EVALUATION OF SERUM ADIPONECTIN LEVELS IN FEMALES WITH POLYCYSTIC OVARIAN SYNDROM

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Abstract

Background: Evaluation of adiponectin levels in PCOS women might help to understand the pathogenesis of the syndrome as well as the complications associated with it. These provide clinical implications for therapeutic interventions targeted at adiponectin in order to prevent the complications associated with polycystic ovary syndrome. Materials and Methods: The present study included a total of sixty (60) women with polycystic ovary syndrome and thirty (30) age matched healthy women were recruited as controls. The blood samples were collected from all the subjects and the biochemical, clinical and experimental parameters were analyzed. Results: Fasting blood sugar levels were similar in PCOS women and controls. Among the lipid parameters studied, total cholesterol and triglycerides were significantly higher in PCOS women when compared to controls, whereas HDL cholesterol levels were similar in PCOS women and controls. Fasting insulin levels and HOMA-IR were similar in PCOS women and controls. Serum adiponectin levels were significantly lower in PCOS women compared to controls. Conclusion: Adiponectin levels are decreased in PCOS women. These decreased levels may further result in the complications associated with polycystic ovary syndrome and hence evaluation of adiponectin levels in these women and measures to improve the levels might provide beneficial effects.

Keywords: Adiponectin, Insulin, HOMA-IR and Polycystic Ovary Syndrome

Introduction

Among women in the reproductive age range, PCOS is one of the most prevalent endocrine-metabolic disorders. While PCOS is thought to be the most prevalent endocrinopathy affecting women who are fertile, estimates of its prevalence range greatly, from 2.2% to 26%. [1-2] The wide range of prevalence reports can be attributed, in part, to variations in the diagnostic criteria employed. PCOS is the most common endocrine condition in women, yet
despite its lengthy history, its etiology is still poorly understood and thought to be complex.\textsuperscript{3-5} It is believed that a complicated interaction between an individual's innate characteristics and environmental variables causes the illness. These interactions cause hormonal disruption, which in turn causes hyperandrogenemia, the hallmark of PCOS and the cause of its clinical symptoms \textsuperscript{[6]}. The development of PCOS is also significantly influenced by genetic factors. Mendelian inheritance occurs in an autosomal dominant manner, and the condition's penetrance varies depending on environmental and epigenetic factors.\textsuperscript{[7]} The cause of the hyperandrogenism is either adrenal or ovarian in origin. Research on genetics and molecular biology has revealed that polycystic ovaries have an underlying steroidogenic abnormality in their theca cells, which leads to an increase in androgen production. Consequently, there is a rise in the activity of three enzymes that function in the steroidogenic pathway: side chain cleavage enzyme, 3-β hydroxyl steroid dehydrogenase, and 17-α hydroxylase.\textsuperscript{[8]} Therefore, it seems that a combination of hereditary and environmental variables that contribute to the hormonal disruption causes PCOS to develop.

Adipose tissue was traditionally considered as an inert organ that is involved in storage of fat. However, since recent times, adipose tissue is regarded as a metabolically active organ, participating in various metabolic functions through release of several locally and systemically biologically active molecules known as adipokines.\textsuperscript{[9-10]} Adiponectin is an important protein synthesized and secreted from adipose tissue and it is composed of 244 amino acids and has a collagen like domain at its N-terminus and a globular domain at its C-terminus.\textsuperscript{[11]} Adipocytokines, in particular adiponectin, have been linked to the pathogenesis of PCOS in recent years. Adiponectin levels were discovered to be impacted by insulin resistance and hyperinsulinemia as well as to correlate inversely with the degree of obesity in healthy persons. According to studies, women with PCOS had reduced amounts of circulating adiponectin, which may be a factor in the difficulties related to PCOS.\textsuperscript{[12]} The increased obesity or insulin resistance that are frequently seen in these women, or any combination of these factors alone, may be the cause of the changed levels. There may be a vicious cycle that develops as a result of the lower adiponectin levels, with less insulin sensitivity leading to insulin resistance. The altered adiponectin levels are proposed to further contribute to the endocrine and metabolic disturbances observed in PCOS women.

