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Original Research

Impact of Thyroid Hormone Replacement Therapy on Lipid Profiles in Patients with Subclinical Hypothyroidism: A Randomized Controlled Trial

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ABSTRACT

Background: Subclinical hypothyroidism (SCH) is associated with dyslipidemia, increasing the risk of cardiovascular diseases. Thyroid hormone replacement therapy (THRT) is commonly employed to restore euthyroidism, but its effect on lipid profiles in SCH patients remains under investigation. This study aimed to evaluate the impact of THRT on lipid profiles in patients with SCH.

Materials and Methods:A randomized controlled trial was conducted with 100 SCH patients, aged 18–65 years, who were divided into two groups: treatment (n=50) and control (n=50). The treatment group received levothyroxine to maintain thyroid-stimulating hormone (TSH) levels within the normal range, while the control group was given a placebo. Lipid profiles, including total cholesterol (TC), low-density lipoprotein (LDL), high-density lipoprotein (HDL), and triglycerides (TG), were measured at baseline and after 12 weeks. Statistical analysis was performed using paired t-tests and ANOVA.

Results: At baseline, lipid parameters were similar in both groups. After 12 weeks, the treatment group showed significant reductions in TC (from 210 ± 15 mg/dL to 180 ± 10 mg/dL, $p<0.01$), LDL (from 130 ± 12 mg/dL to 100 ± 8 mg/dL, $p<0.01$), and TG (from 160 ± 14 mg/dL to 140 ± 12 mg/dL, $p<0.05$). No significant changes were observed in HDL levels or in the control group. The placebo group exhibited no significant alterations in any lipid parameters.

Conclusion: Thyroid hormone replacement therapy significantly improves lipid profiles, particularly by reducing total cholesterol, LDL, and triglyceride levels in patients with subclinical hypothyroidism. These findings support the use of THRT for cardiovascular risk mitigation in SCH patients.

Keywords: Subclinical hypothyroidism, thyroid hormone replacement therapy, lipid profile, cardiovascular risk, randomized controlled trial

INTRODUCTION

Subclinical hypothyroidism (SCH) is characterized by elevated serum thyroid-stimulating hormone (TSH) levels with normal free thyroxine (FT4) concentrations, often presenting without overt symptoms of hypothyroidism [1,2]. It is a relatively common endocrine disorder, affecting approximately 4-10% of the general population, with a higher prevalence in women and the elderly [3,4]. While SCH is often asymptomatic, it has been associated with dyslipidemia, systemic inflammation, and an increased risk of cardiovascular diseases [5,6].

Dyslipidemia in SCH typically involves elevated levels of total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), and triglycerides (TG), which contribute to atherogenesis and cardiovascular morbidity [7,8]. The underlying mechanisms may include reduced hepatic LDL receptor activity and altered lipid metabolism due to thyroid hormone deficiency [9]. Given these associations, early identification and management of SCH are considered critical to mitigating potential cardiovascular complications.

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Thyroid hormone replacement therapy (THRT) with levothyroxine is the standard approach for treating hypothyroidism. However, its role in improving lipid profiles in patients with SCH remains a subject of ongoing research and debate [10,11]. While some studies have demonstrated significant improvements in lipid parameters following THRT, others have reported minimal or no effect, highlighting the need for further investigation [12,13].

This randomized controlled trial aims to assess the impact of THRT on lipid profiles in patients with SCH, contributing to the understanding of its therapeutic benefits and implications for cardiovascular risk reduction.

MATERIALS AND METHODS

Study Design and Participants: This randomized controlled trial was conducted over a 12-week period at a tertiary care hospital. The study enrolled 100 patients aged 18–65 years, diagnosed with subclinical hypothyroidism (TSH levels between 4.5 and 10 mIU/L and normal free thyroxine levels). Exclusion criteria included pregnancy, history of thyroid disorders requiring surgery or radioactive iodine therapy, severe comorbidities, and the use of medications influencing lipid metabolism. Participants provided informed consent for this study.

Randomization and Intervention: Participants were randomized into two groups: the treatment group (n=50) and the control group (n=50). Randomization was performed using a computer-generated random sequence. The treatment group received levothyroxine at a dose adjusted to maintain TSH levels within the normal range (0.5–4.0 mIU/L). The control group was given an identical placebo. All participants were advised to follow a standard diet and maintain consistent physical activity throughout the study period.

Assessment of Lipid Profile: Baseline fasting blood samples were collected from all participants to measure lipid parameters, including total cholesterol (TC), low-density lipoprotein (LDL), high-density lipoprotein (HDL), and triglycerides (TG). These measurements were repeated at the end of 12 weeks. Serum TSH and free thyroxine levels were also monitored to assess thyroid function.

Outcome Measures: The primary outcome was the change in lipid profiles (TC, LDL, HDL, TG) from baseline to the end of the study. Secondary outcomes included changes in TSH and free thyroxine levels.

Statistical Analysis: Data were analyzed using SPSS version 25.0. Continuous variables were expressed as mean ± standard deviation. Paired *t*-tests were used to compare baseline and post-treatment values within groups, while independent *t*-tests were employed to compare changes between groups. A *p*-value of less than 0.05 was considered statistically significant.

RESULTS

Baseline Characteristics: The baseline characteristics of the study participants were comparable between the treatment and control groups (Table 1). The mean age of participants in the treatment group was 42.1 ± 10.5 years, while in the control group, it was 41.6 ± 9.8 years (p=0.85). The female-to-male ratio was 3:2 in both groups. Baseline serum TSH levels were 6.8 ± 0.7 mIU/L in the treatment group and 6.7 ± 0.8 mIU/L in the control group (p=0.62). Lipid profile parameters, including total cholesterol, LDL, HDL, and triglycerides, were similar in both groups at baseline (p>0.05).

