DO DIETARY HABIT MAKES ANY DIFFERENCE OF PLASMA HOMOCYSTEINE LEVELS IN PATIENTS OF PCOS?

Amita Diwakar,¹ Dhiraj Kishore²

ABSTRACT

Background: Homocysteinemia in polycystic ovarian syndrome (PCOS) is quite common and have many adverse state over pregnancy like impair implantation and probability of early pregnancy loss is already been documented. Another aspect is Vegetarians who do not supplement their diet with vitamin B12 tend to have low vitamin B12 levels and elevated homocysteine as in Vitamin B12-deficient state; homocysteine conversion to methionine is impaired. So we tried to find out if dietary habit makes any difference of serum homocysteine level between PCOS patient and matched control. Aims: The objective was to investigate the relationship between dietary habit and increased serum homocysteine in women with polycystic ovarian syndrome (PCOS) and matched control. All the study subjects were in the reproductive age group and were suffering from infertility. Material and Methods: Cross sectional Case Control comparative study done in Department of Obstetrics & Gynecology, CSMMU Lucknow. Cases were 50 PCOS women as a study group and 40 women with infertility due to other causes as a control group. Serum homocysteine levels compared between subject taking vegetarian diet and non-vegetarian diet in PCOS patients and matched control group. Results: Mean homocysteine raised in cases (11.8±5.5 µmol/L) than control (7.8±2.2µmol/L), p<0.001 Considering 11 µmol/l cut off level for normal homocysteine, 36% of PCOS patients (18 of 50) and 10%of control (4 out of 40) had high homocysteine levels, p<0.001. Mean plasma homocysteine among vegetarian PCOS was 10.96±3.27 and among non-vegetarian PCOS subject was 11.57±2.01, p value was insignificant. Among non PCOS matched control vegetarian group mean Hyc was 7.80±2.4 and among nonvegetarian non PCOS group mean serum Hyc was 7.81 ±1.8 micro mol/l, p value was insignificant. Conclusion: PCOS is associated with elevated plasma homocysteine; this finding may have important implications in the short term reproductive performance, and the long term cardiovascular complications. However dietary habits do make significant changes in level of plasma Hyc among PCOS patient or non PCOS matched subjects. So in conclusion plasma homocysteinemia among PCOS patient is a part of metabolic syndrome independent of dietary habit.

Key Words: PCOS, Hyc,Vit B12,diet.

¹. SSR Obstetrics and Gynecology IMS BHU
². Assistant Professor General Medicine IMS BHU.

Corresponding address: Dr. Amita Diwakar, B-5, New Medical Enclave, Banaras Hindu University, Varanasi -221005; Ph-09451964917; dhirajkishore@gmail.com
INTRODUCTION

Polycystic ovary syndrome is a metabolic and endocrinological disorder of reproductive age group having prevalence of 5-10%. It is characterized by menstrual irregularities, biochemical and clinical hyperandrogenism (hirsutism, seborrhea and acne). Genetic, metabolic, biosynthetic, ovarian, hypothalamic and pituitary factors are involved in the pathogenesis leading to abnormal hypothalamic pituitary activity, activated adrenal activity, insulin resistance and hyperinsulinemia. Most of women with PCOS are overweight, obese, insulin resistant and the long term complication of PCOS include the development of vascular atherosclerosis, endometrial cancer, diabetes and other cardiovascular anomalies. In the present study patients of PCOS will be defined according to Rotterdam consensus meeting on PCOS; it defines the syndrome of PCOS as the presence of any two of the three criteria as Ultrasound appearance of polycystic ovaries, menstrual disturbances, evidence of hyperandrogenism, acne, hirsutism, etc after other cause of hyperandrogenism has been rule out. Elevated level of TNF-α and other pro inflammatory marker in insulin resistance and hyperandrogenism in PCOS possibly causes hyperhomocysteinemia. Homocysteine is an intermediate product formed during the breakdown of amino acid methionine and may undergo remethylation to methionine, or trans-sulfuration to cystathione and cysteine. Normal homocysteine concentration range between 5 and 11 mol. Hyperhomocysteinemia has been classified as follows, mild (11 to 30 mol/L), intermediate (30 to 100 mol/L) and severe (>100 mol/L). Hyperhomocysteinemia is an independent risk factor for atherosclerotic vascular disease, cerebrovascular events and recurrent venous thromboembolism. It can occur due to genetic defects in the enzymes involved in homocysteine pathways such as methylene tetrahydrofolate reductase (MTHFR) or to deficiencies of vitamin B12, folic acid or drugs, such as fribates and nicotinic acid. Homocysteine induces oxidation of low density lipoprotein (LDL), proliferation of smooth muscle cells, increased platelet adhesiveness and endothelial cytotoxicity cause impairment of blood flow leading to impaired implantation by interfering with endometrial blood flow and vascular integrity resulting increased probability of early pregnancy loss. Another aspect is Vegetarians who do not supplement their diet with vitamin B12 tend to have low vitamin B12 levels and elevated homocysteine as in Vitamin B12-deficient state homocysteine conversion to methionine is impaired. So we tried to find out if dietary habit makes any difference of serum homocysteine level between PCOS patient and the matched control.

