INFLUENCE OF OBESITY ON INSULIN RESISTANCE IN POLYCYSTIC OVARY SYNDROME

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ABSTRACT

Polycystic ovary syndrome represents the most common endocrine abnormality in women of reproductive age. The aim of this study was to establish the influence of obesity on insulin resistance in polycystic ovary syndrome. A total of 60 polycystic ovary syndrome women were evaluated for the study. The population was separated into three groups namely (i) Polycystic ovary syndrome women with normal body mass index (ii) Polycystic ovary syndrome women with overweight (iii) Polycystic ovary syndrome women with obesity. Abnormalities of glucose metabolism, lipid metabolism and inappropriate gonadotrophin secretion in polycystic ovary syndrome were evaluated in each group by means of fasting glucose, insulin levels, lipid profiles and the ratio of luteinizing hormone and follicle stimulating hormone. Insulin resistance was assessed by the three surrogate markers which are, fasting glucose : insulin ratio, homeostatic model assessment and triglyceride : high density lipoprotein ratio. Obese women showed increasing levels of glucose, insulin, cholesterol, luteinizing hormone and follicle stimulating hormone ratio. Fasting glucose levels are significantly higher in obese women when compared to women with normal body mass index and overweight. It is also found that the insulin levels are increased with increasing body mass index. There is a strong positive correlation between body mass index and insulin resistance. The data suggest that in polycystic ovary syndrome patients increasing body mass index could reflect insulin resistance which may lead to an increased risk of menstrual irregularities and hyperandrogenemia.

KEYWORDS

Insulin resistance, obesity, body mass index, fasting glucose insulin ratio, polycystic ovary syndrome.

INTRODUCTION

Polycystic ovary syndrome (PCOS) is the most common endocrine metabolic disorder among women of reproductive age [1-2] and has been defined as an ovulatory dysfunction associated with hyperandrogenism, with or without hyperandrogenaemia [3-5]. This syndrome shows a prevalence of 5-10% among women of reproductive age [6-8].
Ever since the beginning of the 1980’s there has been evidence of a significant correlation between the levels of androgens and insulin in patients with PCOS[9]. In this regard, these patients show a compensatory hyperinsulinaemia caused by the underlying insulin resistance (IR). The prevalence of IR among PCOS patients is remarkable, appearing in 50 – 70% of the cases. However other studies have found a prevalence as high as 76%[10]. In PCOS, obesity worsens insulin resistance and exacerbates reproductive and metabolic features[11-12].

Obesity plays a central role in the development of PCOS and the majority of women with PCOS are overweight or obese[13]. Obesity is an independent factor associated with IR[14] and sex steroid disturbances[15] which may lead to an increased risk of menstrual irregularities and hyperandrogenemia.

The aim of the present study was to provide insight into the proposed metabolic disturbances in glucose, lipid and the inappropriate luteinizing hormone and follicle stimulating hormone ratio (LH/FSH) and to investigate the role of obesity in women with PCOS. The insulin resistance was also examined and it was correlated with obesity.

MATERIALS AND METHODS

Women (N = 60) of reproductive age diagnosed as having PCOS according to the Rotterdam consensus[16] were included in the present study. Body Mass Index (BMI) was calculated from height and weight measurements and based on BMI levels, the patients are divided in three groups. Group I included the PCOS women with normal BMI (18.5 – 25 kg/m²). Group II with the overweight (BMI 25 – 30 kg/m²) PCOS women and group III comprises the obese (BMI 30 – 40 kg/m²) PCOS women. Blood samples are collected in all the study groups. Blood glucose was assayed by an auto analyzer using the glucose oxidase colorimetric method.

Insulin levels were assayed in all samples by radioimmunoassay method using commercial kits. Based on the values of fasting glucose and insulin, glucose : insulin ratio (G:I) and Homeostatic Model Assessment (HOMA) are calculated. The G:I ratio of less than seven and HOMA value of more than three are considered as markers of insulin resistance.

