Research Article

Assessment of prolactin and insulin resistance in women with polycystic ovarian syndrome

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Abstract

Background: Polycystic ovarian syndrome (PCOS), the most common cause of infertility, is a disorder characterized by chronic anovulation, hyperandrogenism, hyperinsulinemia, and often presence of obesity. Prolactin has been reported as a potent lipogenic and diabetogenic factor, that affecting energy balance and fuel metabolism. The present study was designed to assess serum prolactin and insulin resistance in PCOS women and to compare them with healthy women as controls.

Material and Methods: A comparative study including 30 women diagnosed as PCOS and 30 age and BMI matched healthy women as controls was conducted. The age group for the study was 18-35 years. Fasting blood samples were drawn to assess serum prolactin, serum insulin, HbA1c and fasting blood sugar (FBS). Insulin resistance (IR) was calculated by homeostasis model assessment (HOMA). Body Mass Index (BMI) was also calculated.

Results: A significant increase in fasting serum insulin (p<0.001) and HOMA – IR (p<0.001) were found in patients with PCOS in comparison with controls. Mean BMI, prolactin, HbA1c and FBS were found elevated in the PCOS women but they were not statistically significant. No significant correlations were found between BMI, serum prolactin and serum insulin.

Conclusions: The current study provides further evidence that significantly higher fasting insulin and HOMA in PCOS group indicates presence of IR. IR in PCOS group may have a potential role in the prediction of dysglycemic disease in women with PCOS. We could not find any significant correlation between serum prolactin, serum insulin and BMI because our study consisted of a limited number of PCOS subjects.

Keywords: Polycystic ovarian syndrome, Serum prolactin, Insulin resistance

1. Introduction

Polycystic ovarian syndrome (PCOS) is one of the common endocrine disorders affecting 5 to 10 % of reproductive age women1. According to ESHRE/ASRM consensus workshop at Rotterdam in 2003, the diagnosis of PCOS is based on the presence of any two of (1) chronic anovulation, (2) clinical/biochemical parameters for hyperandrogenism, and (3) polycystic ovaries on ultrasonography. PCOS subjects are often accompanied by obesity, insulin resistance, abnormal glucose metabolism, lipid disorder, hypertension, and other risk factors of cardiovascular disease. It is well known that reproductive function in women with PCOS is strongly dependent on bodyweight and the metabolic status of the patient. Although the pathophysiology of PCOS is not fully understood, insulin resistance and obesity, central obesity in particular, seem to play a key role in the development of PCOS. A large percentage of PCOS women are insulin resistant and suffer from metabolic alterations.

Prolactin (Prl) is a hormone of pituitary origin and a single chain polypeptide involved in several actions, such as lactation, luteal function, reproduction, appetite, suppression of fertility, homeostasis, osmotic balance, immunity, and coagulation. Prolactin has been reported as a potent lipogenic and diabetogenic factor, that affecting energy balance and fuel metabolism. Among the various physiological factors known to augment prolactin, insulin induced hypoglycemia which results in significant release of prolactin in normal subjects. In vitro lactogen treatment, in the form of oral prolactin alters insulin secretory behavior and β cell junctional communication. Hyperprolactinaemia decreases glucose tolerance via an increase in insulin resistance. The present study was designed to assess serum prolactin and insulin resistance in women with PCOS and to compare them with healthy women as controls.

2. Materials and methods

The study was carried out on 30 PCOS subjects in the age group of 18 to 35 years and 30 voluntary age and BMI matched healthy women with normal menstrual cycle as controls. The study was conducted at Kempegowda Institute of Medical Sciences & Hospital. The diagnosis of PCOS was fulfilled as per Rotterdam criteria. Presence of at least two criteria from clinical, hormonal and abdominal USG category was considered diagnostic of PCOS. Patients with diabetes mellitus, hypertension, dyslipidemia, renal and liver failure and other endocrine disorders and patients receiving hormonal / non-hormonal treatment for PCOS were excluded from the study. The institutional ethical committee approved the study protocol. Informed consent was obtained from all the participants.

