

# Dyslipidemia in subclinical hypothyroidism and the effect of thyroxine on lipid profile

Ajay Asranna, R. S. Taneja, Bindu Kulshreshta<sup>1</sup>

Departments of Medicine, and <sup>1</sup>Endocrinology, Post Graduate Institute of Medical Education and Research, Dr. Ram Manohar Lohia Hospital, Guru Gobind Singh Indraprastha University, New Delhi, India

### ABSTRACT

**Introduction:** Subclinical hypothyroidism (SH) has a prevalence between 4% and 10.5% in various studies. The burden of SH in India is expected to increase with increasing iodine sufficiency. Studies have shown conflicting results concerning not only the degree of lipid changes in SH but also the effect of thyroxine substitution therapy. Indian studies on dyslipidemia in SH and the effect of thyroxine on lipid profile are currently lacking. **Aims and Objectives:** (1) To assess the association of SH and lipid profile. (2) To quantify the effect of thyroxine treatment on lipid profile. **Materials and Methods:** About 54 patients who were detected to have SH were compared with 56 healthy controls. Thyroid stimulating hormone (TSH), free T3, free T4, anti thyroperoxidase (TPO) antibodies, total cholesterol, high density lipoprotein (HDL) cholesterol, low density lipoprotein (LDL) cholesterol, Very low density lipoprotein (VLDL) cholesterol, serum triglycerides were measured in all the patients after an overnight fast. Selected patients were started on thyroxine replacement. Twenty-one patients were followed up after 3 months with a repeat lipid profile. **Results:** Mean total cholesterol and mean LDL levels were significantly higher in SH compared to controls, but there was no statistically significant difference in the mean HDL, VLDL, and triglyceride levels. There was a significant reduction in mean T. cholesterol, mean LDL, mean VLDL, and mean triglyceride levels after treatment with thyroxine, while there was no significant difference among the mean HDL levels. **Conclusion:** Dyslipidemia is more common in SH compared to controls. There is a TSH dependent increase in cholesterol, LDL, VLDL, and triglyceride levels. Achieving euthyroid status with thyroxine has a favourable effect on lipid profile.

**Key words:** Dyslipidemia, subclinical hypothyroidism, thyroxine

## INTRODUCTION

Subclinical hypothyroidism (SH) is more frequent in areas of iodine sufficiency as compared to iodine deficient areas. The burden of SH in India is expected to increase with increasing iodine sufficiency. Studies have shown conflicting results concerning not only the degree of lipid changes in SH but also the effect of thyroxine substitution therapy. The effects of thyroxine replacement on lipid levels are at not completely understood. Indian studies on

dyslipidemia in SH and the effect of thyroxine on lipid profile are currently lacking.

## AIMS AND OBJECTIVES

1. To assess the association of SH and lipid profile.
2. To quantify the effect of treatment on lipid profile.

## MATERIALS AND METHODS

Fifty-four patients (49 women and 5 men), who were detected to have SH were compared with 56 healthy controls. TSH, free T3, free T4, anti TPO antibodies, total cholesterol, HDL cholesterol, LDL cholesterol, VLDL cholesterol, serum triglycerides were measured in all the patients after an overnight fast. Selected patients were started on thyroxine replacement. Twenty-one patients were followed up after 3 months with a repeat lipid profile.

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**Corresponding Author:** Dr. Ajay Asranna, Room No. 29, Doctors Hostel, Dr. Ram Manohar Lohia Hospital, Baba Khark Singh Marg, New Delhi - 110 001, India. E-mail: ajayasranna@gmail.com

## RESULTS

Mean TSH in cases was significantly higher than the control group (9.49 mIU/ml vs. 2.91 mIU/ml,  $P$  value < 0.001). No significant difference in the mean free T3 levels of the two groups was seen (2.96 pg/ml vs. 2.87 pg/ml,  $P$  value = 0.509). Mean T4 was significantly lower in cases as compared to controls (0.99 vs. 1.23 ng/dl,  $P$  value = 0.001). Anti TPO antibody levels >50 IU/ml was found in 27 people with SH (50%) compared with the control group which had eight subjects (14.29%) with anti TPO levels >50 IU/ml ( $P$  value < 0.001). Mean BMI among cases was  $21.48 \pm 2.80$  kg/m<sup>2</sup>. Mean BMI in the control group was  $21.36 \pm 1.53$  kg/m<sup>2</sup>. There was no significant difference in the mean BMI of the two groups ( $P$  value: 0.776).

