Serum cobalamin and homocysteine in subclinical hypothyroidism

Reena Bai1, Yasir Ali2, Arsalan Ahmed Uqaili3, Naree mal1 and Zubair Suhail Almani5

1Medical Officer Jinnah Postgraduate Medical Center Karachi, Sindh, Pakistan
2MBBS, FCPS-II Jinnah Postgraduate Medical Center Karachi, Sindh, Pakistan
3Department of Physiology Faculty of Medicine & Allied Medical Sciences Isra University Hyderabad, Sindh, Pakistan.
4Medical Officer Government District Civil Hospital, Kotri, Jamshoro, Sindh, Pakistan
5Medical Officer Asim Clinic Hyderabad, Sindh, Pakistan.

ABSTRACT

The present study intended to evaluate serum homocysteine and serum cobalamin in subclinical hypothyroid patients. Place and Duration: Jinnah Postgraduate Medical Center Hospital, Karachi from January to August 2015. Subjects were divided into Group A Controls- normal subjects (n=50), Group B Cases – diagnosed cases of subclinical hypothyroidism (n=50). 5 ml of venous blood sample was collected and centrifuged at 4000rpm for 10 minutes. The serum obtained was frozen at -20°C and used for estimation of thyroid hormone profile, serum cobalamin and serum homocysteine. The data was analyzed on SPSS version 22.0. Student’s t test and chi square test was used for continuous and categorical data respectively at 95% confidence interval (p ≤ 0.05). Mean ±SD age of controls and cases noted was 52.1 ± 5.6 and 51± 8.7 years respectively. Serum homocysteine in controls and cases was found as 6.89±3.75 and 15.9 ±12.3 µM/L respectively (p=0.0001). Serum cobalamin in controls and cases was noted as 298± 56.5 and 199.7±67.9 pg/dl respectively (p=0.0001). Serum homocysteine was raised with low serum cobalamin in subclinical hypothyroidism patients. The present study reports raised serum homocysteine and low serum cobalamin in Subclinical hypothyroid patients.

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Institutional ethical approval was taken. Signing of informed consent form was mandatory to participate in the study by the volunteer subjects. Patient’s data was noted on a pre-structured proforma. Confidentially of patients information was ensured.

5 ml of venous blood sample was collected and centrifuged at 4000rpm for 10 minutes. The serum obtained was frozen at -20°C and used for estimation of thyroid hormone profile, serum cobalamin and serum homocysteine.

Serum homocysteine levels were estimated by enzyme linked immunosorbent assay (ELISA) kit. Serum cobalamin was determined by competitive EIA technique. The data was analyzed on SPSS version 22.0. Student’s t test and chi square test was used for continuous and categorical data respectively at 95% confidence interval (p ≤ 0.05).

**Results**

Cases and controls showed mean ± S.D age of 52.1 ± 5.6 and 51± 8.7 years respectively. The baseline characteristics of cases and controls are shown in table 1. Age and gender distribution showed non-significant (p>0.05) differences. Complete blood counts, serum T3, serum T4 and serum TSH, blood urea nitrogen and serum creatinine are shown in table 1. Serum homocysteine in controls and cases was noted as 6.89±3.75 and 15.9 ±12.3 µM/L respectively (p=0.0001). Serum cobalamin in controls and cases was noted as 298± 56.5 and 199.7±67.9 pg/dl respectively (p=0.0001). Serum homocysteine was raised with low serum cobalamin in subclinical hypothyroidism patients as shown in table 1. Serum homocysteine and cobalamin as normal, borderline and severe rise or reduction are shown in table 2, graph 1 and 2. Significant differences were noted for the subclinical hypothyroidism patients.

