



## Lipid Profile in Type 2 Diabetes Mellitus with and Without Subclinical Hypothyroidism

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### Abstract

*In clinical practice, Diabetes Mellitus is the most common endocrine disorder. The prevalence of thyroid disorders is higher in diabetic patients as compared to general population and the most common disorder being subclinical hypothyroidism. Subclinical hypothyroidism has been claimed to be a risk factor for coronary artery disease, peripheral vascular disease and various biochemical abnormalities including dyslipidemia.*

*The present study was planned to measure serum lipids such as total cholesterol, triglycerides, low density lipoprotein- cholesterol and high density lipoprotein- cholesterol in type 2 diabetics with and without subclinical hypothyroidism. Study includes 200 patients of type 2 diabetics with subclinical hypothyroidism and 200 type 2 diabetics without subclinical hypothyroidism. The data were evaluated statistically. We found significantly increase in total cholesterol, triglycerides and low density lipoprotein- cholesterol ( $p < 0.001$ ) and significantly decreased high density lipoprotein- cholesterol ( $p < 0.001$ ) in type 2 diabetes mellitus with subclinical hypothyroidism before therapy as compared to type 2 diabetes mellitus without subclinical hypothyroidism.*

*After L-thyroxine therapy we observed highly significant reduction in total cholesterol, triglycerides and low density lipoprotein- cholesterol ( $p < 0.001$ ) and significantly increase in high density lipoprotein- cholesterol ( $p < 0.001$ ) in type 2 diabetes mellitus with subclinical hypothyroidism as compared to before therapy.*

*Subclinical hypothyroidism is associated with atherogenic serum lipid profile pattern. Such pattern may increase the risk of atherosclerosis and CVD. L-thyroxine is of utmost importance to reduce or prevent the risk of development of atherosclerosis and CVD in type 2 DM with SCH patients.*

**Key Words:** Diabetes Mellitus, Subclinical hypothyroidism, Cardiovascular disease, Lipid profile.

## Introduction

In clinical practice, Diabetes Mellitus (DM) is the most common endocrine disorder. India has become the “diabetes capital” of the world with over three crore affected patients (1). The prevalence of thyroid disorders is higher in diabetic patients as compared to general population. In type 2 diabetes mellitus the prevalence of thyroid disorder has been found to be 31%, the most common disorder being subclinical hypothyroidism (SCH) (2).

SCH is the condition characterized by elevated thyroid stimulating hormone (TSH) levels with normal serum free thyroxine (T4) and triiodothyronine (T3) levels (3). Recently, subclinical hypothyroidism has been claimed to be a risk factor for coronary artery disease, peripheral vascular disease and various biochemical abnormalities including dyslipidemia (4).

Lipid disorders are common in diabetes mellitus and play crucial roles in the development of diabetic cardiovascular complications. Presence of thyroid dysfunction may affect diabetic control and thyroid disorders are known to influence on lipid metabolism (5).

However, there is a lack of consistent data on whether and to what extent does SCH affect lipid profile (4). Moreover, there are controversial debates regarding the effect of SCH therapy with levothyroxine on serum lipids (6).

Therefore, we assessed the effect of levothyroxine (L-thyroxine) treatment on lipid profile in diabetics with SCH.

## Materials and methods

The present study was carried out in the Department of Biochemistry, Government medical college and Patwardhan's Endocrine Research Center, Miraj. The study was approved by the ethics committee of Government medical college, Miraj (Maharashtra, India).

## Selection of the study subjects

Study included total 400 subjects and grouped in to two groups.

**Group I:** includes 200 patients suffering from type 2 diabetes mellitus with subclinical hypothyroidism (age 40-60 years) diagnosed by endocrinologist based on WHO criteria for diabetes mellitus and normal T3, T4 with TSH level  $> 4.5 \mu\text{IU/l}$  for SCH at Patwardhan's Endocrine Research Center, Miraj.

L-Thyroxine therapy of  $12.5 \mu\text{g}$  per day was prescribed to diabetics with subclinical hypothyroidism patients for 3 months by endocrinologist.

Pretherapy and post therapy blood samples were collected for various biochemical investigations. Internal comparison of pre and post therapy results was done.

