available and reliable parameters are needed: waist circumference and triglycerides. There was no statistically significant difference in insulin resistance. LAP values were higher in patients in the group with BMI > 25 kg/m2. LAP was a marker for differentiation of insulin – resistant and non-resistant women with PCOS.

Keywords: Polycystic ovary syndrome, insulin resistance, lipid accumulation product.

1. INTRODUCTION

Polycystic ovary syndrome (PCOS) is a reproductive endocrinopathy and metabolic disorder affecting 5-8% of women in reproductive age. In younger women with PCOS the most prevalent feature is hyperandrogenism. Characteristics of older women with PCOS include obesity, cardiovascular and metabolic risk factors. Women with PCOS are at increased risk for dyslipidaemia, hypertension, insulin resistance, gestational diabetes, type 2 diabetes, systemic inflammation and endothelial dysfunction, and the increased risk for cardiovascular morbidity (1). Body mass index (BMI) is used as a medical standard of obesity, and is used in the statistics of the World Health Organization. It is calculated by dividing the body weight (kg) by the square of body height (m2). The prevalence of insulin resistance in women with PCOS is significantly higher compared to the general population. Lipid accumulation product (LAP) is considered a reliable indicator of risk for cardiovascular disease in women with PCOS (2).
cumference and serum triglycerides. LAP (women) = [waist circumference (cm)–58] × [triglycerides (mmol/L)]. Study of Taverna et al. (4) examined it as a predictor of metabolic syndrome and established the LAP cut-off value of 31.77, above which there is a significant increase in factors for metabolic syndrome.

2. MATERIAL AND METHODS

This prospective study included 50 patients at the Clinic of Endocrinology, Diabetes and Metabolic Disorders, Clinical Center University of Sarajevo. All patients were diagnosed with PCOS according to the Rotterdam ES-HRE guidelines (at least two of the following criteria: 1. oligo-anovulation, 2. polycystic ovaries determined by ultrasound, 3. clinical and/or biochemical signs of hyperandrogenism). Patients were divided into two groups according to their BMI. The first group included the patients who had a BMI<24.9 kg/m². The second group included the patients with PCOS whose BMI was greater than 25.0 kg/m² (overweight or obese). Criteria for exclusion from the study: women with PCOS who were treated pharmacologically in the past 12 weeks (oral contraceptives, statins, oral hypoglycemics, other drugs that affect the parameters to be tested), diabetes mellitus or other endocrine disease. A prospective study established the following parameters: anthropometric measurements (waist circumference, height, weight), BMI, serum triglycerides and insulin resistance. LAP was calculated using the formula: LAP (women) = [waist circumference (cm)–58] × [triglycerides (mmol/L)].

3. RESULTS

The group with BMI ≤ 24.9 kg/m² consisted of 18 (36%) patients, while in the group with BMI > 25 kg/m² there were 32 (64%) patients. The waist circumference in women with BMI ≤ 24.9 kg/m² was 31 cm lower compared to women with a BMI > 25 kg/m² (80.0 [77.5–86.5] cm) vs 111.0 [103.7–124.0] cm). Mann-Whitney test showed that the difference in the mean (median) waist circumference between patients in regard to their BMI is statistically significant (p <0.0005). The mean triglyceride value of the patients in group BMI ≤ 24.9 kg/m² was 1.15 mmol/l lower than the mean value of triglycerides in women with a BMI >25 kg/m² (1.10 [0.76 – 1.4]) mmol/l v 2.25 [1.51–3.25] mmol/l). Mann-Whitney test showed that the difference between the mean (median) of triglycerides in women with BMI ≤ 24.9 kg/m² was 1.15 mmol/l, while the difference between the mean values of LAP in relation to patients BMI was 23.9 [14.4 -55.1], and in the group with BMI>25.0 kg/m² was 109.2 [84.4 -218.3]. Mann-Whitney test showed that the difference between the mean values of LAP in relation to patients’ BMI is statistically significant (p <0.0005). It was evaluated that LAP can be a marker of differentiation between insulin-resistant and nonresistant patients (Figure 2).

