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Original Research Article

Can Cardiometabolic Index (CMI) Be Used As An Early Predictor Of Cardiometabolic Status In Patients With Subclinical And Overt Hypothyroidism?

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Abstract:

Objective: The present study was aimed to assess whether Cardiometabolic index (CMI) could be used as an early predictor of cardiometabolic status in patients with subclinical and overt hypothyroidism.

Materials and Methods: Age matched euthyroid, subclinical hypothyroid and overt hypothyroid female subjects were divided into three groups (n=30) in the study. Anthropometric parameters such as body weight, height, Waist circumference and Hip circumference were measured. After an overnight fasting, 5 ml of blood samples were collected and serum thyroid stimulating hormone (TSH), free triiodothyronine (FT3), free thyroxine (FT4), lipid fractions - total cholesterol (TC), triglyceride (TG) high density lipoprotein (HDL), very low-density lipoprotein (VLDL) and low density lipoprotein (LDL) were estimated. Waist-to-height ratio (WHtR) and CMI were calculated.

Results: Bodyweight, TSH, TC, TG, VLDL, LDL and CMI levels were increased in subclinical and overt hypothyroid patients. FT3, FT4 and HDL levels were reduced in patients with overt hypothyroidism. No significant changes were noticed in age, height, waist circumference, hip circumference and WHtR in both hypothyroid groups. CMI positively correlated with TC, TG, VLDL and LDL in both subclinical and overt hypothyroid patients. Negative correlation was found between CMI and HDL levels in patients with overt hypothyroidism.

Conclusion: CMI could be used as an early predictor of any adverse cardiometabolic event in hypothyroid patients as it integrates blood lipid levels and abdominal obesity.

Keywords: Cardiometabolic index, Hypothyroidism, Thyroid stimulating hormone, Thyroid hormones.

Introduction

Hypothyroidism is caused by the reduction in the synthesis of thyroid hormones by the thyroid gland and the diagnosis varies from mild subclinical form to overt hypothyroidism depending upon the severity [1, 2]. Overt hypothyroidism is characterized as elevated thyroid-stimulating hormone (TSH) levels and reduced free thyroid hormone concentrations [3].

Subclinical hypothyroidism (SCH) is defined as increased serum TSH level with normal plasma free thyroid hormone concentrations. It has been evidenced that about 4 to 15% of the general population are affected with SCH [4]. The frequency of SCH is significantly higher in women and increases with age. Decreased thyroid function is positively associated with several cardiovascular risk factors such as dyslipidemia, insulin resistance, hypertension, oxidative stress, inflammation, and endothelial dysfunction and coagulation disorders [5]. Evidence suggests both clinical and subclinical hypothyroidism increases the risk of cardiovascular events [6] and hence it is crucial to identify the development of early signs of cardiometabolic risk in these patients.

Cardiometabolic index (CMI) is a combination of triglyceride (TG)/ High density lipoprotein (HDL)

ratio and waist-to-height ratio (WHtR) [7]. This index integrates blood lipid levels and abdominal obesity and therefore CMI is a clinically accessible and conceptually appealing marker [8, 9]. Several lines of evidence suggest that CMI was positively associated with various diseases such as left ventricular geometry abnormality, peripheral arterial disease, hypertension and stroke [7, 10-12]. There are no studies stating the usefulness of CMI in hypothyroid patients till date. Hence, we designed a comparative study to assess Cardiometabolic index in euthyroid, subclinical and overt hypothyroid female patients attending tertiary care center.

Materials and Methods

The present study is a cross sectional study and was carried out in the Department of Biochemistry, Shri Sathya Sai Medical College and Research Institute (SSSMCRI), Ammapettai after obtaining approval from the Institutional Research Committee and Institutional Human Ethics Committee (IEC No:2020/601). The study was divided into three groups; Group 1: euthyroid healthy controls (n=30), Group 2: subclinical hypothyroidism (n=30), Group 3: overt hypothyroidism (n=30). The study included only females in the age group 20-60 years and all the study participants were recruited from the Department of General medicine, SSSMCRI. Patients diagnosed with Subclinical hypothyroidism (TSH level: 5-10 µIU/ml) [13] and overt hypothyroidism [(TSH level: > 10 µIU/ml) [14] free thyroxine (FT4) level: <0.82 ng/dl] were included as cases and healthy euthyroid persons without any illnesses were included as controls. Patients with history of medical illnesses such as diabetes, hypertension, asthma, renal &liver disease patients who had recent surgery were excluded from the study.