Materials and Methods
The present study included a total of sixty (60) women attending to Endocrinology and Metabolism OPD, Haveri Institute of Medical Sciences and Research center, Haveri, Karnataka and diagnosed with polycystic ovary syndrome based on Rotterdam criteria.\textsuperscript{[13]} Thirty (30) age and Body Mass Index (BMI) matched healthy women were recruited as controls. The study was approved by the institutional ethics committee [HIMS/254/2022-23]. Women of reproductive age diagnosed with PCOS as per Rotterdam criteria were included and women with history of diabetes, hypertension, renal, liver and thyroid disease, smoking and alcoholism, history of CVD, acute infections, on hormone therapy, metformin, thiazolidinediones, oral contraceptives, steroids and whoever not willing to participate in this study were excluded.
Sample collection
Five (5) mL of fasting venous blood sample was collected from all the subjects into two tubes: 1mL into a tube containing anticoagulant, and 4 mL into a plain tube. Plasma samples were separated immediately and plain samples were allowed to clot and separated by centrifugation at 3000 rpm for 15min. The separated samples were transferred into appropriately labeled aliquots and stored at -80°C until biochemical analysis was done.

Methods
The Fasting Blood Sugar (FBS) was determined by using glucose oxidase peroxidase method, Total Cholesterol (TC) and Triglycerides was analyzed by enzymatic end point colorimetric method, High Density Lipoproteins were analyzed by selective inhibitory method, serum adiponectin was estimated by enzyme linked immunosorbent assay (ELISA), insulin was measured by chemiluminescence immunoassay (CLIA) and insulin resistance was calculated as HOMA -IR = Fasting plasma insulin X Fasting plasma glucose / 22.5.

Informed Consent Form
All the participants were included after an informed consent according to Helsinki declaration form.

Statistical analysis
Continuous variables were expressed as mean ± SD. The Kolmogorov-Smirnov test was used to evaluate the distribution of continuous variables. Data which were not normally distributed were expressed as or median (interquartile range). The biochemical parameters studied in patients and controls were compared using unpaired two tailed Student’s t-test or Mann Whitney U test as appropriate. The association between the variables was studied using Pearson or Spearman correlation analysis. A p value<0.05 was considered as statistically significant. Statistical analysis was done using Microsoft excel spread sheets and SPSS version 16.0.

Results
Table 1: Demographic characteristics and biochemical parameters studied in healthy controls and women with polycystic ovary syndrome

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Controls</th>
<th>PCOS women</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>24.21 ± 3.25</td>
<td>23.66 ± 1.34</td>
<td>0.812</td>
</tr>
<tr>
<td>Number of subjects</td>
<td>30</td>
<td>60</td>
<td>-</td>
</tr>
<tr>
<td>BMI (kg/m2)</td>
<td>22.56 ± 3.21</td>
<td>26.54 ± 4.00</td>
<td>0.0001**</td>
</tr>
<tr>
<td>Plasma FBS (mg/dL)</td>
<td>88.21 ± 5.24</td>
<td>92.21 ± 7.14</td>
<td>0.851</td>
</tr>
<tr>
<td>Serum TC (mg/dL)</td>
<td>136.49 ± 16.43</td>
<td>161.32 ± 33.44</td>
<td>0.001**</td>
</tr>
<tr>
<td>Serum TGL (mg/dL)</td>
<td>89.67 ± 24.15</td>
<td>134.22 ± 79.34</td>
<td>0.012**</td>
</tr>
<tr>
<td>Serum HDL-C (mg/dL)</td>
<td>59.24 ± 5.14</td>
<td>58.67 ± 5.33</td>
<td>0.341</td>
</tr>
<tr>
<td>Serum adiponectin (μg/dL)</td>
<td>6.34 ± 4.87</td>
<td>3.49 ± 1.54</td>
<td>0.001**</td>
</tr>
<tr>
<td>Fasting Insulin (μIU/mL)*</td>
<td>8.24 (5.24 - 10.30)</td>
<td>7.56 (9.02 -16.00)</td>
<td>0.324</td>
</tr>
<tr>
<td>HOMA-IR*</td>
<td>3.51 (1.42-2.57)</td>
<td>2.34 (1.12- 5.54)</td>
<td>0.528</td>
</tr>
</tbody>
</table>

Table 1 shows the demographic characteristics and biochemical parameters studied in healthy controls and PCOS women. Both groups were matched with respect to age, PCOS women
were obese when compared to healthy women (p=0.0001**). PCOS women had significantly higher total cholesterol and triglycerides when compared to controls (p=0.001* and 0.012* for total cholesterol and triglycerides, respectively). Serum adiponectin concentration was found to be significantly lower in PCOS women when compared to healthy controls (p=0.001**). Fasting insulin and HOMA-IR were similar between cases and controls.

