Total Antioxidant Capacity and Homocysteine Levels in Obese Women with Polycystic Ovary Syndrome

Keywords: Polycystic ovary syndrome, Total antioxidant capacity, Homocysteine

ABSTRACT

Background: Polycystic Ovarian Syndrome (PCOS) is one of the most common metabolic and reproductive disorders among women of reproductive age. Women suffering from PCOS present with a constellation of symptoms associated with menstrual dysfunction and androgen excess, which significantly impacts their quality of life. They may be at increased risk of multiple morbidities, including obesity, insulin resistance, type II diabetes mellitus, cardiovascular disease (CVD), infertility, cancer, and psychological disorders. The relation between polycystic ovary syndrome and cardiovascular disease remains unclear. In an attempt to provide high-quality evidence on the relation between PCOS and CVD, relevant literature for CVD risk marker is homocysteine (Hcy) in women with PCOS was reviewed and analyzed. Polycystic Ovarian Syndrome is associated with oxidative stress, namely increased production of free radicals followed by decreased serum antioxidant levels and antioxidant enzyme activity. Aim: This study aimed to evaluate the association between total antioxidant capacity and cardiac biomarker (total homocysteine) in obese polycystic ovary syndrome.

Materials and Methods: This study carried out from November 2015 till October 2016 a period of case-control study. We included 30 obese patients with signs and symptoms of polycystic ovary syndrome and another 30 obese control subjects. Total cholesterol, triglyceride, HDL-C, LDL-C, VLDL-C, total antioxidant capacity and total homocysteine were determined and calculated in each sample by various techniques. Then various correlations were measured by SPSS system. Results: There is a high significant p < 0.01 in total antioxidant capacity and total homocysteine when comparison between obese PCOS and obese control. While there is a negative significant correlation between total antioxidant capacity and total homocysteine level in obese PCOS patient. Conclusions: Polycystic ovary syndrome patients clearly present a higher risk of cardiovascular diseases spatially obese PCOS patient in addition to that total antioxidant capacity which had a negative correlation with homocysteine levels as cardiac biomarker.
INTRODUCTION