Detailed history was collected and the anthropometric parameters were measured from the study subjects. After an overnight fasting, 5 ml of blood samples were collected without anticoagulant from the subjects of all groups. The samples were centrifuged at 3500rpm for five minutes and serum was separated and stored at -20˚C till analyses. Age and anthropometric parameters such as body weight, height, Waist circumference and Hip circumference were measured. Serum thyroid stimulating hormone (TSH), free triiodothyronine (FT3) and free thyroxine (FT4) levels were estimated using VIDAS Kits, VIDAS (Vitek® Immuno Diagnostic Assay System) instrument using Enzyme linked Fluorescent Assay (ELFA) technique. The lipid fractions - total cholesterol (TC), triglyceride (TG) and High density lipoprotein (HDL) were measured using kits from ichem Prime, JEEV Diagnostics Pvt Ltd adapted to automated analyzers. Very low density lipoprotein (VLDL) was calculated by dividing triglycerides by 5 [VLDL=TG/5] and low density lipoprotein (LDL) was calculated by friedwald's formula [LDL = TC-(HDL+VLDL)]. Waist-to-height ratio (WHtR) was calculated by Waist circumference (cm) /Height (cm) and Cardiometabolic index (CMI) was calculated by the formula [CMI= TG/HDL×WHtR] [7].

Statistical Analysis: All data were expressed as mean ± S.D. The differences between groups were analyzed with analysis of variance (ANOVA) test followed by an appropriate post-hoc Bonferroni and Tukey's comparison between multiple groups. Spearman correlation analysis was performed to determine the association between various parameters in each group. Statistical analyses were performed using Statistical Package for the Social Sciences (SPSS) software and p-value <0.05 was considered as statistically significant.

Results

Table 1 shows anthropometric measurement, thyroid profile and lipid profile between control, Subclinical hypothyroid and overt hypothyroid subjects

There was significant increase in body weight in groups 2 and 3 when compared with group1. No significant changes were noticed in age, height, waist and hip circumferences in both groups 2 and 3 when compared with group 1. Increased TSH level, decreased FT3 and FT4 levels were noticed in group 3 when compared with group1. Group 2 showed increased TSH level on comparison with group 1. Significantly increased TC, TG, VLDL and LDL levels were observed in groups 2 and 3 when compared with group1. Marked decrease in the HDL levels was seen in group 3 on comparison with group1. No significant changes were seen in the WHtR in both groups 2 and 3 when compared with group 1. There was significant increase in the CMI levels in groups 2 and 3 when compared with group1.

Table 2 shows the correlation analysis of CMI between lipid parameters in Subclinical and Overt hypothyroid patients

CMI positively correlated with TC, TG, VLDL and LDL in groups 2 and 3. There was negative correlation between CMI and HDL levels in group 3.

Table 1: Shows the data on anthropometric measurements, thyroid profile and lipid profile between control, Subclinical hypothyroid and Overt hypothyroid subjects

Sl. No	Parameters	Group 1 Control (N=30)	Group 2 Subclinical hypothyroid (N=30)	Group 3 Overt hypothyroid (N=30)
1	Age (years)	32.23±7.20	31.77±8.03	31.57±7.77
2	Body weight (kg)	58.87±9.45	62.90±6.60[a]	68.37±6.32[a]
3	Height (cm)	157.97±5.41	157.77±4.78	158.40±5.56
4	Waist Circumference (cm)	82.03±9.96	82.87±8.46	84.70±8.30
5	Hip circumference (cm)	98.80±9.95	100.57±9.66	102.60±8.22
6	FT3 (pg/ml)	3.23±0.59	2.89±0.46	0.58±0.14[a]
7	FT4 (ng/dl)	1.25±0.45	1.09±0.36	0.65±0.17[a]
8	TSH (µIU/ml)	2.25±0.77	9.06±2.70[a]	19.58±4.27[a]
9	TC (mg/dl)	164.60±26.38	213.80±38.41[a]	245.53±39.76[a]
10	TG (mg/dl)	119.63±17.09	171.07±27.39[a]	185.57±27.87[a]
11	HDL (mg/dl)	45.60±4.15	44.73±4.53	39.57±4.22[a]
12	VLDL (mg/dl)	24.00±3.42	34.21±5.48[a]	37.11±5.57[a]
13	LDL (mg/dl)	95.00±24.85	134.85±34.39[a]	168.85±38.16[a]
14	WHtR	0.52±0.07	0.53±0.06	0.54±0.06
15	CMI	1.38±0.29	2.03±0.42[a]	2.58±0.74[a]

Data were expressed as mean±S.D. (N=30) p-value <0.05 was considered as statistically significant. [a]-significant when compared with group 1(control), Kg = Kilogram, cm = centimeter, pg/ml = picogram/milliliter, ng/dl = nanogram/deciliter, µIU/ml = micro international units/milliliter, mg/dl = milligram/deciliter, S.D. = Standard deviation

Table 2: Shows the correlation analysis of CMI between control, Subclinical hypothyroid and Overt hypothyroid subjects

Parameters	Group 2 Subclinical hypothyroid (N=30)		Group 3 Overt hypothyroid (N=30)	
	R value	p-value	R value	p-value
TC	0.679**	0.000	0.772**	0.000
TG	0.840**	0.000	0.890**	0.000
HDL			-0.843**	0.000
VLDL	0.840**	0.000	0.890**	0.000
LDL	0.645**	0.000	0.768**	0.000

*Correlation is significant at the 0.05 level (2-tailed), **Correlation is significant at the 0.01 level (2-tailed).

