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Cardiometabolic and Hematological Consequences of Subclinical Hypothyroidism – A Hospital-based Study

Prabir Kumar Saha[1], Dipayan Choudhuri[2]*

Abstract

Introduction: Cardiometabolic syndrome is a major public health problem that effects various groups of population world over. Overt hypothyroidism is reported to be associated with both adverse cardiometabolic events as well as hematological picture. However, cardiometabolic and hematological consequences of subclinical hypothyroidism (SCH) are yet to be evaluated in different population. In the present study, we evaluated cardiometabolic and hematological consequences of SCH in a middle aged population from Agartala, Tripura, India. **Methodology:** The study was conducted on 193 patients attending the ENT OPD of Tripura Medical College and Dr. B.R. Ambedkar Memorial Teaching Hospital, Hapania, Agartala. Subjects having diabetes mellitus, hypertension, patients having thyroxin, antithyroid drugs and antilipidemic drug users, established cancer patients, pregnant woman, and women receiving oral contraceptive pills were excluded from inclusion in the study. **Results:** The mean age of the subjects was 40.13 years, and females constituted around 65 % of total subjects. The analyses showed a significant difference the RBC count, HB concentration, and a non-significant difference in WBC count between euthyroid and hypothyroid subjects, while platelets showed no significant difference between the groups. There was a significant increase in total cholesterol level and level of LDL cholesterol as well as blood pressure, blood sugar level, and waist circumference in hypothyroid subjects in comparison to euthyroid subjects. **Conclusion:** The study concluded that the subjects with hypothyroidism have worse cardiometabolic parameters with alteration in lipid profile. Thyroid dysfunction affects all blood parameters except platelets. The follow-up of patients with hypothyroidism should include the complete blood count and evaluation of lipid profile and other cardiometabolic parameters.

Keywords: Hematological parameters, Lipid profile, MetS, T3, T4, TSH

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Introduction

Globally cardiovascular disease (CVD) is one of the leading causes of death.[1] It is now well established that cluster of major risk factors (Hypertension, diabetes, dyslipidemia, obesity, inappropriate diet, alcohol, and physical inactivity) governs the occurrence of CVDs. Much before these are firmly established as diseases, all these cardiometabolic risk factors were clustered as ardiometabolic syndrome or simply metabolic syndrome (MetS).[2] Despite the controversy on its definition, it is estimated that one out of four people around the world suffers from MetS.[3] The prevalence of these are increasing all over the world with different regions having individual clusters of epidemic risk factors. Distinctly, there is an evidence of high prevalence of MetS in India and other South-Asian countries.[4]

Decreased function of thyroid gland is one of the common endocrine disorders effecting general population globally and is identified as a major endocrine disorder among Indians.[5]

Overt hypothyroidism adversely affects cardiovascular morbidity and mortality. In thyroid disease, dyslipidemia and the coexisting metabolic abnormalities in combination with the thyroid hormone-induced hemodynamic alterations explain the high risk of CVD. Thyroid disease is associated with various metabolic abnormalities, due to the effects of thyroid hormones on nearly all major metabolic pathways. Thyroid hormones regulate the basal energy expenditure through their effect on protein, carbohydrate, and lipid metabolism. Dyslipidemia is a common metabolic abnormality in patients with thyroid disease either in the overt or subclinical forms of the disease and constitutes the end result of the effect of thyroid hormones in all aspects of lipid metabolism leading to various quantitative and/or qualitative changes of triglycerides, phospholipid, cholesterol, and other lipoproteins.[6,7]

[1]Department of ENT, Tripura Medical College and Dr. B.R. Ambedkar Memorial Teaching Hospital, Hapania, Agartala, Tripura, India.

[2]Department of Human Physiology, Tripura University (A Central University), Agartala, Tripura, India.

Corresponding Author: Dipayan Choudhuri, Department of Human Physiology, Tripura University (A Central University), Suryamaninagar, Agartala, Tripura, India. E-mail: dipayanchoudhuuri@tripurauniv.ac.in

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Subclinical hypothyroidism (SCH) commonly defined as plasma thyroid stimulating hormone (TSH) above the reference range (above 4–4.5 ml/L) together with a free plasma thyroxin level within the reference range is a well-recognized entity in clinical settings. More recently, the concept is emerging that low normal thyroid function that is higher TSH and or lower FT4 levels within the euthyroid reference range, even when determined at a single time point, could have a negative cardiometabolic impact. The consequences of SCH are variable at several levels and may depend on the duration and the degree of elevation of TSH. Hence, a number of important questions arise relating to SCH, including whether it raises cardiovascular risk and therefore mortality and whether it negatively influences metabolic parameters.[8,9]

Alteration of lipid profile is a common observation associated with thyroid dysfunction.[10,11] However, current knowledge on relationship between lipids and thyroid hormone levels in euthyroid as well as hypothyroid state is insufficient. Therefore,

it is important to determine the association between thyroid hormones and TSHs with lipid profile in euthyroid as well as hypothyroid subjects. This will help in proper management of subject suffering from hypothyroidism vis-a-vis their future cardiovascular consequences. Thyroid gland regulates blood cell metabolism and proliferation as all other cells in the body. Reports suggest that thyroid dysfunction is associated with alteration of various hematological parameters.[12]

In view of the above, the present study aims to evaluate the cardiometabolic risk profile of hypothyroid subjects along wither lipid profile and hematological profile and compare the same with euthyroid subjects of same age and sex.