Polycystic Ovarian Syndrome (PCOS), refers to hyperandrogenic anovulation (HA), or Stein–Leventhal syndrome (1), described since 1935 by Stein and Leventhal (1935), is one of the most common endocrine system disorders that affect women in their reproductive age affecting 7–10% of this group (2, 3). The clinical features of the syndrome include oligomenorrhea, acne, hirsutism, obesity and insulin resistance (IR). Insulin resistance is present in the majority of women with PCOS, regardless of Body mass index (BMI). Women with PCOS have an increased risk for impaired glucose tolerance (IGT). IGT or type two diabetes mellitus (T2DM) develops in 40% of obese women with PCOS by the age of 30, decreased high-density lipoprotein cholesterol (HDL-C) levels, and increased total cholesterol, low-density lipoprotein cholesterol (LDL-C) and triglyceride levels are also associated with PCOS (4). Both polycystic ovary syndrome (PCOS) and cardiovascular disease (CVD) are common in women, CVD remains the leading cause of death in women, and age remains one of the strongest risk factors for the development of atherosclerosis and death from a cardiovascular event (5). Despite the higher prevalence of CV risk factors and subclinical markers of CV disease in women with PCOS, studies have failed to show a consistent association between PCOS and increased CV events or mortality (6). The direct evidence for a link between oxidative stress and cardiovascular disease, ROS-induced oxidative stress plays a role in various cardiovascular diseases such as atherosclerosis, ischemic heart disease, hypertension, cardiomyopathies, cardiac hypertrophy and congestive heart failure (7). Therefore, PCOS is accompanied by oxidative stress in which increased production of free radicals is followed by decreased serum total antioxidant levels. Furthermore, it has been shown that even lean women with PCOS exhibit oxidative stress (8). Hyperhomocysteinemia (HHCY) has been described as an independent risk factor for cardiovascular disease. Hyperhomocysteinemia either by elicitation of oxidative stress, systemic inflammation and/or endothelial dysfunction is known to promote insulin resistance and β-cell dysfunction (9). Homocysteine (Hcy) in plasma is an independent risk factor for cardiovascular disease. It has often been shown to be related to occlusive vascular disease independently of other known risk factors. Hyperhomocysteinemia induces endothelial injury, oxidative stress, smooth muscle hypertrophy and oxidation of LDL-cholesterol (10). Approximately half of all women with PCOS are overweight or obese. Independently of the presence of obesity, these women are frequently insulin resistant and therefore they have hyperinsulinemia, which may play a pathogenic role in the disease (11). Recent studies have
documented increased oxidative stress in patients with PCOS (12, 13), which may increase the risk of CVD in such patients. Elevated plasma Hcy levels are considered to be an independent risk factor for CVD (14). In recent studies, serum Hcy concentrations were found to be elevated in PCOS women, suggesting that an alteration in Hcy metabolism may play a role in the increased cardiovascular risk associated with PCOS (15-19). Hyperhomocysteinaemia-induced oxidative stress may occur as a consequence of either decreased expression and activity of key antioxidant enzymes or increased enzymatic generation of superoxide anions (20-24). Mounting data suggest that obesity induces oxidative stress in humans. Several studies have reported increased levels of reactive species or oxidant products in obesity (25, 26). These levels decrease in response to weight reduction, caloric restriction and diets rich in antioxidants (27, 28). Possible contributors to oxidative stress in obesity include hyperglycemia, hyperlipemia, augmented muscle activity to carry excessive weight, hyperleptinemia, chronic inflammation and inadequate antioxidant defenses (27). Oxidative stress is increased in diabetes and also in obesity (29). Studies also demonstrated elevated oxidative stress in insulin-resistant women with PCOS (12). Increased reactive oxygen species generation induced by hyperglycemia and/or hyperinsulinemia has been reported in this population. However, there were conflicting results about the levels of antioxidants in these studies. Some investigators found decreased levels of antioxidants, whereas others have observed increased activities of some antioxidants as a compensatory mechanism in PCOS (13, 30).

MATERIALS AND METHODS

The study was conducted during the period from Nov. 2015 to Oct. 2016 a period of case-control study. Sixty women within the reproductive age (18-45 years old). Thirty obese Patient women out of sixty were attended from gynecological and obstetric hospital in Karbala province, and they all diagnosed by their physicians as Polycystic Ovary Syndrome, and they compared with thirty obese healthy control women with comparable age. The study protocol was approved by the ethical research committee of the College of Medicine-University Karbala and Karbala Health Directorate.

Inclusion Criteria

Consisted of all patients with PCOS were already diagnosed and the diagnosis was confirmed according to European society of human reproduction and embryology and American society for reproductive medicine criteria: PCOS is diagnosed if there are any two of the following:
Presence of polycystic ovary on ultrasound examination.

Menstrual dysfunction with an ovulation.

Clinical or biochemical hyperandrogenemia.

Exclusion Criteria

- All patients with hormonal therapy or any medication known to interfere with follicular development or hormonal levels under the study for last 3 months of samples expect metformin.
- All patients with oligomenorrhea, amenorrhea due to other than PCOS causes.
- Diabetic patients.
- All patients suffered from heart diseases or congenital abnormality of the heart.

About 5 ml of venous blood sample was drawn from each patient and control groups. The sera were separated by centrifugation at (3000 runs per minute) for 5 min. Each serum sample was analyzed directly for total cholesterol, Triglyceride, HDL-C, LDL-C, VLDL-C by using Auto Analyzer Biochemistry while then analyzed total antioxidant capacity and total homocysteine by using ELIZA technique.

