

Original Article

Study of Fasting Lipid Profile in Patients with Subclinical Hypothyroidism in a Tertiary Care Hospital in Bangladesh

MA Hossain¹, Atiquzzaman², M Sharifuzzaman³, F Amin⁴, L Kabir⁵, D Sultana⁶, MSI Bhuiyan⁷

Abstract:

Subclinical hypothyroidism (SCH) is a metabolic disorder with prevalence about 4-10% in general population. This study was conducted to observe the pattern of fasting lipid profile in SCH and to correlate the components of it with thyroid stimulating hormone and free thyroxine level. This cross sectional observational study included 31 newly diagnosed cases of SCH and 17 age and BMI matched healthy control subjects with normal thyroid function test. Fasting lipid profile was recorded and compared. TSH was significantly higher in SCH compared to controls (9.09±2.79 vs 2.31±0.92 μ IU/ml; p=0.001). FT4 was comparable between the groups (1.17±0.18 vs 1.28±0.20 ng/dl; p=0.938). Significantly higher level of Total cholesterol and LDL-C were observed in SCH compared to controls (TC 194.77±29.70 vs 156.59±20.45 mg/dl; p=0.042 and LDL-C 124.81±27.85 mg/dl vs 88.59±18.41mg/dl; p=0.045 respectively). Triglycerides and HDL-C were comparable between the groups (TG 134.90±80.97 vs 118.12±49.14 mg/dl; p=0.171 and HDL-C 42.87±4.83 vs 44.47±5.66; p=0.633 respectively). TSH showed significant positive correlation with TC and LDL-C (r=0.591, p<0.001 and r=0.644, p<0.001 respectively), but not with TG or HDL-C (r=0.011, p=0.943 and r=0.115, p=0.435 respectively). FT4 only showed significant negative correlation with LDL-C (r=0.302; P=0.037) but not with TC, TG or HDL-C (TC: r=0.245, P=0.093; TG: r=0.121, p=0.411 and HDL-C: r=0.108, p=0.466 respectively). SCH is associated with raised TC and LDL-C. So patients with SCH are more vulnerable to develop future adverse cardio-metabolic complications.

Key words: Subclinical hypothyroidism, Fasting lipid profile, Total cholesterol, Triglycerides, HDL-C, LDL-C, Thyroid stimulating hormone, Thyroxine.

Introduction:

Subclinical hypothyroidism (SCH) is defined as a condition where biochemically thyroid stimulating hormone (TSH) is elevated above the reference value but thyroid hormones including thyroxine (T4) and triiodothyronine (T3) are normal¹⁻³. This is a common

endocrine condition with prevalence about 4-10% in general population and the prevalence is higher among female and increases with age^{4,5}. This condition may progress to overt hypothyroidism specially when thyroid auto antibody is raised or TSH is more elevated⁶.

1. Dr. Mohammad Afjal Hossain, MBBS, MD (Endocrinology and Metabolism), Assistant Professor, Department of Endocrinology, US-Bangla Medical College, Narayanganj.

2. Dr. Atiquzzaman, MBBS, FCPS (Medicine), Assistant Professor, Department of Medicine, US-Bangla Medical College, Narayanganj.

3. Dr. Mirza Sharifuzzaman, MBBS, MD (Endocrinology and Metabolism), Assistant Professor, Department of Endocrinology, Dhaka Medical College, Dhaka.

4. Dr. Farzana Amin, MBBS, Medical Officer, South East Model Hospital, Dhaka, Bangladesh.

5. Dr. Lutful Kabir, MBBS, MD (Endocrinology and Metabolism), Assistant Professor, Department of Endocrinology, Rangpur Medical College, Rangpur.

6. Dr. Dahlia Sultana, MBBS, MD (Endocrinology and Metabolism), Assistant Professor, Department of Endocrinology, Sir Salimullah Medical College, Dhaka.

7. Dr. Mohammed Shafiqul Islam Bhuiyan, MBBS, MD (Gastroenterology), Associate Professor, Department of Gastroenterology, US-Bangla Medical College, Narayanganj.

Address of correspondence :

Dr. Mohammad Afjal Hossain, MBBS, MD (Endocrinology and Metabolism), Assistant Professor, Department of Endocrinology, US-Bangla Medical College, Narayanganj, Bangladesh.
Phone: +88-01673826979, E-mail: afjal62.k61@gmail.com

It is well established that overt hypothyroidism is associated with atherogenic lipid profile and thus increases the risk of cardiovascular diseases^{7,8}. Actually hypothyroidism is a common cause of secondary dyslipidemia^{9,10}. Various mechanisms like reduction of cell surface LDL receptor, reduced secretion of cholesterol in bile, decreased activity of cholesteryl ester transferase and decreased activity of lipoprotein lipase may play role in development of this dyslipidemia¹¹⁻¹³.