**Group II:** includes 200 type 2 Diabetes Mellitus patients without subclinical hypothyroidism (age 40-60 years) were diagnosed by endocrinologist based on WHO criteria and having normal T3, T4 and TSH levels.

Subjects having history or symptoms of cardiovascular diseases, receiving other medications that alter thyroid functions and lipid levels were excluded from the study.

## Sample (Blood) collection

An informed consent was obtained from participants after complete explanation of procedure. Every patient was advised for at least 12-14 hours overnight fast. About 3 ml venous blood was collected in plain blue tube taking aseptic precautions and used for lipid parameter investigations.

After two hours of collection, samples were centrifuged at 3000 R.P.M. for 10 minutes, clear and un-hemolysed serum was separated and used for estimation of Total cholesterol (TC), HDL cholesterol (HDL-C), LDL cholesterol (LDL-C) and triglycerides (TG).

Total cholesterol estimated by Enzymatic-colorimetric (Trinder – Endpoint) (7,8), Triglycerides by Enzymatic-colorimetric (Endpoint) method (8-10) and direct High density lipoprotein cholesterol (HDL-C) (11) and direct Low density lipoprotein cholesterol (LDL-C) (12)

on Selectra Junior analyzer by using Merck specialties private limited kit. The data was analyzed by student's 't', 'z' test and Karl Pearson's correlation coefficient. P values <0.001 were considered significant.

### Results

Table no 1 show lipid parameters in subjects. We found highly significant increase ( $p<0.001$ ) in total cholesterol, triacylglycerol, LDL-C and highly significant decrease ( $p<0.001$ ) in HDL-C

in type 2 DM with SCH patients as compared to type 2 DM without SCH.

Comparison of lipid parameters in type 2 DM with SCH patients before and after therapy is given in table no 2. We observed highly significant reduction in total cholesterol, TG and LDL-C and highly significant increase in HDL-C after therapy as compared to before therapy.

We found only significant correlation of TSH with TG before treatment ( $p<0.05$ ) (table no.3).

**Table No 1:** Serum lipid parameters in subjects

Parameters	Type 2 DM (n=200)	Type 2 DM with SCH before treatment (n=200)	P value
Total cholesterol (mg/dl)	227 ± 19.683	237.621 ± 20.054	0.001
Triglycerides (mg/dl)	184.905 ± 26.139	223.317 ± 23.045	0.001
HDL (mg/dl)	23.625 ± 3.672	21.25 ± 4.350	0.001
LDL (mg/dl)	104.2 ± 18.48	123.293 ± 17.432	0.001

**Table No 2:** Comparison of lipid parameters in patients before and after treatment

Parameters	Type 2 DM with SCH Before treatment (n=200)	Type 2 DM with SCH After treatment (n=200)	t value	P value
Total cholesterol (mg/dl)	237.621 ± 20.0543	219.482 ± 16.643	15.39	0.001
Triglycerides (mg/dl)	223.317 ± 23.045	210.169 ± 23.615	20.87	0.001
HDL (mg/dl)	21.25 ± 4.350	24.04 ± 4.457	-18.60	0.001
LDL (mg/dl)	123.293 ± 17.432	115.737 ± 17.191	17.31	0.001

**Table No 3:** Correlation between TSH level and lipid parameters of type 2 DM with SCH patients before treatment

	Lipid parameters	R	P
TSH in (μIU/l)	TC (mg/dl)	-0.072	0.311
	TG (mg/dl)	-0.139*	0.05
	HDL-C (mg/dl)	0.036	0.612
	LDL-C (mg/dl)	0.036	0.615

\* $p<0.05$ , Significant

**Table No 4:** Correlation between TSH level and lipid parameters of type 2 DM with SCH patients after treatment

	Lipid parameters	R	P
TSH in (μIU/l)	TC (mg/dl)	-0.077	0.280
	TG (mg/dl)	0.086	0.225
	HDL-C (mg/dl)	0.036	0.608
	LDL-C (mg/dl)	0.066	0.353

### Discussion

In the present study we have demonstrated that patients with type 2 DM with SCH had altered lipid profile when compared to type 2 DM without SCH. This indicates lipid abnormalities in type 2

DM with SCH. High level of TSH may associated with deleterious changes in serum lipids such as total cholesterol, low density lipoprotein cholesterol, high density lipoprotein cholesterol and triglycerides.

