

Impact of Levothyroxine Therapy on Lipid Profile Value in Patients of Subclinical Hypothyroidism

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ABSTRACT

Aim: The aim of this study is to study the effect of levothyroxine treatment on lipid profile in patients of subclinical hypothyroidism.

Materials and methods: A randomized control trial, prospective study conducted on 22 cases of subclinical hypothyroidism with 22 control at the Downtown Hospital, Guwahati. Inclusion and exclusion criteria were undertaken. Levothyroxine therapy was given and was followed up after 3 months with thyroid and lipid profiles. Pretreatment and posttreatment values were compared using the paired *t* test using the statistical software SPSS v.19.

Results: A statistical significance between pretreatment and posttreatment values is found to be in values of thyroid-stimulating hormone (TSH), cholesterol, high-density lipoprotein (HDL), low-density lipoprotein (LDL), and triglyceride ($p < 0.05$). There was no significant difference in the pretreatment and posttreatment T3 and T4 values. There was a mild increase in the value of HDL, a significant decrease in the value of TSH, cholesterol, very low-density lipoprotein (VLDL), and triglyceride.

Conclusion: Lipid profiles are altered in patients with subclinical hypothyroidism compared to controls. Levothyroxine therapy has beneficial effect on lipid profile in patients with subclinical hypothyroidism.

Keywords: Levothyroxine, Lipid profile, Subclinical hypothyroidism.

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INTRODUCTION

The term “subclinical hypothyroidism” is used to describe a state where there is a raised TSH concentrate with a normal concentration of T4. It is common with a prevalence of 7–8% in women and 2–4% in men.¹ Patients with subclinical thyroid disease have a few or no symptoms or signs of thyroid dysfunction and vary in nature, thus, subclinical thyroid disease is a laboratory diagnosis. Levothyroxine therapy in mild elevation of serum TSH is generally agreed to be appropriate.^{2,3} Management of patients with a serum TSH level of less than 10 mIU/L is also controversial.⁴ HMG coenzyme A reductase (HMGCR) is the rate-limiting enzyme in cholesterol synthesis. In the hypothyroid state, *HMGCR* mRNA levels are reduced and treatment with thyroid hormone restores it to normal level. Thyroid hormone stimulates *HMGCR* transcription and increases its stability.⁵ The abnormality of lipid profiles in subclinical hypothyroidism may be related to gradually decreased thyroid hormone (TH) levels in the serum and tissues.⁶ Additionally, high TSH level stimulates *HMGCR* expression by stimulating the cyclic adenosine monophosphate/protein kinase A/cyclic adenosine monophosphate-responsive element binding protein (cAMP/PKA/CREB) cassette.⁷ Conversion of cholesterol into bile acids is important for maintaining whole body cholesterol homeostasis. The rate-limiting enzyme in bile acid synthesis is controlled by cholesterol 7-hydroxylase which is regulated by thyroid hormone.⁸

Thus, TH also reduces cholesterol through enhancing cholesterol clearance pathway. Over time, the subclinical may develop to overt hypothyroidism. This study will also help patients prevent in the development of overt hypothyroidism

MATERIALS AND METHODS

A randomized control trial, prospective study conducted on 22 cases of subclinical hypothyroidism with 22 control at the Downtown Hospital, Guwahati.

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Conflict of interest: None

Inclusion Criteria

- All patients with subclinical hypothyroidism
- Patients willing to participate in the study.

Exclusion Criteria

- Patients not willing to participate in the study
- A past history of thyroid disease
- Patients on treatment for thyroid disorder
- Patient not on antidiabetic drugs.

The study was approved by Downtown Hospital Ethical Committee. TSH, T3, T4, total cholesterol, HDL cholesterol, LDL cholesterol, VLDL cholesterol, and serum triglycerides will be measured in all the patients after an overnight fast. In all patients, subclinical hypothyroidism will be started with levothyroxine. Levothyroxine daily dose of 25–75 µg depending on the level of thyroxine and the serum TSH level. Serum TSH will be checked after 8 weeks, and the dose will be adjusted. Patients will be followed up after 3 months from the first date of visit with a repeat lipid profile and thyroid profile.

Descriptive statistical analysis was carried out in the present study. The paired *t* test is applied to analyze the data. The SPSS v19 is used to generate data.

RESULTS

About 22 patients and 22 control were taken in the study. The mean age of patients were 43.22 years and 40.45 years of control. Among cases, the female predominance was 86.36%. The mean value of variables (Table 1) was compared with control (Table 2) after levothyroxine therapy. The mean TSH value was significantly higher, i.e. 7.24 than control i.e. 2.67 after levothyroxine therapy (p value = 0.00091). There was no significant change in the T3 value when compared with control (p value = 0.165746) and T4 value (p value = 0.967266). The mean total cholesterol levels were significantly higher in patients with SH as compared to controls

(372.1364 vs 205.5909, p value = <0.0001). The mean LDL levels were reduced from 97.4545 to 85.2727 and the mean VLDL value is decreased from 28.2273 to 27.8636 and is statistically significant when compared with control, p value = 0.003102. The mean triglyceride value decreased from 169.8636 to 166.9545 and is statistically significant when compared with the control, p value < 0.00001. The mean HDL value is increased from 34.7727 to 35.2273 and is statistically significant when compared with the control, p value < 0.00001.

The statistical significance between pretreatment and posttreatment values is found to be in values of TSH, cholesterol, HDL, LDL, and triglyceride, p < 0.05 (Table 3). There was no significant difference in the pretreatment and posttreatment T3 and T4 values. There was a mild increase in the value of HDL and a significant decrease in the value of TSH, cholesterol, VLDL, and triglyceride.

