Available online at www.elixirpublishers.com (Elixir International Journal)

Physiology and Anatomy

Elixir Physio. & Anatomy 95 (2016) 41166-41168

ISSN: 2229-712X

Serum cobalamin and homocysteine in subclinical hypothyroidism

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ARTICLE INFO

Article history:

Received: 9 May 2016;

Received in revised form: 17 June 2016;

Accepted: 22 June 2016;

Keywords

Subclinical hypothyroidism, Homocysteine, Cobalamin.

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 ($p \leq 0.05$). 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 .

Introduction

Hypothyroidism is a clinical condition of low physiological functioning of thyroid gland with reduced synthesis and secretion of thyroid hormones. Hypothyroidism is of 2 types; one overt hypothyroidism and the other subclinical hypothyroidism. Subclinical hypothyroidism (SCH) is defined biochemically as persistently raised serum thyroid stimulating hormone with normal thyroid gland hormones.[1, 2] clinically, the subclinical hypothyroidism remains asymptomatic, but 30% of patients May complaint of one or other symptom of thyroid gland failure.[3]Recently, the SCH is linked with atherosclerosis and ischemic heart disease in elderly. Recently, interest has increased on the subclinical hypothyroidism as a risk factor for the cardiovascular disease.[4, 5] similarly, serum homocysteine (Hcy) is an emerging risk factor for ischemic heart disease. Serum Hcy is a sulfur containing amino acid which is produced during interconversion of methionine and cysteine.[6] Hyperhomocysteinemia (HHcy) is identified as an independent risk factor of vascular endothelial injury and atherosclerotic vascular disorders.[7] Previous studies had reported relationship of SCH and serum Hcy, however, results are controversial.[8-10] However, 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]

Serum cobalamin is commonly known as the vitamin B12. Cobalamin is essential for deoxyribose nucleic acid (DNA) synthesis along with folate. It also participate role in the metabolic reactions of Hcy metabolism.[14, 15] Cobalamin functions as co enzyme for the methionine synthetase enzyme, which converts Hcy into methionine. Cobalamin is also needed for the conversion of methyl malonate into Succinate.[16, 17]

Keeping in view, all the conflicting results, the present study was planned to evaluate the serum cobalamin and serum homocysteine in subclinical hypothyroid patients presenting at the Jinnah Postgraduate Medical Center Hospital, Karachi.

Subjects and Methods

The present comparative case control study was conducted prospectively at Jinnah Postgraduate Medical Center Hospital, Karachi from January to August 2015. Subjects were selected as per criteria of inclusion and exclusion. Sampling was non-probability purposive sampling. Group A. Controls- normal healthy subjects (n=50) Group B. Cases – diagnosed cases of subclinical hypothyroidism (n=50). All subjects were screened by a medical officer and were diagnosed by a consultant physician or a chest specialist. Only diagnosed cases of subclinical hypothyroidism were included. Subclinical hypothyroidism was defined as normal serum thyroxine with elevated serum TSH with or without clinical symptoms. While subclinical hypothyroidism with diabetes mellitus, systemic hypertension, ischemic heart disease, multivitamin pill therapy and chronic kidney disease subjects were excluded from study protocol. Written informed consent was obtained and a copy was given to the patient. The patients were assigned a study number. All the participants were informed about advantages and disadvantages of study, harm and or losses.

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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 ($p \leq 0.05$).

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.

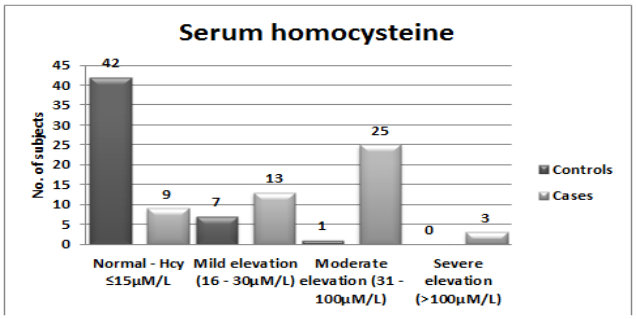
	Control (n=50)	Case (n=50)	p-value
Age (years)	52.1±5.6	51± 8.7	0.056
Male	29 (58%)	30 (60%)	0.09
Female	21 (42%)	20 (40%)	0.07
BMI (kg/m^2)	29 ± 3.5	29.5± 9.4	0.06
Hemoglobin (g/dl)	14.7 ±3.9	11.0± 2.8	0.011
RBC counts (x10^9/µl)	4.3± 1.7	2.39± 4.1	0.013
WBC counts (/µl)	7078±51	6073±71	0.072
Platelets (x10^9/µl)	3.73±1.4	3.57±2.1	0.071
Serum T3 (ng/ml)	96.7±29.4	97±27.8	0.0001
Serum T4 (µg/ml)	7.3± 2.1	7.5±2.13	0.0001
Serum TSH (µU/ml)	3.5±0.9	7.8±1.53	0.0001
Serum homocysteine (µM/L)	6.89±3.75	15.9 ±12.3	0.0001
Serum cobalamin (pg/ml)	298± 56.5	199.7±67.9	0.0001
Blood urea nitrogen (mg/dl)	7.90±1.9	9.3±0.7	0.002
Serum creatinine (mg/dl)	2.13±0.4	2.15±0.6	0.05

Table 2. Serum homocysteine in controls and cases

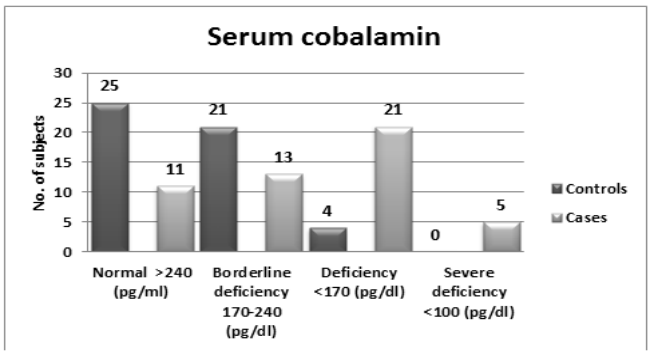
	Controls (n=50)	Cases (n=50)	p-value
Normal - Hcy ≤15µM/L	42 (84%)	9 (18%)	0.0001
Mild elevation (16 - 30µM/L)	7 (14%)	13 (26%)	
Moderate elevation (31 - 100µM/L)	1 (2%)	25 (50%)	
Severe elevation (>100µM/L)	0 (0%)	3 (6%)	

Table 3. Serum cobalamin in controls and cases

	Controls (n=50)	Cases (n=50)	p-value
Normal >240 (pg/ml)	25 (50%)	11 (22%)	0.0001
Borderline deficiency 170-240 (pg/dl)	21 (42%)	13 (26%)	
Deficiency <170 (pg/dl)	4 (8%)	21 (42%)	
Severe deficiency <100 (pg/dl)	0 (0%)	5 (10%)	



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 studies[8-10] are in contradistinction to present and previous studies.[18-20]

Ciccone et al[20] 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[19] has 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[22] 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[18] 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 with diabetes mellitus, systemic hypertension, ischemic heart disease, multivitamin pill therapy and chronic kidney disease subjects were excluded from study protocol.

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.

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