RESULTS

The results showed a significant difference in total antioxidant capacity, total homocysteine and HDL-C between obese patients and obese healthy P < 0.01 as shown in Table 1. There was statistically negative significant correlation between T-AOC and HCY as shown in Table 2 and figure 1.
Table 1: Comparison between obese polycystic ovary syndrome patient group and obese control group in the measured parameter

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Control group N= 60 Mean ± SE</th>
<th>Patient group N= 60 Mean ± SE</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (20 – 35)</td>
<td>27.733 ± 3.808</td>
<td>26.383 ± 4.741</td>
<td>NS</td>
</tr>
<tr>
<td>BMI (Kg/m²)</td>
<td>28.217 ± 5.197</td>
<td>28.891 ± 5.957</td>
<td>NS</td>
</tr>
<tr>
<td>Cholesterol (mg/dl)</td>
<td>139 ± 21.637</td>
<td>141.082 ± 23.322</td>
<td>NS</td>
</tr>
<tr>
<td>TG (mg/dl)</td>
<td>83.753 ± 32.172</td>
<td>85.458 ± 39.089</td>
<td>NS</td>
</tr>
<tr>
<td>HDL-C (mg/dl)</td>
<td>54.51 ± 5.72</td>
<td>41.747 ± 9.387</td>
<td>P&lt; 0.01</td>
</tr>
<tr>
<td>LDL-C (mg/dl)</td>
<td>73.101 ± 10.38</td>
<td>78.295 ± 12.95</td>
<td>P&lt; 0.05</td>
</tr>
<tr>
<td>VLDL-C (mg/dl)</td>
<td>16.75 ± 6.434</td>
<td>17.091 ± 7.817</td>
<td>NS</td>
</tr>
<tr>
<td>T-AOC (U/ml)</td>
<td>26.029 ± 20.515</td>
<td>10.783 ± 5.039</td>
<td>P&lt; 0.01</td>
</tr>
<tr>
<td>HCY (nmol/ml)</td>
<td>14.411 ± 13.732</td>
<td>7.392 ± 2.407</td>
<td>P&lt; 0.01</td>
</tr>
</tbody>
</table>

Table (2): Correlation between T-AOC and HCY

<table>
<thead>
<tr>
<th>T-AOC (U/ml)</th>
<th>HCY (nmol/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>r = - 0.342</td>
<td>p = 0.045</td>
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</tbody>
</table>

Citation: Fadhil Jawad Al-Tu’ma et al. Ijppr.Human, 2017; Vol. 8 (3): 78-86.
DISCUSSION

The results indicated that homocysteine levels were significantly elevated in obese PCOS patients. These findings were agreeing with many studies (31–33). Homocysteine may have several actions on vascular cells impairment of endothelial function, enhancement of low-density lipoprotein oxidation, promotion of smooth muscle cell proliferation and accelerated elastin degradation, as a result of increased free radical generation leading to a reduction in total antioxidant capacity in woman with PCOS. It was also observed that elevated serum Hcy levels are present in PCOS women, suggesting that an alteration in Hcy metabolism may be implicated in the increased risk of cardiovascular disease in such patients (16). Lowering plasma Hcy improves endothelial function in individuals with coronary artery disease and decreases the incidence of major cardiac events (34). This is lead to widely accept that Hcy is a major independent risk factor for cardiovascular disease (35). Also, the results showed high significant differences in total antioxidant capacity between patient and control. Fenkci et al. detected lower TAOC levels in the PCOS group, but these levels did not reach a level of statistical significance. This observation suggested that the oxidative status imbalance in PCOS women might contribute to their increased risk of cardiovascular diseases. Polycystic ovary syndrome is also associated with decreased antioxidant concentrations and is thus considered an oxidative state (36). Therefore the result indicated that the correlation between TAOC and HCY is a significant negative correlation in obese PCOS. This is due to the influential factors is obesity, where they considered as a positive impact on oxidative stress (37, 38).
CONCLUSION

Polycystic ovary syndrome patients clearly present a higher risk of cardiovascular diseases. Obesity appeared to be a major factor associated with elevated cardiac markers. Homocysteine was high in PCOS patient. From the presented results which revealed that PCOS is associated with dyslipidemia and altered oxidative status. Total antioxidant capacity had a negative correlation with Homocysteine in obese women.

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REFERENCES


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