Like overt hypothyroidism, SCH may be associated with deranged lipid profile and may lead to atherogenic cardiovascular disease and peripheral vascular disease¹⁴⁻¹⁶. However the controversy persists regarding the lipid profile alterations in SCH. Some studies found increased levels of serum total cholesterol, triglycerides and LDL-C in subjects with SCH compared with euthyroid controls^{17,18} where other studies found no significant differences^{15,16}. Very few study has been conducted regarding this issue, specially

in Bangladesh. So this study was conducted to observe the pattern of fasting lipid profile in patients with subclinical hypothyroidism and to correlate different components of it with thyroid stimulating hormone (TSH) & free thyroxine (FT₄) level.

Materials and Methods:

This cross sectional observational study was conducted in Medicine and Endocrinology outpatient department of US- Bangla Medical College and Hospital, Narayanganj from September 2019 to February 2020. Subclinical hypothyroidism was diagnosed when TSH $\geq 5.1 \mu\text{IU/ml}$ and Free T₄ remained in reference range (0.83-1.8 ng/dl). Patients suffering from overt hypothyroidism (primary/secondary), undergoing treatment with thyroxine/antithyroid drugs, lipid lowering agents or oral contraceptives, patients with diabetes mellitus, cardiac, liver or renal diseases or any chronic disease and pregnant women were excluded from the study. Thirty one subjects with newly diagnosed SCH aged 20 to 50 years were included. Seventeen age and BMI matched healthy subjects with normal thyroid function test were included as euthyroid control group. Informed written consent was taken from each participant. Detailed clinical history was taken and demographic & anthropometric data was recorded in a data collection sheet. Blood sample was collected in the morning at least after 12-hours overnight fasting. TSH & FT₄ were measured by ELFA (Enzyme Linked Fluorescent Assay) in Biomerieux MINI VIDAS Automated Immunoassay Analyzer, FRANCE. Total cholesterol (TC), HDL cholesterol (HDL-C) and triglycerides (TG) were estimated by Enzymatic method in SELECTRA PRO M, FRANCE. LDL cholesterol (LDL-C) was calculated from TC, HDL-C and TG, using Friedwald's Formula¹⁹ [LDL-C= TC - (HDL-C + TG/5)].

After editing and coding, the coded data was directly entered into the computer by using Statistical Package for the Social Sciences (SPSS) version 22.0 software. Data were expressed as mean \pm standard deviation (SD) and were compared between groups using Student's t test. Correlation of TSH & FT₄ with the different components of fasting lipid profile was done by Pearson's correlation analysis. A p value of less than or equal to 0.05 was considered as statistically significant.

Results:

Total sample size was 48 which included 31 cases of subclinical hypothyroidism (SCH) and 17 age and BMI matched controls. Total 37 female (23 cases of SCH & 14 controls) and 11 male (8 cases of SCH & 3 controls) were included.

Table I shows comparison of different demographic and biochemical parameters between the cases of SCH and control subjects which indicates significantly higher

TSH, total cholesterol and LDL cholesterol among SCH subjects where age, BMI, Free thyroxine (FT₄), Triglycerides and HDL cholesterol are comparable between the groups.

Table I: Comparison of age, BMI, Thyroid hormones and fasting lipid profile between SCH subjects and controls

Characteristics	SCH (n=31)	Control (n=17)	p value
Age (years)	35.84 \pm 7.05	33.71 \pm 7.45	0.896
BMI (kg/m ²)	23.83 \pm 2.12	23.47 \pm 3.23	0.091
TSH ($\mu\text{IU/ml}$)	9.09 \pm 2.79	2.31 \pm 0.91	0.001
FT ₄ (ng/dl)	1.17 \pm 0.18	1.28 \pm 0.20	0.938
Total Cholesterol (mg/dl)	194.77 \pm 29.70	156.59 \pm 20.45	0.042
Triglycerides (mg/dl)	134.90 \pm 80.97	118.12 \pm 49.14	0.171
HDL-C (mg/dl)	42.87 \pm 4.83	44.47 \pm 5.66	0.633
LDL-C (mg/dl)	124.81 \pm 27.85	88.59 \pm 18.41	0.045

*p \leq 0.05 indicates statistically significant, p \leq 0.001 indicates highly significant

Table II shows correlation of different components of fasting lipid profile with TSH and FT₄ which indicates significant positive correlation between TSH and total cholesterol & LDL cholesterol level where FT₄ negatively correlated with LDL cholesterol level.