Table 1. Age, gender, blood parameters, serum homocysteine and serum Cobalamin in controls and cases.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Control (n=50)</th>
<th>Case (n=50)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>52.1±5.6</td>
<td>51± 8.7</td>
<td>0.056</td>
</tr>
<tr>
<td>Male</td>
<td>29 (58%)</td>
<td>30 (60%)</td>
<td>0.09</td>
</tr>
<tr>
<td>Female</td>
<td>21 (42%)</td>
<td>20 (40%)</td>
<td>0.07</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>29 ± 3.5</td>
<td>29± 5.9</td>
<td>0.06</td>
</tr>
<tr>
<td>Hemoglobin (g/dl)</td>
<td>14.7± 3.9</td>
<td>11± 2.8</td>
<td>0.011</td>
</tr>
<tr>
<td>RBC counts (x10⁸/µl)</td>
<td>4.3± 1.7</td>
<td>2.39± 4.1</td>
<td>0.013</td>
</tr>
<tr>
<td>WBC counts (µl)</td>
<td>707± 51</td>
<td>607± 47</td>
<td>0.072</td>
</tr>
<tr>
<td>Platelets (x10³/µl)</td>
<td>3.73±1.4</td>
<td>3.57±2.1</td>
<td>0.071</td>
</tr>
<tr>
<td>Serum T3 (mg/dl)</td>
<td>96.7±29.4</td>
<td>97±27.8</td>
<td>0.0001</td>
</tr>
<tr>
<td>Serum T4 (µg/ml)</td>
<td>7.3± 2.1</td>
<td>7.5± 2.13</td>
<td>0.0001</td>
</tr>
<tr>
<td>Serum TSH (µU/ml)</td>
<td>3.5±0.9</td>
<td>7.8±1.53</td>
<td>0.0001</td>
</tr>
<tr>
<td>Serum homocysteine (µM/L)</td>
<td>6.89±3.75</td>
<td>15.9± 12.3</td>
<td>0.0001</td>
</tr>
<tr>
<td>Serum cobalamin (pg/ml)</td>
<td>298± 56.5</td>
<td>199.7±67.9</td>
<td>0.0001</td>
</tr>
<tr>
<td>Blood urea nitrogen (mg/dl)</td>
<td>7.90±1.9</td>
<td>9.3±0.7</td>
<td>0.002</td>
</tr>
<tr>
<td>Serum creatinine (mg/dl)</td>
<td>2.13±0.4</td>
<td>2.15±0.6</td>
<td>0.05</td>
</tr>
</tbody>
</table>

Graph 1. Serum homocysteine in cases and controls.

Graph 2. Serum cobalamin in cases and controls.

**Discussion**

In the present study, serum homocysteine and cobalamin were investigated in the subclinical hypothyroid subjects. To achieve authentic results, strict inclusion and exclusion criteria were observed. Serum homocysteine in controls and cases was noted as 6.89±3.75 and 15.9 ±12.3 µM/L respectively (p=0.0001). Serum cobalamin in controls and cases was noted as 298± 56.5 and 199.7±67.9 pg/dl respectively (p=0.0001). The present study reports raised serum homocysteine and low serum cobalamin in subclinical hypothyroidism patients as shown in table 1. The findings of present study are consistent with previous studies. 18-20

Serum Hcy levels are found low in hyperthyroid patients compared to hypothyroid subjects who have raised serum Hcy levels. Serum FT4 concentration reported an independent determinant of serum Hcy level.8,9

Previous studies had reported relationship of SCH and serum Hcy, however, results are controversial.8-10 However, and previous studies had reported a positively lowering effect of levothyroxine (L-T4) therapy on the serum Hcy. However, the consensus does not exist on the levothyroxine therapy and serum Hcy.11-13 Previous studies8-10 are in contradistinction to present and previous studies.18-20

Ciccone et al20 reported that the obese female with hypothyroidism have increased intima-media thickness (IMT) which is an indicator of atherosclerosis and risk of Cerebrovascular and cardiovascular diseases. They concluded that the hypothyroidism was an independent factor for the atherosclerosis. They reported raised serum Hcy in their hypothyroid subjects which might be accelerating the
atherosclerosis. The findings are consistent to the present study.

Wang et al. reported a study on the serum Hcy and serum cobalamin in anti-thyroid antibodies positive hypothyroid subjects. They reported raised serum Hcy and low serum cobalamin in the cases. The findings of above study are in agreement with the present study.

Topaloglu et al. reported increased carotid IMT, normal serum Hcy and serum cobalamin in their study subjects. Normal serum Hcy and serum cobalamin is in contrast to presents study.

Owecki et al. has recently reported a case control study, in which hypothyroid cases were treated with levothyroxine. They reported reduction of serum Hcy with levothyroxine therapy compared to controls. They concluded that the hypothyroid subjects are at risk of increased atherosclerosis due to elevated serum Hcy levels. The findings of above study support the observations of the present study.

The present study has its some strengths and limitations. Low sample size and anti-thyroid antibody profile are the main limitation of the present study. However, the strength of study lies in its exclusion criteria of; subclinical hypothyroidism and atherosclerosis because of raised serum homocysteine which is an independent risk factor. However, further studies are recommended to validate the findings.

Conclusions

The present study reports raised serum homocysteine level and low vitamin Cobalamin levels in subclinical hypothyroid patients. The observation adds evidence to the debate of the possible association of subclinical hypothyroidism and atherosclerosis because of raised serum homocysteine which is an independent risk factor. However, further studies are recommended to validate the findings.

References