Study of Shivleela Biradar et al <sup>(4)</sup> found similar findings in SCH, which supports our study but patients included in their study were non-diabetic. Another study of Sarika Singh et al <sup>(13, 14)</sup> observed significant increase in TC, TG LDL-C and non-significant decrease in HDL-C in SCH patients without DM compared to controls.

Dyslipidemia is a common finding in patients with thyroid disease, explained by the adverse effects of thyroid hormones in almost all steps of lipid metabolism <sup>(4,14)</sup>. SCH by different mechanisms can be associated with lipid alterations, mainly total and LDL-C and less often HDL-C, TG, and Lp (a), which may increase the risk of heart diseases <sup>(14)</sup>.

Hypercholesterolemia is a common feature in hypothyroidism because thyroid hormones upregulate LDL-receptor expression<sup>(15)</sup>. The reported mechanisms for the development of hypercholesterolemia and an increase in low density lipoproteins in hypothyroidism include decreased fractional clearance of LDL by a reduced number and reduced activity of LDL receptors in the liver <sup>(4, 13)</sup>.

In vivo and in vitro studies of Wei Zhang et al <sup>(16)</sup> showed the presence of TSH receptor on liver cells. TSH itself upregulates the expression of HMG-COA -reductase by acting on a TSH receptor in hepatocyte membrane and therefore promotes cholesterol synthesis in liver <sup>(17)</sup>. Such mechanisms may initiate lipid abnormalities in SCH.

Increase in serum TSH levels may decrease the activities of hepatic lipase, lecithin cholesterol acyl transferase and ATP binding cassette transporter resulting in reduction in HDL-C levels <sup>(4)</sup>

High level of TG may be due decreased activity of lipoprotein lipase enzyme <sup>(4)</sup> and poor clearance of endogenous and exogenous triglycerides from circulation in subclinical hypothyroidism <sup>(13)</sup>. Thyroid hormones affect lipoprotein lipase activity and which regulates hydrolysis of TG in VLDL and chylomicrons into fatty acids and glycerol. In hypothyroidism, lipoprotein lipase

activity in the adipose tissue has been found normal or decreased in addition to decreased hepatic lipase activity resulting in normal or high levels of TG <sup>(14)</sup>.

TG- rich lipoproteins such as chylomicron remnants and VLDL remnants still play an important role in atherogenesis. These remnants are taken up by macrophages in the arterial walls to produce foam cells and thus may be a risk factor for atherosclerosis in SCH <sup>(4)</sup>.

#### **Effect of thyroxine therapy on lipid profile**

After therapy in our study, we found highly significant decrease in TC, TG, LDL-C and highly significant increase in HDL-C values compared to before therapy in type 2DM with SCH. This may indicate reduction in the cardiovascular risk factors.

Similarly Sarika Singh et al <sup>(14)</sup> and Amit Saxena et al <sup>(18)</sup> found significant decrease in TC, TG, LDL-C and significant increase in HDL-C levels after L-thyroxine therapy as compared to before therapy in non-diabetic SCH patients <sup>(14)</sup>.

After L-thyroxine therapy in SCH serum TSH concentration decreases as serum T4 concentration rises that may lead to increased conversion of cholesterol into bile acids in liver, activity of lipoprotein lipase may be elevated, increased synthesis of proteins required for HDL synthesis and more expression and synthesis of LDL receptors. All these mechanisms may results in reduction in the concentration of TC, TG and LDL-C and increased concentration of HDL-C in type 2 DM with SCH after therapy.

#### **Conclusion**

SCH is associated with atherogenic serum lipid profile pattern. Such pattern (atherogenic lipid profile that is TC, HDL-C, TG, and LDL-C) may increase the risk of atherosclerosis and CVD. Therefore there is a potential association between SCH and atherosclerosis. So assessment, monitoring of serum lipid profile and treatment of L-thyroxine is of utmost importance to reduce or prevent the risk of development of atherosclerosis and CVD in type 2 DM with SCH patients.

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