Table 1: Paired samples statistics of cases

		Mean	N	Std. deviation	Std. error mean
Pair 1	T3-B	1.7182	22	0.23048	0.04914
	T3-A	1.7359	22	0.24325	0.05186
Pair 2	T4-B	107.3636	22	18.86934	4.02296
	T4-A	105.7727	22	27.57489	5.87899
Pair 3	TSH-B	9.9627	22	3.36084	0.71653
	TSH-A	7.2364	22	2.09433	0.44651
Pair 4	CHOL-B	384.2273	22	118.21245	25.20298
	CHOL-A	372.1364	22	122.48121	26.11308
Pair 5	HDL-B	34.7727	22	5.07029	1.08099
	HDL-A	35.2273	22	5.10771	1.08897
Pair 6	LDL-B	97.4545	22	20.63222	4.39880
	LDL-A	85.2727	22	20.82394	4.43968
Pair 7	VLDL-B	28.2273	22	6.20239	1.32235
	VLDL-A	27.8636	22	6.34932	1.35368
Pair 8	TG-B	169.8636	22	21.01767	4.48098
	TG-A	166.9545	22	19.90089	4.24288

Table 2: Paired samples statistics of controls

		Mean	N	Std. deviation	Std. error mean
Pair 1	CONTROL T3-B	1.8455	22	0.33684	0.07182
	CONTROL T3-A	1.8532	22	0.34295	0.07312
Pair 2	CONTROL T4-B	108.0455	22	22.91283	4.88503
	CONTROL T4-A	108.0909	22	22.80541	4.86213
Pair 3	CONTROL TSH-B	2.6782	22	1.25158	0.26684
	CONTROL TSH-A	2.6782	22	1.25158	0.26684
Pair 4	CONTROL COL-B	205.1818	22	25.52429	5.44180
	CONTROL COL-A	205.5909	22	26.05426	5.55479
Pair 5	CONTROL HDL-B	47.3636	22	7.41649	1.58120
	CONTROL HDL-A	47.2273	22	7.52730	1.60482
Pair 6	CONTROL LDL-B	72.1818	22	28.20273	6.01284
	CONTROL LDL-A	72.6364	22	27.99583	5.96873
Pair 7	CONTROL VLDL-B	22.6364	22	4.59343	0.97932
	CONTROL VLDL-A	22.5909	22	4.66659	0.99492
Pair 8	CONTROL TG-B	112.2727	22	27.64086	5.89305
	CONTROL TG-A	112.2727	22	27.64086	5.89305

Table 3: Paired samples statistics of pretreatment and posttreatment values

		Paired differences					t	df	p value
		Mean	Std. deviation	Std. error mean	95% confidence interval of the difference				
					Lower	Upper			
Pair 1	T3-B-T3-A	-0.00955	0.02663	0.00568	-0.02135	0.00226	-1.681	21	0.108
Pair 2	T4-B-T4-A	-1.04545	22.02915	4.69663	-10.81263	8.72172	-0.223	21	0.826
Pair 3	TSH-B-TSH-A	2.72636	2.13675	0.45556	1.77898	3.67375	5.985	21	0.000
Pair 4	CHOL-B-CHOL-A	12.09091	11.93199	2.54391	6.80056	17.38126	4.753	21	0.000
Pair 5	HDL-B-HDL-A	-0.45455	0.59580	0.12703	-0.71871	-0.19038	-3.578	21	0.002
Pair 6	LDL-B-LDL-A	12.18182	4.87595	1.03956	10.01994	14.34369	11.718	21	0.000
Pair 7	VLDL-B-VLDL-A	0.36364	0.58109	0.12389	0.10600	0.62128	2.935	21	0.008
Pair 8	TG-B-TG-A	2.90909	4.12783	0.88006	1.07891	4.73927	3.306	21	0.003

DISCUSSION

The Colorado study, which screened 25,862 subjects, found that the mean total cholesterol and LDL cholesterol progressively increased with increasing levels of serum TSH and hypercholesterolemia was associated with mild elevations of TSH levels.⁹ In this study, the mean age of patient is 43.22 years which is similar to Rigdway:¹⁰ 44 years, Bell:¹¹ 42 years, and Elder:¹² >40 years. Female predominance in this study 86.36% which is close to study by Bandyopadhyay et al.¹³ where females constituted 78% of study populations. In this study, the mean total cholesterol levels were significantly higher in patients with subclinical hypothyroidism supported by Asranna et al.¹⁴ and Bandyopadhyay et al.¹³ An increased level of LDL and hypertriglyceridemia has been shown to increase the risk of cardiovascular disease. In this study, mean LDL, VLDL, and triglyceride levels were reduced after levothyroxine therapy but only a decreased value of VLDL and triglyceride was statistically significant (p value < 0.05). There was a reduction in the LDL value but this might be due to the presence of confounding factor like low-fat diet intake. Subclinical hypothyroidism was associated with raised LDL levels and, thus, had larger cardiovascular risk (Bakker et al.)¹⁵ and reduced level seen with levothyroxine therapy (Meier et al.).¹⁶ The value of triglyceride is reduced after levothyroxine therapy in this study which is statistically significant. A similar reversal of changes following treatment has shown by Atthans et al.¹⁷ and Monzani et al.¹⁸ A mild increase in the HDL value is also observed which is statistically significance.

There is an increasing prevalence of cardiovascular morbidity. Even a small decrease in the levels of T. cholesterol, LDL, and triglyceride levels results in substantial reductions in cardiovascular morbidity.

CLINICAL SIGNIFICANCE

Levothyroxine therapy is patients of subclinical hypothyroidism reduces the TSH level and, thus, preventing conversion to overt hypothyroidism and also reduces cardiac morbidity.

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