A STUDY OF LIPID PROFILE AND ASSESSMENT OF CARDIOVASCULAR RISK IN SUBCLINICAL HYPOTHYROIDISM

Kishore Chander Prem Kumar¹, Prakash Subramanian²

¹Postgraduate Student, Department of General Medicine, Government Stanley Medical College and Hospital, Chennai, Tamilnadu, India.

²Assistant Professor, Department of General Medicine, Government Stanley Medical College and Hospital, Chennai, Tamilnadu, India.

ABSTRACT

BACKGROUND

Studies on association between subclinical hypothyroidism and lipid profile have produced conflicting results. The assessment of cardiovascular risk in subclinical hypothyroid patients is rare in Indian scenario. We wanted to study the lipid profile in subclinical hypothyroid patients and assess the cardiovascular risk in subclinical hypothyroid patients by using atherogenic indexes.

METHODS

In this study, newly diagnosed untreated subclinical hypothyroid patients were studied for dyslipidaemia and cardiovascular risk is assessed using lipid ratios- Atherogenic Index of Plasma and Castelli Risk Index. To find the significant difference between the bivariate samples in independent groups, unpaired sample t-test was used and to find the significance in categorical data, Chi-Square test and Fisher's Exact test were used. In all the above statistical tools, the probability value 0.05 was considered as significant.

RESULTS

Total cholesterol, triglyceride and VLDL-C levels shows statistically significant association among subclinical hypothyroid patients compared to euthyroid subjects. Castelli Risk Index-II showed statistically significant association in subclinical hypothyroid patients compared to euthyroid controls.

CONCLUSIONS

The positive association of subclinical hypothyroid patients and dyslipidaemia warrants that all patients with subclinical hypothyroidism should be evaluated for deranged lipid profile parameters. Castelli Risk Index-II calculated as LDL-C/HDL-C could be used as a better predictor of cardiovascular risk compared to the other risk assessment ratios Atherogenic Index of Plasma and Castelli Risk Index I.

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BACKGROUND

Subclinical hypothyroidism is defined as a biochemical evidence of thyroid hormone deficiency with few or no apparent clinical features of hypothyroidism. Subclinical hypothyroidism is characterized by normal serum free thyroxine (fT4) and normal serum free triiodothyronine (fT3) and elevated levels of serum thyroid stimulating hormone (TSH).^[1]

Subclinical hypothyroidism is a common disorder with a prevalence of 2.8-4.4% in males and 7.5-8.5% in females world-wide.^[2]

Overt hypothyroidism has been associated with abnormal lipid profile parameters such as elevated levels of total cholesterol (TC), low density lipoproteins (LDL-C), triglycerides (TG) and reduced levels of high-density lipoproteins (HDL-C) as established by various studies. Such deranged lipid profile parameters are well associated with cardiovascular disease morbidity and mortality.^[3]

Studies conducted to establish the relationship between subclinical hypothyroidism and abnormalities in lipid profile have produced conflicting results.^[4] Some studies have established a significant relationship between subclinical hypothyroidism and metabolic syndrome thereby increased risk of cardiovascular diseases.

Apart from individual lipid parameters that has been measured in conventional lipid profile, serum lipid profile ratios such as LDL-C/HDL-C, TC/HDL-C, TG/HDL-C have been widely used and is shown to be a better predictor of cardiovascular risk than individual lipid parameters.^[5] Small dense lipoproteins (sdLDL-C), a subtype of LDL-C is well known for its atherogenic potential. The Atherogenic Index of Plasma (AIP) is calculated as $\log [TG/HDL-C]$ and is a surrogate marker of sdLDL-C there having a superior prediction advantage for cardiovascular risk assessment than the previously used lipid parameters.^[5,6]

Thyroid hormone has inotropic and chronotropic effects on the heart. Reduced blood volume and increased peripheral vascular resistance causes prolonged circulation and reduced blood flow to tissues.^[7]

Both Subclinical and overt hypothyroid patients aged 65 & above showed correlation with cardiovascular outcome in a prospective study.^[8]

Some studies suggest a benefit in cardiovascular outcome following treatment primarily in middle age.^[9,10]

The effects of overt hypothyroidism on lipid parameters has been extensively studied. However, the studies relating the association between the subclinical hypothyroidism and

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Corresponding Author:

Dr. Prakash Subramanian,

14/20, P. C. Hostel Road,

Chetpet, Chennai-600031,

Tamilnadu, India.