The levels of LH and FSH are assessed by enzyme linked immune sorbent assay. Serum levels of triglyceride (TGL) are measured by GPO - POD method and the levels of cholesterol and high density lipoprotein (HDL) cholesterol levels are measured by CHOD-PAP method. Lipids are expressed as mg/dl and the ratio of TGL: HDL is calculated for each group. A TGL: HDL ratio is of more than three was considered as a surrogate marker of insulin resistance.

Statistical analyses were performed using the statistical package for social sciences 12.0 (SPSS 12.0). Values are reported as mean ± standard deviation. Statistical significance was found using paired t-test and was attributed to P < 0.01.
Table 1 | Levels of glucose, insulin, lipid patterns and hormonal profiles of PCOS

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<th>NORMAL BMI</th>
<th>OVERWEIGHT</th>
<th>OBESE</th>
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<tr>
<td>GLUCOSE (mg/dl)</td>
<td>105.69 ± 4.07</td>
<td>122.92 ± 3.54</td>
<td>157.32 ± 7.52</td>
<td>18.70*</td>
<td>p &lt; 0.01</td>
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<td>INSULIN (µU/ml)</td>
<td>17.88 ± 2.30</td>
<td>24.88 ± 1.89</td>
<td>33.40 ± 2.25</td>
<td>9.15*</td>
<td>p &lt; 0.01</td>
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<td>CHOLESTEROL (mg/dl)</td>
<td>216.9 ± 32.29</td>
<td>232.55 ± 37.11</td>
<td>276.7 ± 38.32</td>
<td>1.52</td>
<td>NS</td>
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<td>TG (mg/dl)</td>
<td>198.25 ± 33.02</td>
<td>220.75 ± 55.68</td>
<td>245.75 ± 57.73</td>
<td>2.19</td>
<td>NS</td>
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<td>HDL (mg/dl)</td>
<td>59.65 ± 6.04</td>
<td>56.2 ± 6.75</td>
<td>52.25 ± 7.40</td>
<td>1.89</td>
<td>NS</td>
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<td>LDL (mg/dl)</td>
<td>90.10 ± 25.75</td>
<td>97.3 ± 23.78</td>
<td>121.75 ± 27.91</td>
<td>0.97</td>
<td>NS</td>
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<td>LH (mIU/ml)</td>
<td>4.1 ± 0.38</td>
<td>5.83 ± 0.12</td>
<td>6.37 ± 0.14</td>
<td>18.60*</td>
<td>p &lt; 0.01</td>
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<td>FSH (mIU/ml)</td>
<td>2.67 ± 0.14</td>
<td>3.04 ± 0.15</td>
<td>2.99 ± 0.14</td>
<td>9.35*</td>
<td>p &lt; 0.01</td>
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<tr>
<td>LH/FSH RATIO</td>
<td>1.53</td>
<td>1.9</td>
<td>2.1</td>
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Values are given as mean ± SD

*Comparison between normal and overweight PCOS women

**Comparison between normal and obese PCOS women
Fig. 1 Change in the levels of glucose in normal BMI, overweight and obese women

![Graph showing glucose levels in normal BMI, overweight, and obese women.]

Fig. 2 Change in the levels of insulin in normal BMI, overweight and obese PCOS women.

![Graph showing insulin levels in normal BMI, overweight, and obese PCOS women.]

Fig. 3 Change in the levels of TGL, HDL and LDL in normal BMI, overweight and obese PCOS women.

Table 2 Levels of HOMA, G:I ratio and TG:HDL ratio

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<th>NORMAL BMI</th>
<th>OVERWEIGHT</th>
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<tr>
<td>HOMA</td>
<td>8.3</td>
<td>13.5</td>
<td>23.3</td>
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<td>G : I ratio</td>
<td>5.9</td>
<td>4.9</td>
<td>4.7</td>
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<td>TGL : HDL ratio</td>
<td>3.7</td>
<td>3.9</td>
<td>4.1</td>
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RESULTS

Table 1 shows the mean values of glucose, insulin, lipid profiles, LH and FSH. The levels of glucose in obese PCOS women (157.32 ± 7.52) are highly significant (p < 0.01) when compared to overweight (122.92 ± 3.54) and normal BMI PCOS women (105.69 ± 4.07)(Fig 1). The level of glucose was increased by 32% and is statistically significant. Increasing BMI also induced an increase in the level of insulin in obese PCOS women (33.40 ± 2.25) when compared...
with overweight (24.88 ± 1.89) and PCOS women with normal BMI (17.88 ± 2.30)(Fig 2). Although the slight increase in BMI did not alter the values of insulin, prominent increase may increase the levels of insulin and it was statistically significant (p <0.01).