A pre-structured and pre-tested proforma was used to collect the data. Baseline data including age, BMI, detailed medical history, clinical examinations and relevant investigations were included as part of the methodology. Serum prolactin, serum insulin, HbA1c and blood sugar were measured in all participants from morning blood samples collected after 12 hours of fasting. Serum prolactin and serum insulin were measured by electrochemiluminescence immunosassay (Elecsys 2010 analyzer, Roche Diagnostics). IR was estimated via the homeostasis model assessment insulin resistance index (HOMA-IR), as follows: HOMA-IR = fasting insulin (mU/L) × fasting glucose (mmol/L)/22.5. HbA1c was
measured by boronate affinity method (Nycocard HbA1c Glycated Hemoglobin Assay k993131). Body mass index (BMI) was calculated as the ratio of weight (Kg) to height squared (m²). Blood sugar was estimated by GOD/POD method.

2.1 Statistics analysis

SPSS software version 13.0 was used for statistical analysis. Comparisons between groups were performed using the Mann-Whitney test. Correlation analysis between BMI, serum prolactin and serum insulin were done using Spearman’s rank order correlation coefficients. A P value < 0.05 was considered statistically significant.

3. Results

Results on continuous measurements are presented as Mean ± SD. The basic characteristics and mean distribution of biochemical parameters in the cases and controls are depicted in Table 1. There was no significant difference in age between two groups. Slightly higher mean BMI was recorded in cases as controls in the difference of mean BMI between the two groups was not statistically significant (P>0.05). Higher mean fasting serum Insulin and higher mean HOMA-IR were recorded in cases compared to controls and the difference between them were found to be statistically significant (P<0.001). Higher mean prolactin, HbA1c and FBS were recorded in cases compared to controls but differences between cases and controls were not statistically significant (P>0.05). Correlation of prolactin with insulin, HOMA-IR and BMI is depicted in Table 2. No significant correlation could be found between BMI and serum Insulin in cases (ρ= 0.283, p = 0.130) or controls (ρ= -0.163, p = 0.388). No significant correlation could be found between prolactin and serum Insulin in cases (ρ= 0.042, p = 0.825) or controls (ρ= -0.295, p = 0.113). Prolactin was not significantly correlated with HOMA-IR in cases (ρ= 0.131, p = 0.492) or controls (ρ= -0.281, p = 0.133) in our study. Similarly, no significant correlation could be found between BMI and prolactin in cases (ρ= -0.117, p = 0.537) or controls (ρ= -0.075, p = 0.694).

Table 1: Mean distribution of biochemical parameters in PCOS cases and controls.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Cases (n=30)</th>
<th>Controls (n=30)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>23.37 ± 4.09</td>
<td>23.73 ± 3.81</td>
<td>0.744</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>24.00 ± 4.41</td>
<td>22.51 ± 2.31</td>
<td>0.126</td>
</tr>
<tr>
<td>Serum Prolactin</td>
<td>14.08 ± 6.87</td>
<td>10.78 ± 6.72</td>
<td>0.065</td>
</tr>
<tr>
<td>Serum Insulin</td>
<td>12.01 ± 6.74</td>
<td>6.80 ± 3.10</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>HOMA-IR</td>
<td>2.35 ± 1.40</td>
<td>1.27 ± 0.58</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>HbA1c</td>
<td>5.91 ± 0.97</td>
<td>5.63 ± 0.36</td>
<td>0.432</td>
</tr>
<tr>
<td>FBS</td>
<td>80.33 ± 10.53</td>
<td>74.67 ± 9.59</td>
<td>0.050</td>
</tr>
</tbody>
</table>

*denotes significant difference; Values are expressed as means ± SD

Table 2: Correlation between various parameters

<table>
<thead>
<tr>
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<th>Cases</th>
<th>Controls</th>
<th>P value</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prolactin and Insulin</td>
<td>0.042</td>
<td>0.825</td>
<td>-0.295</td>
<td>0.113</td>
</tr>
<tr>
<td>Prolactin and HOMA-IR</td>
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<td>-0.075</td>
<td>0.694</td>
</tr>
</tbody>
</table>

4. Discussion

The consequences of the polycystic ovary syndrome extend beyond the reproductive axis; women with the disorder are at substantial risk for the development of metabolic, endocrine and cardiovascular abnormalities.

