Insulin resistance in obese and lean women with polycystic ovarian syndrome

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ABSTRACT

Background: According to NIH criteria for PCOS, the estimated prevalence of this disorder has been reported to range from 4% to 10% of women in their reproductive years, which designates PCOS as the most common endocrinopathy of women. Insulin resistance is common in PCOS and obesity contributes an additional component to insulin resistance in obese PCOS.

Methods: The study was a prospective study. One-hundred and twenty PCOS women were divided into two groups: Group O - obese (n = 60) and Group L - lean (body mass index [BMI] cutoff <23 kg/m2). Oral glucose tolerance test, serum fasting insulin and HOMA-IR were compared between these groups.

Results: Impaired glucose tolerance was seen in 33.3% of lean PCOS and 36.7% of obese PCOS women. 5% of lean PCOS and 10% of obese PCOS women had hyperinsulinemia. 38.3% of lean PCOS and 51.7% of obese PCOS women had insulin resistance. But the differences were not statistically significant. However, HOMA-IR and fasting insulin values showed a significant positive correlation with BMI.

Conclusions: Both obese and lean women with PCOS are vulnerable to the problems of insulin resistance irrespective of BMI and insulin resistance shows a positive correlation with BMI.

Keywords: Fasting Insulin, HOMA-IR, Lean PCOS, Obese PCOS

INTRODUCTION

Polycystic ovarian syndrome (PCOS) was first reported by Stein and Leventhal in 1935. It is one of the most common endocrine disorders in reproductive age, affecting 5% to 10% of women worldwide. A high prevalence of up to 35% reported for the Indian women is of great concern. The 2003 Rotterdam Consensus Workshop concluded that PCOS is a syndrome of ovarian dysfunction along with cardinal features of hyperandrogenism and polycystic ovary (PCO) morphology.

Achard and Thiers described the association between a disorder of carbohydrate metabolism and hyperandrogenism in 1921 and was called “the diabetes of bearded women”.

A study conducted on 100 lean women with PCOS found that 47% were insulin resistant. This shows the need for evaluating both obese and lean women with PCOS as its prevalence is high and to prevent the reproductive, metabolic and cardiovascular consequences. The presence of hyperinsulinemia in PCOS, independent of obesity, was confirmed by a number of groups worldwide.

This study was done to evaluate the biochemical markers of insulin resistance (fasting insulin, HOMA-IR (Homeostatic Model Assesment and Insulin Resistance).
and oral glucose tolerance test) in obese (BMI>23) and lean women with PCOS (BMI≤23) and compare their values between them.

**METHODS**

This was a prospective study done on patients coming to OBG OPD of JSS hospital, Mysuru, satisfying inclusion and exclusion criteria.

One hundred and twenty patients between 14 and 40 years of age meeting at least two of the three parameters in Rotterdam criteria were included in the study.

**Inclusion criteria**

- Oligomenorrhea-Amenorrhea
- Biochemical and/or clinical hyperandrogenism
- PCO morphology in USG.

**Exclusion criteria**

- Patients with suspicion of androgen secreting tumour,
- Hyperprolactinemia, cushing’s syndrome,
- Congenital adrenal secreting tumour,
- Thyroid dysfunction and pregnant women.

The patients were further divided into obese (Group O) and lean (Group L) PCOS groups. The body mass index (BMI) cut-off was taken as ≤23 kg/m² for lean PCOS. The patients were informed about the study and its confidential nature. A written and informed consent was taken.

This study was approved by and conducted according to the guidelines of the Institutional Ethical Committee.

Detailed history was taken including presenting complaint(s), menstrual history, pattern of menstrual cycle, duration and extent of hair growth, voice changes, acne and weight gain.

Past history of diabetes mellitus, hypertension, thyroid disorders, hirsutism or galactorrhoea, treatment history for irregular cycles, diabetes, PCOS, infertility, baldness, excessive hair growth, treatment for acne or weight gain and family history of similar complaints were noted.

Height was measured to the nearest 0.1 cm using a stadiometer with the subject in the erect position, with her head held in Frankfurt horizontal plane.

Weight was measured to the nearest 0.1 kg, without shoes and wearing light clothes, using an electronic digital weighing machine. BMI was calculated by the formula weight (kg)/ [height (m²)].

Clinically insulin resistance was diagnosed subjectively by the presence of acanthosis nigricans. Hormonal evaluation was done after an overnight fasting using commercial kits in our laboratory. The hormonal profile included prolactin, thyroid-stimulating hormone and serum fasting insulin (FI).

Oral glucose tolerance test (OGTT) was done by obtaining fasting plasma glucose and plasma glucose 2 hours after 75 g oral glucose load. Samples were stored at −20°C until the assay.

The glucose oxidase–peroxidase method was used for measurements of plasma glucose.

Serum fasting insulin level was measured using commercial kits and an electro-chemiluminescence device. Insulin resistance (IR) was calculated by using the HOMA model [HOMA-IR=fasting serum insulin(μU/L) x fasting plasma glucose (mmol/L)/22.5].

HOMA-IR value more than 2.5 was considered as insulin resistance. Statistical methods applied were descriptive statistics, inferential statistics, Cramer’s V test and Pearson correlation. P value <0.05 was considered statistically significant.

**RESULTS**

The present study was conducted in the Department of Obstetrics and Gynecology, J.S.S Medical College and Hospital, Mysore. One hundred and twenty patients diagnosed as having PCOS by Rotterdam criteria were divided into obese and lean PCOS patients.

In the present study 40% of lean PCOS patients were within the age group of 16–20 years with a mean age of 22.5 years. 46.7% obese PCOS women were in the age group of 21-25 years with a mean age of 24 years.