The mean total cholesterol levels were significantly higher in patients with SH as compared to controls (173.72 mg/dl vs. 150.77 mg/dl,  $P$  value = 0.004). The mean HDL was lower in patients with SH (38.63 mg/dl) as compared to controls (42 mg/dl). However, it was not statistically significant. The mean LDL levels were significantly higher among cases compared to controls (106.07 mg/dl vs. 80 mg/dl,  $P$  value < 0.001). There was no significant increase to the VLDL levels among patients with SH as compared to controls (32.98 mg/dl vs. 28.73 mg/dl,  $P$  value = 0.112). There was no significant increase to the triglyceride levels in cases of SH compared to controls (165.01 mg/dl vs. 140.57 mg/dl,  $P$  value = 0.063). Twenty-one subjects were followed up after starting treatment with thyroxine. A fasting thyroid and lipid profile was obtained after achieving euthyroid status with incremental doses of thyroxine replacement at the end of 3 months.

The mean dose of thyroxine used was  $47.62 \pm 15.62$  µg. There was a significant decrease in mean TSH after treatment ( $11.65 \pm 6.66$  mIU/ml vs.  $3.18 \pm 1.68$  mIU/ml,  $P$  value < 0.001). There was no significant difference in the pre-treatment and post-treatment T3 values. There was a significant increase in the mean free T4 levels after treatment ( $0.95 \pm 0.20$  ng/dl vs.  $1.03 \pm 0.21$  ng/dl,  $P$  value = 0.011).

There was a significant decrease in T. cholesterol from pre-treatment mean levels of 175.48 mg/dl to 161.86 mg/dl ( $P$  value = 0.003). There was a mild increase in HDL from mean pre-treatment levels of 41.14 mg/dl to 43.43 mg/dl. However, it was not statistically significant ( $P$  value = 0.220). There was a significant decrease in the mean LDL levels from 102.19 mg/dl to 88.37 mg/dl ( $P$  value 0.002). There was a significant decrease in mean VLDL levels from 32.14 mg/dl to 27.91 mg/dl ( $P$  value 0.008). There was

a significant decrease in the mean triglyceride levels from pre-treatment values of 161.57 mg/dl to 140.28 mg/dl ( $P$  value 0.014).

## DISCUSSION

Various population-based studies like the Colorado study which screened 25,862 subjects found that mean total cholesterol and LDL cholesterol progressively increased with increasing serum TSH levels.<sup>[1]</sup> In a population-based sample from Northern India of 100 patients in the age range of 15-65 years having SH, a significant increase in triglycerides and VLDL-cholesterol levels were observed in patients of SH with respect to euthyroid controls while a nominal increase in serum cholesterol, LDL and HDL levels were recorded. However, there was no statistical difference found in any of the lipid fraction levels with change in the severity of SH.<sup>[2]</sup> In another study of dyslipidemia in an Indian population of 100 patients with SH and 52 euthyroid controls, serum lipoprotein (a) above the age of 20 years, and total cholesterol, triglyceride and LDL in the age group of 40-50 years were significantly elevated.<sup>[3]</sup> The higher mean triglyceride levels and low HDL levels seen in the present study could, in fact, be a reflection on the difference in pattern of dyslipidemia in Indian populations.

It is not yet established whether or not replacement therapy with thyroxine lowers serum lipid levels in patients with SH. Two meta-analyses have been carried out regarding the effects of thyroxine therapy on serum cholesterol levels in patients with mild thyroid failure.<sup>[4,5]</sup> In the first meta-analysis of 13 studies from 1976 to 1995, thyroid hormone replacement therapy decreased total cholesterol (TC) in patients with SH by 15 mg/dl independently of the initial plasma level; however, plasma levels remained elevated in most patients.<sup>[4]</sup> In the other meta-analysis performed in 2000 on 247 patients from 13 selected studies, serum TC was reduced by about 8 mg/dl and serum LDL-C by about 10 mg/dl after thyroxine treatment, whereas triglyceride and HDL-C levels did not change.<sup>[5]</sup> The variable changes in the various lipid parameters depend on factors like age, sex, race, pre-treatment lipid values, etc. Even small reductions in levels of T. cholesterol, LDL-C, and triglyceride levels result in substantial reductions in cardiovascular morbidity. This, and the fact that the prevalence of SH in India is increasing undermines the importance of studies investigating the effect of thyroxine on lipid profile.

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