E-mail: pvastanlee@gmail.com

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the lipid parameters are few. In the Indian clinical scenario such studies are lacking. Subclinical hypothyroidism having been diagnosed with greater frequency in recent times particularly among the women population it has become necessary to study extensively the relation between SH and cardiovascular risk related to deranged lipid profile.

Aims & Objectives

To study the lipid profile in subclinical hypothyroid patients and to assess the cardiovascular risk in subclinical hypothyroid patients by using atherogenic indexes.

METHODS

Type of Study

Comparative Cross-Sectional Study.

Cases

Patients with few or no clinical manifestation of hypothyroidism, but elevated Serum-TSH Levels.

Controls

Patients with normal Serum-TSH Levels.

Patients of both sexes attending the Outpatient Department of Endocrinology, Government Stanley Medical College Hospital, Chennai, having one or more clinical manifestations of hypothyroidism, e.g., fatigue, weakness, loss of strength, loss of stamina, weight gain, coarse dry hair, dry, rough and pale skin, hair loss, cold intolerance, muscle cramps, frequent muscle aches, constipation, depression, irritability, memory loss, and in women abnormal menstrual cycle were recruited for the study, for a duration of Six Months.

RESULTS

Parameters	Values	Cases	Controls	'p' Value
Total Cholesterol	<240 mg% >240 mg%	44 (88%) 6 (12%)	50 (100%) 0	0.040
Triglycerides	<200 mg% >200 mg%	41 (82%) 9 (18%)	48 (96%) 2 (4%)	0.075
HDL-Cholesterol	<40 mg% >40 mg%	12 (24%) 38 (76%)	8 (16%) 42 (84%)	0.384
LDL-Cholesterol	<130 mg% >130 mg%	39 (78%) 11 (22%)	48 (96%) 2 (4%)	0.078
VLDL-Cholesterol	<30 mg% >30 mg%	32 (64%) 18 (36%)	50 (100%) 0	0.000
Atherogenic Index of Plasma (Log [TG/HDL-C])	0.11-0.21 >0.21	5 (10%) 45 (90%)	4 (8%) 46 (92%)	1.000
Castelli Risk Index-I (TC/HDL-C)	<5 >5	41 (82%) 9 (18%)	47 (94%) 3 (6%)	0.163
Castelli Risk Index-II (LDL-C/HDL-C)	< 3 >3	38 (76%) 12 (24%)	49 (98%) 1 (2%)	0.002

Table 1. Analysis of Study Parameters in Cases & Controls

There is a statistically significant association among cases with elevated total cholesterol, triglycerides, VLDL-C and Castelli Risk Index-II than Controls.

There is no statistically significant association with HDL-C, LDL-C, Atherogenic Index of Plasma and Castelli Risk Index-I among cases and controls.

These patients were screened for fT3, fT4, and TSH. 50 patients with raised TSH (TSH >5mIU/L) with normal fT3, fT4 were included in the study and evaluated further for lipid profile pertaining to TC, TGs, High density lipoprotein cholesterol (HDL), and Low-density lipoprotein-cholesterol (LDL-C). 50 patients with normal TSH were kept as control. Based on the lipid profile values the following atherogenic indices were calculated-

1. Atherogenic Index of Plasma-Log[TG/HDL}
2. Castelli Risk Index -I - TC/HDL-C
3. Castelli Risk Index-II - LDL-C/HDL-C

The sample size was taken based on the convenience of the study.

Inclusion Criteria

Newly diagnosed and untreated cases of subclinical hypothyroidism

Exclusion Criteria

Known hypothyroidism cases, thyroidectomy cases, patient with history of external radiation, previous radioactive iodine therapy.