Methodology

The study was conducted on the freshly diagnosed overt or subclinical hypothyroid subjects attending ENT OPD of Tripura Medical College and Dr. BRAM Teaching Hospital, Hapania, Agartala before initiation of the treatment. Subjects with diabetes mellitus, hypertension, patients having thyroxin, antithyroid drugs and antilipidemic drug users, established cancer patients, pregnant woman, and women receiving oral contraceptive pills were excluded from inclusion in the study. We have evaluated 193 total hypothyroid subjects. All subjects signed an informed consent before inclusion in the study. The study protocol is approved by Human Ethical Committee of Tripura University.

The cardiometabolic parameters evaluated in the subject included waist circumference as measure of the central obesity, both systolic and diastolic blood pressure, lipid profile, and fasting blood glucose level. All hematological parameters (Hb content, total RBC count, total WBC count, and platelet count) are estimated using automated hematological analyzer. To evaluate thyroid function, status of the subjects (Serum T3, Serum T4, and Serum TSH) level were estimated by Elisa method. All data were computerized and analyzed using Data Analysis Tool of MS-Excel.

Results

Total of 193 subjects were evaluated for the study. Out of that, 127 cases were euthyroid and 66 cases were hypothyroid. Among the euthyroid study population, 48 were male and 79 were female. Whereas, among hypothyroid subjects, 19 were male and 47 were female. Total male population in this study was 67 out of 193 (34%) and female were 126 out of 193 (66%). Analysis revealed that general anthropometric characteristics such as BMI, body weight, and waist circumference were significantly higher in both male and female hypothyroid subjects in comparison to euthyroid subjects. Among cardiometabolic risk parameters, blood pressure and fasting blood glucose level was found to be significantly higher in hypothyroid subjects of both male and female groups [Table 1]. There was significantly higher values of TSH in hypothyroid subjects whereas T3 and T4 were within normal limits in both groups [Table 2]. Analysis of lipid profile of the subjects revealed that total cholesterol and LDL cholesterol were significantly higher in hypothyroid subjects in comparison to the euthyroid subjects. Variation in triglyceride level and HDL cholesterol level were not significant [Table 3]. Among the hematological parameters such as RBC count, WBC count, platelet count, and Hb concentration analyzed, there was a significant decrease in Hb concentration and total RBC count in hypothyroid subjects whereas there was a non-significant increase in total WBC count. Platelet count did not show much differences between the groups [Table 4].

Discussion

We observed a substantially higher prevalence of SCH among the male (28%) and female (37%) subjects. Such a high prevalence of SCH seem clinically significant due to risk of progression to overt hypothyroidism and cardiac and metabolic consequences associated with this. The anthropometric observations of the study revealed that body weight, BMI, and waist circumference of subjects with SCH are significantly higher than the euthyroid subjects.

A number of studies have reported that SCH is associated with increased risk of coronary heart diseases and results in significant increase in cluster of cardiometabolic risk factors.[13,14] Similar to earlier studies, we also found preponderance of cardiometabolic risk factors in subjects with SCH in comparison to euthyroid subjects. In subjects with SH, there is a significant increase in diastolic blood pressure, total, and LDL cholesterol as well as fasting blood sugar levels.[15-17] Results of our study so far revealed that SH may lead to diastolic hypertension and hypercholesterolemia along with a mild increase in fasting blood sugar levels. The altered lipid profile in SH subjects may lead to atherosclerosis which has serious consequences such as development of coronary artery disease and stroke.

The study revealed that there was a significant decrease in RBC count and hemoglobin concentration in hypothyroid subjects in comparison to euthyroid and control subjects. Although there was a slight increase in the number of WBC in hypothyroid subjects but the difference was not significant. Platelet count did not show any significant difference between the groups. Reports from earlier studies revealed that anemia and other blood abnormalities are common in thyroid function abnormalities specially hypothyroidism.[18] Analysis showed that

Table 1: Details of anthropometric and cardiometabolic parameters evaluated in the subjects (values are in mean±SD)