There is an elevated levels of cholesterol, triglycerides and low density lipoprotein and decreased levels of high density lipoprotein with increasing BMI. The cholesterol level in obese PCOS women (276.7 ± 38.32) is increased by 21% when compared to PCOS women with normal BMI (216.9 ± 32.29). The levels of triglycerides in obese PCOS women (245.75 ± 57.73) showed an increase of 20% when compared with PCOS women with normal BMI (198.25 ± 33.02). Negative correlation exists between the BMI and high density lipoprotein in which increasing BMI causes a decrease in high density lipoprotein. The levels of high density lipoprotein in obese PCOS women (52.25 ± 7.40) was decreased by 7% when compared with PCOS women with normal BMI (59.65 ± 6.04)(Fig 3). In contrast to high density lipoproteins, low density lipoproteins showed an increase with increasing BMI and it was statistically significant (p <0.01). There is also the presence of hormone imbalance which is reflected in the levels of LH and FSH. The LH level is highly increased (6.37 ± 0.14) that leads to the increased ratio of LH/FSH (2.1) in obese PCOS women when compared to the PCOS women with normal BMI.

Table 2 reflects the insulin resistance by the HOMA, G:I ratio and TGL:HDL ratio. The HOMA value of 23.3 in obese PCOS women shows highest level of IR. G:I ratio shows an insulin resistance of 4.7 in obese PCOS women and 4.9, 5.9 in overweight and normal BMI PCOS women respectively. Similarly on the basis of TGL:HDL ratio, the insulin resistance was highest in obese PCOS women (4.1) when compared to overweight (3.9) and normal BMI PCOS women (3.7).

DISCUSSION

The present study was performed to elucidate the intriguing relationship between insulin resistance in PCOS and obesity. There is a significant association between the BMI and insulin. Increasing BMI causes hyperinsulinaemia in PCOS women which maybe central to the pathogenesis of PCOS, since it can induce hyperandrogenism and anovulation. It is highly supported by the previous studies by [17-20].

The present study also reflects the impaired glucose tolerance by the elevated levels of glucose in obese PCOS women. This may be due to the synergistic effects of insulin resistance and obesity which is sufficient to account for the predisposition to diabetes in PCOS. The impaired glucose tolerance was 7 fold higher in obese patients [21-22]. In the current study, PCOS is associated with significant increase of triglycerides, low density lipoprotein and decrease of high density lipoprotein. The results of the study are in line with the findings of the researchers who have evaluated the effect of obesity and PCOS on glucose, lipid and insulin metabolism [23-24].

From table 2, it is evident that increasing BMI strongly influence the insulin resistance. The HOMA IR of greater than 3 and the G:I ratio of less than 7 are the main factors selected as
markers of IR for comparison because it is easily calculated and can be applied in any clinical setting and so also the lipid parameters. The insulin resistance is highest in the obese PCOS women when compared with PCOS women with normal BMI on the basis HOMA IR, G:I and TGL:HDL ratio which implies the lowest degree of insulin sensitivity. Insulin resistance is present in less than 10% of non-obese patients with PCOS[25-26], but the prevalence largely increases in obese or overweight women [27-28].

Obesity is also associated with hormonal disturbances which is reflected in the levels of LH and FSH. This may induce functional hyperandrogenism which may be due to an increased androgen production in fatty tissue and also due to higher insulin levels, inhibiting hepatic sex hormone binding globulin production. It was found that obese women with PCOS had more severe ovulatory dysfunction[29].

In conclusion, the present study reflects the strong relationship between BMI and insulin resistance. The methods used to assess the IR are inexpensive which would be potentially useful in clinical practice. The present also proved that the overweight/obesity amplifies the clinical severity of PCOS and increases the risk of metabolic dysfunction.

REFERENCES