Patient on statins, oral contraceptive pills and drugs that affect thyroid status [Alpha blockers, glucocorticoids, dopamine analogues-reduces TSH] and lipid profile.

Patients with Diabetes mellitus, renal failure, Hepatic failure. Pregnant women.

Statistical Methods

The data was collected and analysed using standard statistical chi-square test, $P < 0.05$ statistically significant. Data was entered in Microsoft excel and analysis was done using SPSS version 22.

DISCUSSION

In our study the mean age of cases was 34.88 +/- 14.081 and the mean age for control subjects were 32.50 +/- 9.368. Out of 50 subjects in the case group, 24% were in the age group of

13 to 20 years, 42% were in the age group of 21 to 40 years, 30% of subjects belongs to the age group between 41 to 60 years and 4% were > 60 years of age. In the case group 98% (49 patients) of subjects were female and 2% were male.

Subclinical hypothyroid patients with TSH values more than 10 mIU/L are invariably treated with thyroxine replacement. Our study taking into consideration the subclinical hypothyroid subjects with TSH values less than 10 mIU/L and analysing the lipid profile and cardiovascular risk index ratios, we intended to formulate a guide for thyroxine replacement in such patients with regard to benefit from cardiovascular morbidity and mortality.

In the lipid profile parameters, 12% of case subjects had total cholesterol levels of ≥ 240 mg/dl which is in the high-risk range group for developing cardiovascular morbidity and mortality. In the control group no subjects had total cholesterol values in the high-risk group. There is a statistically significant association among cases with elevated total cholesterol compared to controls.

58% of subjects in the case group had triglyceride levels of < 150 mg/dl which falls in the desirable range. 24% of cases had triglyceride values between 150-199 mg/dl and 18% of patients had values between 200-499 mg/dl which falls into normal risk and high risk for cardiovascular morbidity/ mortality respectively. Among the controls 11% of subjects had triglyceride levels in the high-risk range. There is a statistically significant association among the cases with triglyceride levels compared to the controls.

In the case group 24% of subjects had HDL-C values < 40 mg/dl which falls in the high risk for developing cardiovascular disease. In the control group 16% of subjects had HDL-C levels in the high-risk group. There is no statistically significant association with HDL-C among cases and controls.

In the case group 4% had LDL-C levels in the high-risk range and only 2% had levels in the very high-risk range. In the control group 2% and 1% of subjects had LDL-C levels in the high risk and very high-risk range respectively. There is no statistically significant association among cases and controls with LDL-C levels.

36% of cases had VLDL-C levels > 30 mg/dl which is in the high-risk range for developing cardiovascular events. 18% of subjects among the control group falls in the high-risk range. There is a statistically significant association among cases with VLDL-C than controls.

The Atherogenic Index of Plasma is calculated as Log [TG/HDL-C] . 90% of cases and 92% of controls had values > 0.21 which is in the high-risk range. There is no statistically significant association among cases and controls with Log [TG/HDL-C] values.

Castelli Risk Index-I is calculated as ratio of TC/ HDL-C. 18% of subjects in the control group had ratio of > 5 which is in the high-risk range, while 12% subjects of the control group had ratios in the high-risk group. 46% and 36% of the

case group subjects had ratios in the borderline risk and low risk respectively for developing cardiovascular event. There is no statistically significant association among cases and controls with Castelli Risk Index-I [TC/HDL-C].

Castelli Risk Index- II is calculated as ratio of LDL-C/ HDL-C.

CONCLUSIONS

Subclinical hypothyroid patients have significantly deranged lipid parameters including statistically significant elevated total cholesterol, triglycerides and VLDL-C compared to euthyroid individuals. Among the lipid ratios the Castelli Risk Index II calculated as LDL-C/HDL-C shows statistically significant association and could be used as a better predictor of cardiovascular risk compared to the other risk ratios Atherogenic Index of Plasma and Castelli Risk Index-I.

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