Parameters	*Study subjects (193)*			
	Male (67)		*Female (126)*	
	Euthyroid (48)	*Hypothyroid (19)*	*Euthyroid (79)*	*Hypothyroid (47)*
Age in years	41.20±11.71	43.22±11.43 (NS)	37.67±11.17	39.10±12.84 (NS)
Height (cm)	161.46±9.87	163.96±5.88 (NS)	153.94±7.74	157.14±7.55 (NS)
Weight in kg	63.57±10.18	66.44±9.90	55.16±7.60	60.40±9.57**
Body mass index (kg/m^2)	24.56±4.42	26.68±3.22*	23.98±2.98	26.31±2.40**
Waist circumference	89.87±4.29	91.67±5.23**	83.96±3.92	87.35±2.31***
Systolic blood pressure-SBP (mmHg)	123.30±11.31	128.33±7.28**	123.65±8.58	127.14±8.58**
Diastolic blood pressure-DBP (mmHg)	79.18±6.01	87.77±9.35**	77.36±4.84	88.08±4.75**
Fasting blood glucose-FBG (mg/dl)	102.79±17.57	107.33±23.16**	103.35±20.28	117.21±37.26**

*P≤0.5, **P≤0.01, ***P≤0.001. NS: Not Significant

Table 2: thyroid function status of subject (values are in mean±sd)

Parameters	*Study subjects (193)*			
	Male (67)		*Female (126)*	
	Euthyroid (48)	*Hypothyroid (19)*	*Euthyroid (79)*	*Hypothyroid (47)*
S.T3	1.263878±0.254786	1.322±0.288 (NS)	1.236±0.306	1.606±1.154 (NS)
S.T4	8.928571±1.621498	8.584±1.324 (NS)	8.710±2.153	6.940±3.572*
S. TSH	3.324±1.164	9.978±3.672***	3.545±1.272	14.695±8.693***

*P≤0.5, **P≤0.01, ***P≤0.001. NS: Not Significant

Table 3: the details of lipid profile parameters evaluated in the subject (values are in mean±sd)

Parameters	*Study subjects (193)*			
	Male (67)		*Female (126)*	
	Euthyroid (48)	*Hypothyroid (19)*	*Euthyroid (79)*	*Hypothyroid (47)*
Triglyceride (mg/dl)	170.74±60.14	192.66±63.11	153.61±40.33	184.65±52.213
Total cholesterol (mg/dl)	175.96±35.24	185.77±26.48**	171.09±33.99	201.19±34.46***
HDL-C (mg/dl)	45.49±5.833576	47.22±6.52	45.89±6.045	47.77±4.45*
LDL-C (mg/dl)	107.01±31.42	108.55±15.28 (NS)	106.27±23.039	122.91±25.87**

*P≤0.5, **P≤0.01, ***P≤0.001. NS: Not Significant

Table 4: Details of hematological parameters recorded in the subject (values are in mean±sd)

Parameters	*Control Subjects (50)*		*Study subjects (193)*			
			Male (67)		*Female (126)*	
	Male (25)	*Female (25)*	*Eutrhyroid (48)*	*Hypothyroid (19)*	*Eutrhyroid (79)*	*Hypothyroid (47)*
Total RBC count (millions/mn^3)	5.940±0.308	4.827±0.512**	5.0246±0.389	4.6342±0.280**	4.987±8.207	4.367±7.597*
Total WBC (Thousand/mn^3)	8.321±1.534	7.196±1.723**	8.350±1.459	8.552±1.777 (NS)	7.952±1.555	8.229±1.820 (NS)
Platelet Count (Lakhs/mn^3)	1.932±0.47	1.632±0.46*	1.886±0.178	1.90±0.22 (NS)	179.7±0. 168	180.2±0.101 (NS)
Hemoglobin (g%)	11.704±1.577	11.532±1.714 (NS)	13.114±1.870	12.288±1.092*	11.986316±1.826	11.089±1.371*

*P≤0.5, **P≤0.01, ***P≤0.001. NS: Not Significant

the most affected blood parameters by thyroid dysfunction were the RBC count, Hb concentration, and WBC count, respectively. Many studies indicated that these parameters were affected initially before development of other parameters. Some studies also showed that platelets are affected by thyroid dysfunction.[19,20] However, our study showed that platelets were the only parameter that did not show any correlation with thyroid dysfunction. This may be due to the fact that platelets are non-nucleated and have short life span with continuous rapid turnover.[21]

The most of the studies on status of hematological parameters revealed low hemoglobin and reduced RBC counts in hypothyroidism. Microcytic anemia is the most common type of anemia seen in thyroid dysfunction.[22,23] Red cell distribution width (RDW) that represents degree of RBC anisocytes is found to be increased in thyroid dysfunction similar to that of the patients with iron deficiency anemia, B12, and folate deficiency. However, RDW may be affected by other clinical conditions such as inflammatory processes, cardiac diseases, and rheumatoid arthritis.[24,25]

The study concluded that female is worst effected by hypothyroidism than their male counterparts at that middle age of their life. The SCH also adversely effects various cardiometabolic parameters as well as hematological parameters which might affect the well-being of subjects with hypothyroidism. However, one of the major limitations of the present study is less number of subjects. Larger number of subjects are required to increase the accuracy of the findings and some population based data are required to determine the normal geographical and age-related variation regarding the test parameters.

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