Insulin resistance is a metabolic disorder caused by the impairment of insulin function in inducing glucose uptake and utilization. Sergus et al. demonstrated that IR in PCOS involves both receptor and postreceptor defects, including defects in phosphatidylinositol 3-kinase and the GLUT-4 glucose transporter. In addition, women with PCOS frequently exhibit impaired peripheral insulin-stimulated glucose utilization and higher basal insulin levels, probably caused by increased insulin secretion and/or decreased hepatic clearance of the hormone; such abnormalities were independent of obesity. Insulin resistance is defined clinically as the inability of a known quantity of exogenous or endogenous insulin to increase glucose uptake and utilization in an individual as much as it does in a normal population. In present study, Higher mean fasting serum Insulin and higher mean HOMA-IR were recorded in PCOS subjects compared to controls and the difference between them were found to be statistically significant (P<0.001). This was consistent with Shou-Kal et al. They found in their study that the HOMA-IR of the PCOS women was significantly higher than that of age-matched healthy women, which suggested that insulin resistance had a crucial role in pathogenesis of PCOS. Higher mean HbA1c and FBS were recorded in PCOS women in our study compared to controls but differences between cases and controls were not statistically significant (P>0.05). We could not find any significant correlation between BMI and serum insulin level in either of the groups mostly because of the limited number of subjects. Puder et al also showed in their study that women with PCOS were more insulin resistant compared to a group of age and BMI matched controls. Sunita et al concluded in their study that insulin resistance is common in Indian PCOS women and this is independent of obesity.

Studies showed mild hyperprolactinemia has been reported in 5% to 30% of patients with PCOS. In present study, higher mean prolactin was recorded in PCOS women compared to controls but differences between cases and controls were not statistically significant (P>0.05). This finding was consistently with Ansam, Soodabeh and Sunita et al. In contrast to this, Roy et al found in their study that serum insulin and prolactin both are significantly increased in PCOS women. This increased prolactin may augment adrenal androgen secretion by the inhibition of 3beta-hydroxysteroid dehydrogenase activity or, less often, through selective action on the sulfation of DHEA in adrenal or extra-adrenal sites. However, prolactin inhibits FSH-induced ovarian aromatase, leading to intraovarian hyperandrogenemia. Cristianne et al also found prolactin is significantly higher in PCOS women.

In our study, no significant correlation could be found between prolactin and serum Insulin in PCOS cases (ρ= 0.042, p = 0.825) or controls (ρ= -0.295, p = 0.113). Similarly, no significant correlation could be found between BMI and serum prolactin in PCOS cases (ρ= -0.117, p = 0.537) or controls (ρ= -0.075, p = 0.694). The role of prolactin on glucose metabolism and insulin resistance depends on its circulating level. A high levels of prolactin exacerbate whole-body and hepatic insulin resistance and impair the insulin secretory capacity in diabetic mice. Differential effects on gene expression are associated with synergistic effects of glucose and PRL on islet DNA synthesis. PRL up-regulates β-cell glucose uptake and utilization, whereas glucose increases islet PRL receptor expression and potentiates the effects of PRL on cell cycle gene expression and DNA...
synthesis. Available in-vitro studies suggest an influence of prolactin on β-cell secretion via increased glucokinase activity, improved β-cell specific survival, or inhibition of intrinsic β-cell apoptosis.

5. Conclusion

Fasting Serum Insulin and HOMA-IR were found to be significantly higher in PCOS subjects compared to controls in our study. All the above derangements confirm that PCOS is associated with insulin resistance and places the subject at a higher risk of metabolic syndrome. We could not find any significant correlation between serum prolactin, serum insulin and BMI. Because our study consisted of a limited number of PCOS subjects and controls from a single population, further studies with larger number of PCOS subjects will polycystic ovarian syndrome for evaluating risk of metabolic and endocrine disorders.

References