Discussion

In the present study, elevated TSH levels and reduced FT3, FT4 levels were noticed in overt hypothyroid patients. There was increase in the TSH levels and FT3, FT4 levels were within the normal reference range in patients with subclinical hypothyroidism. The inability of the thyroid gland to synthesize adequate levels of thyroid hormones for the metabolic requirements of the body leads to hypothyroidism. The cause for hypothyroidism might be due to primary thyroid gland failure or inadequate stimulation of the thyroid gland by the pituitary or hypothalamus [15]. Several lines of evidence document that increased TSH levels in subclinical hypothyroidism reveals mild and initial form of thyroid failure accompanied with noticeable signs of tissue hypothyroidism [16, 17]. Chronic hypothyroidism is positively associated with the development of dyslipidemia, infertility, hypertension, neuromuscular dysfunction and cognitive impairment [15].

We found marked increase in the bodyweight and lipid fractions - TC, TG, VLDL and LDL levels of patients with both subclinical and overt hypothyroidism. There was also significant reduction in the HDL levels of overt hypothyroid patients. Thyroid hormones influence the lipid homeostasis by affecting the synthesis, transport and degradation of lipids. Thyroid disease, either overt or subclinical form is associated with the development of dyslipidemia leading to alterations in cholesterol, triglycerides, phospholipids and lipoproteins [18]. Stimulation of hepatic 3-hydroxy-3-methyl-glutaryl coenzyme A reductase by the thyroid hormones enhances synthesis of cholesterol [19]. The activity of lipoprotein lipase (LPL) is chiefly up regulated by the thyroid hormones which cause the breakdown of triglyceride rich lipoproteins such as VLDL and chylomicrons. Reduction in the thyroid hormones impairs these effects and hence increases serum triglycerides in hypothyroidism [20].

Thyroid hormones influence the activities of cholesteryl ester transfer protein and hepatic lipase which are found to be reduced in hypothyroidism affecting the total and subtraction levels of HDL

[21]. Thus, it is evident that thyroid hormones play vital role in the lipid homeostasis and reduced levels of thyroid hormones are associated with dyslipidemia, a well-known atherogenic factor. Dyslipidemia is frequently associated with oxidative stress and insulin resistance [22]. Thyroid disease per se leads to inflammation, oxidative stress, hypertension, insulin resistance and coagulation deficits independently of dyslipidemia. Therefore, thyroid hormone deficiency enhances cardiovascular risk with dyslipidemia playing a central role. Several lines of evidence document that the hemodynamic alterations in thyroid disease could probably increase the risk of cardiovascular disease. The chief hemodynamic alterations in hypothyroidism include decreased blood volume, reduced cardiac output, reduced heart rate, increased peripheral vascular resistance and elevated diastolic blood pressure [2, 23].

Both overt and subclinical hypothyroid patients have increased chances of cardiovascular risk and early prediction of the same can aid in the better management of these patients. Cardiometabolic index is a combination of TG/HDL ratio and WHtR. It has been documented that CMI correlated with atherosclerosis in patients with peripheral arterial disease [10]. The association of CMI has also been reported in diseases like left ventricular geometry abnormality, hypertension and stroke [7, 11, 12].

In the present study, there was significant increase in the CMI levels in both subclinical and overt hypothyroid patients. CMI positively correlated with TC, TG, VLDL and LDL in both subclinical and overt hypothyroid groups and negatively correlated with HDL levels in overt hypothyroid patients in this study. CMI integrates both blood lipids and abdominal obesity, and hence it can be considered as a reliable marker in the early prediction of cardiovascular risk. As the estimation of CMI is cost effective, early assessment of the same will aid in the better management of both subclinical and overt hypothyroid patients.

Conclusion

Both subclinical and overt hypothyroidism is positively associated with various cardiometabolic risk factors and the likelihood of developing several metabolic and cardiovascular diseases are greater. CMI serves as a clinically accessible and conceptually appealing marker to predict any adverse cardiometabolic event at an early stage in both subclinical and overt hypothyroid patients.

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