There is a significant difference in the age group of lean women with PCOS compared to obese women, with more number of women being in the 16 to 20 years age group (Table 1).

Acanthosis nigricans, a clinical manifestation of insulin resistance, was seen in 3.3% of lean PCOS patients and 10% of obese PCOS patients. There is no statistically significant difference between the two groups (Table 2).

Present study shows that 33.3% of lean PCOS and 36.7% of obese PCOS patients had impaired glucose tolerance. There is no significant difference between obese and lean women with respect to glucose intolerance. None of the women in both groups had type 2 diabetes mellitus (Table 3).
Hyperinsulinemia was found in 5% of lean PCOS and 10% of obese PCOS patients. There is no statistically significant difference between both groups (Table 4). HOMA-IR of ≥2.5, indicating insulin resistance, was found in 38.3% of lean PCOS and 51.7% of obese PCOS patients. The difference is not statistically significant (Table 5). There is a significant positive correlation of HOMA-IR and fasting insulin with BMI (Table 6).
Table 5: HOMA-IR

<table>
<thead>
<tr>
<th>Group</th>
<th>L</th>
<th>O</th>
<th>Total</th>
<th>p value</th>
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<tbody>
<tr>
<td>HOMA-IR&lt;sup&gt;†&lt;/sup&gt; ≥2.5</td>
<td>23</td>
<td>31</td>
<td>54</td>
<td>0.142</td>
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<tr>
<td></td>
<td>% within group</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>38.3</td>
<td>51.7</td>
<td>45.0</td>
<td></td>
</tr>
<tr>
<td>HOMA-IR&lt;sup&gt;†&lt;/sup&gt; &lt;2.5</td>
<td>37</td>
<td>29</td>
<td>66</td>
<td></td>
</tr>
<tr>
<td></td>
<td>% within group</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>61.7</td>
<td>48.3</td>
<td>55.0</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>60</td>
<td>60</td>
<td>120</td>
<td></td>
</tr>
<tr>
<td></td>
<td>% within group</td>
<td></td>
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<td></td>
<td>100.0</td>
<td>100.0</td>
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<sup>†</sup> Homeostatic model assessment and insulin resistance

Table 5: Correlation with BMI.

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<th>BMI</th>
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<tbody>
<tr>
<td></td>
<td>HOMA-IR&lt;sup&gt;†&lt;/sup&gt;</td>
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<tr>
<td></td>
<td>Fasting Insulin</td>
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<tr>
<td></td>
<td>OGTT&lt;sup&gt;‡&lt;/sup&gt;</td>
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DISCUSSION

PCOS constitutes a spectrum of symptoms starting from the early pre-pubertal years and continuing after menopause.

The phenotypic expression varies through time, depending on several internal (e.g. ovarian/ adrenal steroidogenesis, insulin resistance) and external factors (e.g. quality and quantity of food, exercise).<sup>6</sup>

Burghen et al in 1980 found that PCOS women had major metabolic as well as reproductive morbidity.

They reported that women with hyperandrogenic disorders like PCOS had basal and glucose stimulated hyperinsulinemia compared to weight matched controls suggesting presence of insulin resistance.<sup>7</sup>

The presence of hyperinsulinemia in PCOS, independent of obesity, was confirmed by a number of groups worldwide. Hughesdon reported in his study that hyperinsulinemia had an impact on ovarian morphology as well as function.<sup>8</sup>

Hyperinsulinemia exacerbates ovarian hyperandrogenism by

- Increasing 17 α-hydroxylase activity in theca cells a
- Promoting androstenedione and testosterone production; promoting LH- and IGF1-stimulated androgen production.
- Elevating free testosterone by decreasing the production of sex hormone binding globulin (SHBG).

Hyperandrogenism in turn results in arrest in the follicle development and anovulation. Metformin is the first line treatment for insulin resistance in PCOS.

In present study we evaluated two groups of PCOS patients, obese and lean. Relatively young population of PCOS women were enrolled in the present study with a majority of them presenting in the age group of 16-25 years.

Acanthosis nigricans (AN), a velvety, mossy, hyper pigmented skin disorder, which is a cutaneous manifestation of insulin resistance and correlates with the magnitude of peripheral insulin resistance was seen in 3.3% of lean PCOS patient and 10% of patients in obese group. In a study conducted by Akshaya et al also, the incidence of AN was similar in both the groups.<sup>9</sup>

In present study, 33.3% of lean PCOS and 36.7% of obese PCOS women had impaired glucose tolerance (IGT). None of the women in both the groups had type 2 diabetes mellitus.

There is no significant difference between obese and lean women with respect to glucose intolerance. In contrast to this, Gupta et al in their study found IGT in 12% and 8% of obese and non-obese group, respectively.<sup>10</sup> Gambineri et al.,11 also reported similar results among PCOS subjects screened from Mediterranean region.<sup>11</sup>

A National Survey of Diabetes and IGT conducted in the year 2000 in six major cities of India showed a 13.1% prevalence of IGT and 5% prevalence of diabetes in the younger age group (20-40 years) of the general population.<sup>12</sup> Majumdar et al. reported a higher prevalence of IGT and type-2 DM in obese PCOS women when compared with lean ones.<sup>13</sup>

Legro et al. reported 31% IGT and 7.5% type-2 DM in obese PCOS patients and 10.3% IGT and 1.5% DM in non-obese PCOS which was 3 times that of general population. They found that PCOS women are at a
Both obese and lean women with PCOS are vulnerable to the problems of insulin resistance irrespective of BMI.

PCOS itself is a risk factor for insulin resistance and its long-term complications. When evaluating PCOS subjects, metabolic features and insulin resistance should also be evaluated irrespective of BMI to prevent long term complications.

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