Table 2: Correlation of serum adiponectin with the studied parameters in women with PCOS

<table>
<thead>
<tr>
<th>Adiponectin</th>
<th>(n=60)r</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>-0.442</td>
<td>0.073</td>
</tr>
<tr>
<td>BMI</td>
<td>-0.503</td>
<td>0.289</td>
</tr>
<tr>
<td>FBS</td>
<td>0.341</td>
<td>0.280</td>
</tr>
<tr>
<td>TC</td>
<td>-0.051</td>
<td>0.717</td>
</tr>
<tr>
<td>TGL</td>
<td>0.214</td>
<td>0.642</td>
</tr>
<tr>
<td>HDL-C</td>
<td>-0.636</td>
<td>0.941</td>
</tr>
<tr>
<td>Insulin</td>
<td>-0.001</td>
<td>0.986</td>
</tr>
<tr>
<td>HOMA-IR</td>
<td>-0.021</td>
<td>0.920</td>
</tr>
</tbody>
</table>

The correlation of serum adiponectin with the parameters studied using Pearson correlation analysis is presented in table-2. Adiponectin did not show significant correlation with any of the parameters.

Figure 1: Serum adiponectin concentrations in controls and women with PCOS

Figure 1 shows mean serum adiponectin concentrations in controls and women with polycystic ovary syndrome. PCOS women showed significantly lower adiponectin levels than controls.

Discussion

Polycystic ovary syndrome (PCOS) is one of the most common endocrine-metabolic disorder of women of reproductive age group. PCOS occurs as a result of interaction between environmental factors and intrinsic factors and begins to appear early in the reproductive age. Insulin resistance, which is commonly observed in PCOS women is another contributing factor for PCOS. In addition to the hormonal changes, metabolic disturbances including glucose intolerance and dyslipidemia are also a common feature of polycystic ovary
syndrome. Obesity, which is observed in more than half of women with PCOS plays an important role in the metabolic complications associated with PCOS.\[^{15}\]

In the present study, serum adiponectin levels were found to be significantly lower in women with polycystic ovary syndrome than in healthy females (6.34 ± 4.87 Vs 3.49 ± 1.54, P=0.002) [Table-1]. Several studies have evaluated the relationship between PCOS and adiponectin. Majority of studies have reported significantly lower adiponectin levels in PCOS women when compared to BMI matched healthy controls. In the present study, PCOS women were overweight and had significantly higher BMI than controls (22.56 ± 3.21 Vs 26.54 ± 4.00, 0.0001**) [Table-1]. Several factors have been proposed to be responsible for the lower adiponectin levels in PCOS women. While some of the studies have suggested that the alterations in adiponectin levels are a result of insulin resistance and glucose intolerance, others have shown that adiponectin concentration varies with the degree of adiposity and is not influenced by insulin resistance.\[^{16-18}\]

Additionally, another recent study has reported that hypoadiponectinemia is present in both obese and lean women with PCOS with variable degrees of insulin resistance.\[^{19}\] On the other hand, previous study’s also observed decreased total adiponectin and HMW adiponectin levels in PCOS women suggested that the lowered adiponectin levels occur independent of BMI and insulin resistance and that the posttranscriptional/translational modifications contribute to the low levels of HMW adiponectin in PCOS.\[^{20}\]

The increased adiposity as indicated by a higher BMI in women with polycystic ovary syndrome in the present study might be responsible for the lower adiponectin levels observed in them. In contrast to the above studies, another recent study reported higher adiponectin levels in young non-obese women newly diagnosed with PCOS when compared to controls.

The correlation of serum adiponectin with the clinical and biochemical parameters was analyzed using Pearson correlation analyses. Adiponectin showed a negative but non-significant correlation with age and BMI [Table-2]. Recent study also observed significant inverse correlation between adiponectin and age in PCOS women, whereas another cross sectional study on sixty women with PCOS have reported that adiponectin was associated with obesity.\[^{21}\]

Further, adiponectin levels in PCOS women in the present study showed non-significant inverse correlation with fasting insulin levels and HOMA-IR [Table-1]. Similar findings another study have reported that the adiponectin showed significant negative correlation with insulin resistance.\[^{22}\]

The discrepancy in the results could be due to a small sample size and the difference in the study groups.

Thus, findings of the present study indicate that serum adiponectin levels are significantly lower in women with polycystic ovary syndrome compared to healthy women. The hyperandrogenemia that is one of the characteristic features of PCOS leads to a state of adiposity which further results in decreased adiponectin levels. The low adiponectin levels further contribute to the metabolic complications associated with PCOS including insulin resistance and dyslipidemia. The insulin resistance and the resultant hyperinsulinemia in turn lead to ovarian hormonal disturbances, thus forming a vicious cycle. Thus, the altered adiponectin levels in polycystic ovary syndrome appear to form an important link between obesity and the complications of PCOS.
Conclusion
Adiponectin levels are decreased in PCOS women. These decreased levels may further result in the complications associated with polycystic ovary syndrome and hence evaluation of adiponectin levels in these women and measures to improve the levels might provide beneficial effects.

References