Table II: Correlation of TSH and FT₄ with different components of fasting lipid profile

	Total cholesterol	Triglycerides	HDL-C	LDL-C
TSH r	0.591	0.011	-0.115	0.644
p	<0.001	0.943	0.435	<0.001
FT ₄ r	-0.245	0.121	-0.108	-0.302
p	0.093	0.411	0.466	0.037

*r= Pearson correlation coefficient

*p \leq 0.05 indicates statistically significant, p \leq 0.001 indicates highly significant

Discussions:

Subclinical hypothyroidism (SCH) is a common metabolic disorder. As thyroid hormones play an important role in synthesis and degradation of different components of blood lipids, dyslipidemia may be present in SCH. This study was conducted in newly diagnosed subclinical hypothyroid patients to observe the pattern of fasting lipid profile among them.

In this study, significantly higher serum total cholesterol (TC) and LDL cholesterol (LDL-C) were found in SCH patients compared to control subjects. This finding is supported by some previous studies^{17,18,20-22}. Although thyroid hormones deficiency leads to slightly reduced cholesterol synthesis due to decrease activity of HMG Co A reductase, TC & LDL-C level may be increased^{23,24}. Thyroid hormones deficiency leads to reduced LDL receptors on the cell surface for which degradation of LDL-C is impaired¹¹. Moreover cholesterol secretion in bile is also impaired which leads to decrease clearance of cholesterol¹². All these conditions may lead to increase serum level of TC and LDL-C in SCH. However very few study found no significant difference regarding TC & LDL-C level among SCH & control subjects¹⁶.

Like TC & LDL-C, relationship of HDL-C with SCH is highly controversial²⁵. Some studies found significantly lower HDL-C in SCH compared to control¹⁵⁻¹⁸ whenever few studies found higher HDL-C in SCH¹⁴. In contrast to those findings, present study found that HDL-C was comparable among the groups. However this finding is also supported by few studies^{5,15,17}.

Like cholesterol, TG metabolism is also impaired in hypothyroidism. Thyroid hormones stimulate lipoprotein lipase which degrades TG and thyroid hormones deficiency may be associated with raised TG level in blood¹¹. Some previous studies found increased TG in SCH compared to control subjects^{14,16,18,26,27}. In contrast to this finding, present study did not found any significant difference in the level of TG between the groups. Actually cholesterol metabolism is more affected than TG metabolism in thyroid hormones deficit. Moreover TG & HDL-C are more associated with dietary habit, physical activity, body weight and metabolic syndrome. As thyroid hormones deficiencies lead to weight gain, patients with hypothyroidism may present with obesity and metabolic syndrome which may lead to hypertriglyceridemia and low HDL-C. Our control group was age & BMI matched, where most of the previous studies included SCH patients with higher BMI compared to control. As a result, raised TG and low HDL-C were found in those studies which differ from our result. However few studies supported our findings^{5,17,28}.

In this study, TSH showed significant positive correlation with TC & LDL-C, but not with TG & HDL-C. A previous study in Bangladesh among overall hypothyroid patients also found similar result⁹. Some other studies found positive correlation between TSH and TC, TG & LDL-C and negative correlation between TSH & HDL-C in subclinical hypothyroid patients which support our result in term of correlation of TSH with TC & LDL-C but not in term of TG &

HDL-C^{18,22,28}. In this study, FT₄ was negatively correlated with LDL-C but not with any other component of fasting lipid profile. A previous study observed significant negative correlation between FT₄ and TC, TG & LDL-C among overall hypothyroid patients²⁹ whether another study found no correlation between FT₄ and any component of fasting lipid profile¹⁸. Difference in sample size and inclusion criteria, difference in age, ethnicity, dietary habits & BMI may be the cause of this variation.

Conclusions:

Subclinical hypothyroidism is associated with atherogenic lipid profile. Therefore patients with this condition are more prone to develop atherosclerosis and adverse cardiovascular outcome. So every subclinical hypothyroid patient should be advised for exploring metabolic parameters including fasting lipid profile. The sample size of the study was small. We did not assay free triiodothyronine (FT₃) and thyroid autoantibodies including anti thyroid peroxidase (anti TPO) & anti thyroglobulin antibody which may have effect on serum lipid. Lipoprotein (a) was not measured which may affect cardiovascular outcome. LDL-C was calculated by Friedwald's formula, not measured directly; so full actual scenario of LDL-C may not be revealed. Effect of thyroid hormone replacement was not observed in this study. A large sample study should be conducted with above mentioned parameter for definite conclusions.

Acknowledgement:

We are grateful to Prof. Dr. Swapna Bhattacharjee and Prof. Dr. Shekhar Bhattacharjee, Professors of Medicine, US-Bangla Medical College for their kind supervision. We also express our gratitude to all lab technicians of US-Bangla Medical College Hospital for their technical support. We like to thank all the participants for their cooperation.

Conflicts of interest:

There are no conflicts of interest.

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