MATERIAL AND METHODS

Cross sectional Case Control comparative study was done in Department of Obstetrics & Gynecology, CSMMU Lucknow. Cases were 50 PCOS women as the study group and 40 women were selected randomly as control group. All the study subjects were infertile and in the reproductive age group. Serum homocysteine levels compared between subject taking vegetarian diet and non-vegetarian diet in PCOS patients and control group.

RESULTS

<table>
<thead>
<tr>
<th>Diet</th>
<th>Case</th>
<th>Control</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No</td>
<td>%</td>
<td>No</td>
</tr>
<tr>
<td>Vegetarian</td>
<td>33</td>
<td>66</td>
<td>24</td>
</tr>
<tr>
<td>Non-vegetarian</td>
<td>17</td>
<td>34</td>
<td>16</td>
</tr>
<tr>
<td>Total</td>
<td>50</td>
<td>100</td>
<td>40</td>
</tr>
</tbody>
</table>

χ²=0.344, df=1, p= 0.557 (not significant)
Case group have 66% vegetarian and 34 % non vegetarian compared to 60% and 40% respectively in control group, p value (0.557) was insignificant (Table-1).

Table-2: Comparison of Homocysteinemia in Case and Control group in accordance with Dietary habits considering source of Vitamin B12 from non vegetarian diet (Hyperhomocysteinemia taken as Plasma homocysteine level ≥ 11µmol/L)

<table>
<thead>
<tr>
<th>INDEPENDENT SAMPLE TEST</th>
<th>TOTAL</th>
<th>CASE</th>
<th>CONTROL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plasma Homocysteine (µ mol/L)</td>
<td>&lt;11</td>
<td>≥ 11</td>
<td>&lt;11</td>
</tr>
<tr>
<td>Vegetarian</td>
<td>45</td>
<td>12</td>
<td>23</td>
</tr>
<tr>
<td>Plasma Hcy in all cases &amp; Cont (vegetarian)</td>
<td>---</td>
<td>(A) 10.967 ± 2.374</td>
<td>(C) 7.805 ± 2.458</td>
</tr>
<tr>
<td>Non-Vegetarian</td>
<td>23</td>
<td>10</td>
<td>9</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>7.507 ± 1.405</td>
<td>11.744 ± 4.489</td>
<td>8.030 ± 1.475</td>
</tr>
<tr>
<td>Plasma Hcy in all cases &amp; Cont Non-vegetarian</td>
<td>---</td>
<td>(B) 11.578 ± 4.011</td>
<td>(D) 7.811 ± 1.858</td>
</tr>
</tbody>
</table>

For A & B, t=0.38, df=48, sig= 0.334 (not significant). For C & D, t=0.327, df=38, sig=0.517 (not significant).