Lipid accumulation product is proven to be a marker for the differentiation of insulin-resistant and insulin-nonresistant patients (p = 0.049). Cut-off value for LAP is 17.91 (test sensitivity 97%, specificity 50%), as shown in Table 1.

![Figure 1. Insulin resistance in women with PCOS in regard to their BMI. n= number of patients; BMI - body mass index.](image1)

<table>
<thead>
<tr>
<th>Insulin resistance</th>
<th>Total</th>
<th>Not present</th>
<th>present</th>
</tr>
</thead>
<tbody>
<tr>
<td>LAP ≤ 17.90</td>
<td>6</td>
<td>3</td>
<td>9</td>
</tr>
<tr>
<td>LAP &gt; 17.91</td>
<td>8</td>
<td>33</td>
<td>41</td>
</tr>
<tr>
<td>Total</td>
<td>14</td>
<td>36</td>
<td>50</td>
</tr>
</tbody>
</table>

Table 1. Predictive values of insulin resistance for the LAP cut-off value of 17.91.

The proportion of patients with LAP ≤ 17.90 without insulin resistance: negative predictive value: 6/9 = 0.67, or 67%. The proportion of patients with LAP ≥ 17.91 with insulin resistance: the positive predictive value of 33/41 = 0.80 or 80%.

4. DISCUSSION

Unlike earlier studies of Legro et al., Robinson et al. (5,6) in which the metabolic disorders in women with PCOS were compared to those of healthy women, this study compared the metabolic disturbances of PCOS patients divided into two groups with regard to their BMI.

Women with PCOS are often overweight, and there are conflicting opinions in the literature whether patients are obese due to PCOS, or pre-obese women have a predisposition to PCOS. Hoegen and Oberfield study (7) investigated this dilemma. There is evidence to indicate slow metabolism and subsequent predisposition to obesity in women with PCOS. In contrast, the literature found no link between excess weight and PCOS, but the difference in obesity rates between countries is explained by environmental factors and sedentary lifestyle.
The patients in this study were divided into two groups, and evaluated for the uniformity of characteristics that could have an impact on the results of laboratory tests. They were uniform in age, body height and dietary habits. The basic difference between the two groups was value of body weight, and anthropometric measurements including waist circumference. Having examined the lipid profile of the patients in the sample, it was shown that the values of triglycerides were higher in patients in the group with BMI ≥ 25 kg/m². Kauffmann et al. (8) had shown that overweight women with PCOS are significantly affected by dyslipidemia, with increased level of triglycerides, which correlates with the results of our study.

Our study showed that women in both groups had a uniform incidence of insulin resistance. The incidence of insulin resistance in patients in the sample was 70.0%, which is slightly higher than the results of the study by Pontes et al. (9) where insulin resistance was present in 56.4% of women with PCOS. Comparing the patients with PCOS and a group of healthy women, Sarapatková et al. (10) found that patients with PCOS require a greater amount of insulin to maintain normoglycemia. Karabulut et al. (11) showed that increased BMI and type of abdominal (central) obesity in women with PCOS is very closely associated with insulin resistance. Of great importance was the finding that 66.7% of women in the group with BMI ≤ 24.9 kg/m² had insulin resistance. This data correlates with the results of study of Kim et al. (12), which proved defective glucose metabolism in patients with PCOS with normal weight.

LAP is confirmed as a marker for differentiation of insulin-resistant and insulin-nonresistant patients regardless of their BMI, with the upper limit (cut-off) value of 17.81. These results correlate with the study of Wehr et al. (13) where LAP is shown to be a readily available and inexpensive marker linked with glucose metabolism disturbances in patients with PCOS as well as women without PCOS.

5. CONCLUSION
Patients with PCOS and BMI ≤ 24.9 kg/m² were not significantly different from those with a BMI > 25 kg/m² in relation to age and dietary habits. Regardless of this, patients with PCOS and BMI ≤ 24.9 kg/m² were significantly different from those with BMI>25 kg/m² in the values of body weight, waist circumference and values of triglycerides. There was no statistically significant difference in presence of insulin resistance with regard to BMI of the patients. The values of lipid accumulation product (LAP) were higher in patients in the group with BMI > 25 kg/m². LAP is a marker for differentiation of insulin-resistant and insulin non-resistant women with PCOS.

REFERENCES