Changes in Lipid Profiles: After 12 weeks, the treatment group showed significant reductions in total cholesterol, LDL, and triglyceride levels compared to baseline, while the control group showed no significant changes (Table 2). In the treatment group, total cholesterol decreased from 210 ± 15 mg/dL to 180 ± 10 mg/dL (p<0.01), LDL from 130 ± 12 mg/dL to 100 ± 8 mg/dL (p<0.01), and triglycerides from 160 ± 14 mg/dL to 140 ± 12 mg/dL (p<0.05). HDL levels remained stable in both groups (p>0.05).

Thyroid Function: The treatment group achieved euthyroid status, with a significant reduction in TSH levels (from 6.8 ± 0.7 mIU/L to 3.1 ± 0.5 mIU/L, p<0.01), while no significant change was observed in the control group (Table 3).

Table 1. Baseline Characteristics of Participants

Characteristic	Treatment Group (n=50)	Control Group (n=50)	*p*-value
Age (years)	42.1 ± 10.5	41.6 ± 9.8	0.85
Female-to-male ratio	3:2	3:2	-
TSH (mIU/L)	6.8 ± 0.7	6.7 ± 0.8	0.62
Total cholesterol (mg/dL)	210 ± 15	208 ± 14	0.78
LDL (mg/dL)	130 ± 12	129 ± 11	0.84
HDL (mg/dL)	50 ± 5	51 ± 6	0.71
Triglycerides (mg/dL)	160 ± 14	159 ± 15	0.83

Table 2. Changes in Lipid Profiles After 12 Weeks

Lipid Parameter	Baseline (mg/dL)	12 Weeks (mg/dL)	*p*-value
Treatment Group			
Total cholesterol	210 ± 15	180 ± 10	<0.01
LDL	130 ± 12	100 ± 8	<0.01

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HDL	50 ± 5	51 ± 4	0.45
Triglycerides	160 ± 14	140 ± 12	<0.05
Control Group			
Total cholesterol	208 ± 14	206 ± 13	0.52
LDL	129 ± 11	128 ± 10	0.67
HDL	51 ± 6	50 ± 5	0.58
Triglycerides	159 ± 15	157 ± 14	0.63

Table 3. Thyroid Function Parameters

Parameter	Baseline	12 Weeks	*p*-value
Treatment Group			
TSH (mIU/L)	6.8 ± 0.7	3.1 ± 0.5	<0.01
Free thyroxine (ng/dL)	1.2 ± 0.2	1.4 ± 0.3	<0.05
Control Group			
TSH (mIU/L)	6.7 ± 0.8	6.6 ± 0.7	0.72
Free thyroxine (ng/dL)	1.2 ± 0.2	1.2 ± 0.2	0.89

The baseline characteristics (Table 1) demonstrate similar demographic and clinical parameters between groups. Lipid profile changes (Table 2) were significant in the treatment group, particularly for total cholesterol and LDL. Thyroid function improvement was observed only in the treatment group (Table 3).

DISCUSSION

This study aimed to evaluate the effect of thyroid hormone replacement therapy (THRT) on lipid profiles in patients with subclinical hypothyroidism (SCH). The findings demonstrated that THRT significantly reduced levels of total cholesterol (TC), low-density lipoprotein (LDL), and triglycerides (TG) in the treatment group, while no significant changes were observed in the control group. These results align with existing evidence, highlighting the potential of THRT in improving lipid metabolism and mitigating cardiovascular risk in SCH patients [1,2].

The reduction in TC and LDL levels observed in this study is consistent with prior research suggesting that thyroid hormones regulate lipid metabolism by increasing hepatic LDL receptor activity, promoting cholesterol clearance from the bloodstream [3,4]. Additionally, the significant decrease in TG levels could be attributed to improved lipoprotein lipase activity, which enhances triglyceride breakdown [5]. Similar outcomes have been reported in other randomized controlled trials and meta-analyses [6,7].

In contrast, high-density lipoprotein [HDL] levels did not show significant changes post-treatment, which has also been noted in previous studies [8]. This finding may indicate that thyroid hormone replacement primarily influences atherogenic lipids such as LDL and TG, while its effect on HDL remains minimal or inconsistent [9].

The relationship between SCH and dyslipidemia is well-documented, with elevated TSH levels contributing to impaired lipid metabolism [10]. By normalizing TSH levels, THRT may not only improve lipid parameters but also reduce inflammation and endothelial dysfunction, further lowering cardiovascular risk [11,12]. These benefits underscore the importance of early diagnosis and management of SCH in patients with lipid abnormalities.

While this study provides valuable insights, some limitations should be acknowledged. The relatively short duration of the study (12 weeks) may not fully capture long-term changes in lipid profiles and cardiovascular outcomes. Additionally, the sample size, though adequate for detecting significant differences, may limit the generalizability of the findings to broader populations. Future studies with larger sample sizes and extended follow-up periods are warranted to confirm these results and assess their clinical implications.

The controversy surrounding the treatment of SCH arises from conflicting evidence on its cardiovascular benefits [13,14]. While some studies argue against routine THRT due to potential overtreatment, others emphasize its role in improving lipid profiles and reducing subclinical atherosclerosis [15]. This study adds to the growing body of evidence supporting the use of THRT, particularly in patients with significant dyslipidemia.

CONCLUSION

In conclusion, this study demonstrated that thyroid hormone replacement therapy significantly improves lipid profiles in patients with subclinical hypothyroidism, particularly by reducing TC, LDL, and TG levels. These findings reinforce the potential role of THRT in reducing cardiovascular risk and highlight the importance of personalized treatment approaches for SCH patients.

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