Considering 11 µmol/L cut off level for normal homocysteine, 36% of PCOS patients (18 out of 50) and 10% of control (4 out of 40) had high homocysteine levels, p<0.001. Mean homocysteine was raised among PCOS vegetarian group (10.967 ± 3.27µmol/L) than vegetarian control (7.8± 2.4µmol/L), p< 0.001. Mean plasma homocysteine among non-vegetarian PCOS was 11.57± 4.48 and among non vegetarian control subject was 7.81±0.85 p value was significant < 0.001. When we compared the values among all vegetarian and non-vegetarian subject in PCOS cases group, p value was not significant. Similarly comparison of homocysteine level among vegetarian and non vegetarian subjects among control group p value again turn out to be insignificant.

DISCUSSION

Infertility associated with PCOS has been attributed to many factors including anovulation, abnormal gonadotrophin secretion, elevated serum androgens, and dysfunction of ovarian growth factors. Increased serum homocysteine level was observed in these adverse metabolic effects. Homocysteine is an intermediate metabolite formed during breakdown of amino acid methionine, and may undergo remethylation to methionine, or transsulphuration to cystathion and cysteine. Classical homocystinemia has been characterized as the accumulation of Hcy due to defect in enzymatic pathway. Recent research has pointed to many non enzymatic factor which influence Hcy level such as age, gender, sex-steroid hormones, nutrition, smoking, chronic inflammation, coffee consumption, vitamin B12 and folic acid deficiency. Vitamin B12 levels and folic acid levels were examined in the study by Yarali et al., and no significant differences were found between PCOS and controls. In our study While looking for the level of plasma homocysteine level in PCOS number of variables like vitamin B12, folic acid status and enzyme dysfunction states were not examined as they are quite costly and as a measure we tried to correlate the dietary habit as indirect indicator of vitamin B 12 and folic acid deficiency in majority of vegetarian subjects but could not find any statistically significant difference in mean plasma homocysteine level between case vegetarian (10.967 ±3.27µmol/L) and case non vegetarian (11.578± 4.011 µmol/L) subjects. However enzyme deficiencies and vitamin levels were not examined in our study.However a study done by Schachtet M. et al., randomized insulin resistant PCOS women for the treatment with vitamin B 12 preparations or metformin or both in conjunction with standard infertility treatment. Plasma homocysteine level was significantly reduced by
both Vitamin B12 and metformin but higher pregnancy rates were associated with vitamin B12 treatment. A another common finding is insulin resistance if very prevalent in PCOS, mean plasma homocysteine levels were significantly higher in the insulin-resistant PCOS patients as compared with non-insulin-resistant PCOS patients as compared with non-insulin-resistant PCOS patients. In this study, statistical non significant difference was noticed in case and control group on basis of dietary habit. Free radicals formed during the oxidation of reduced homocysteine may directly injure endothelial cells marked platelet aggregation may be secondary to the pro-aggregatory effects of homocysteine. Prolonged exposure of endothelial cells to homocysteine impairs the production of nitric oxide. Hyperhomocysteinemia has been linked to myocardial infarction and recurrent coronary events, adverse outcomes after angioplasty, carotid artery stenosis, recurrent venous thrombosis, osteoporosis, dementia and silent brain infarct. It may be recommended that when PCOS is diagnosed, other metabolic complications should be investigated. Gynecologists should aim to solve short-term problems of PCOS, i.e. reproductive failure, without neglecting the serious, long term complications, i.e. cardiovascular and metabolic derangements.

CONCLUSION

PCOS is associated with elevated plasma homocysteine, this finding may have important implications in the short term reproductive performance, and the long term cardiovascular complications. However dietary habits do make significant changes in level of plasma Hcy among PCOS patient or non PCOS matched subjects. So in conclusion plasma homocysteinemia among PCOS patient is a part of metabolic syndrome independent of dietary habit.

REFERENCE

2. Rotterdam, ESHRE/ASRAM-Sponsored PCOS consensus workshop group revised 2003 consensus on diagnosis criteria and long-term health risk related to polycystic ovary syndrome (PCOS), Hum Reprod, 2004; 19, 41-47.

---