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Thyroid function parameters, body mass index and serum lipid profile in subclinical hypothyroidism: a hospital-based study of effect of levothyroxine replacement therapy in Srinagar, Jammu and Kashmir State

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Abstract

Introduction: The Present study aimed to assess the effect of levothyroxine replacement therapy on serum lipid profile and thyroid function parameters of patients on subclinical hypothyroidism. We also aimed to correlate the lipid profile parameters with body mass index.

Methods: Ninety patients of subclinical hypothyroidism treated with levothyroxine for three months were included in the study. Fifty three euthyroid subjects served as controls. Levels of serum TSH, total cholesterol were assayed before and after levothyroxine therapy in patients with subclinical hypothyroidism. Levels of serum TSH, total cholesterol, LDL-cholesterol, HDL-cholesterol, T3 and T4 in subclinical hypothyroidism patient's post-levothyroxine therapy were compared with those of euthyroid controls, and correlated with body mass index.

Results: The study demonstrated significant decrease in serum total cholesterol levels in subclinical hypothyroidism patients on levothyroxine treatment (P <0.001). Male hypothyroid subjects showed significantly lower serum triglycerides, post thyroxine therapy, when compared to euthyroid males (P <0.001). In females, hypothyroid subjects post-thyroxine treatment showed significant difference with euthyroid controls with respect to triglycerides and LDL-cholesterol (P<0.001). Male obese and normal weight hypothyroid subjects (post-thyroxine) differed significantly with respect to LDL-cholesterol, and total cholesterol (significantly higher levels in obese; P <0.001). The obese and overweight groups differed significantly (P<0.001) with respect to LDL-cholesterol. In female hypothyroid subjects post-thyroxine treatment, LDL-cholesterol and triglycerides were significantly higher (p<0.001) in overweight and obese when compared to normal weight females.

Conclusions: Subjects with subclinical hypothyroidism showed significant improvement in dyslipidemia and thyroid hormones on treatment with L-thyroxine.

Keywords: Subclinical Hypothyroidism; Levothyroxine; Lipid Profile; Body mass Index.

Introduction

Thyroid function regulates a wide variety of metabolic pathways. Thyroid function significantly affects lipoprotein metabolism and some cardiovascular risk factors, thus influencing the overall CVD risk.[(1)] Hypothyroidism and subclinical hypothyroidism are the most common endocrine disorders which induce metabolic dysfunction and cardiovascular disease.[(1,2)]

Thyroid dysfunction is also associated with changes in body weight, body composition, body temperature and resting energy expenditure independent of physical activity.[(3)] Thyroid also influences adipocyte metabolism production of adipokines, which regulate body weight through various processes.[(4)] Several population studies have shown a significant relationship between TSH levels and body mass index.[(5)] Clinical trials have demonstrated that L-thyroxine therapy improved energy level, feeling of well-being and reduced serum cholesterol levels in individuals with subclinical hypothyroidism.[(6)]

The association between thyroid function and lipid abnormalities has not been established in Indians.[(7)] The present study made an attempt to evaluate the effect of thyroxine substitution therapy on body mass index and serum lipid profile in patients with subclinical hypothyroidism in Jammu and Kashmir. Earlier a hospital based study conducted by our research group revealed that Subclinical hypothyroidism.[(8)] In the present study we aimed to assess effect of L-thyroxine therapy on serum lipid profile, and effect of change in body weight on serum lipid profile and TSH, in subjects with subclinical hypothyroidism.

Materials and Methods

1. **Detailed description of the materials used and their components:** The present study was done at Sri Ramakrishna Mission Clinic, Srinagar. Study period was from January 2014 to March 2014. The study protocol was approved by Institutional Ethics Committee, and voluntary informed consent was taken from all study subjects.

Subjects: Categorization of subjects was based on TSH, T3 and T4 levels.[(9)]

Category	Serum TSH (μIU/ml)	Serum T3 (ng/ml)	Serum T4 (μg/dl)
Reference Range	0.27 to 4.2	0.8 to 2.0	4.8 to 12.7
Euthyroid	2.2 ± 1.5	1.5 ± 0.4	7.6 ± 1.8

Subclinical hypothyroidism	6.5 ± 12.2	Normal	Normal

Group-I: Included 275 Patients(Females n=200; males n=75) with confirmed diagnosis of subclinical hypothyroidism, aged 21-50 years, who were put on L-thyroxine therapy. These patients had serum TSH levels of 5.5 to 10 μIU/ml, and serum cholesterol levels of 230-250 mg%. Treatment with L-thyroxine was for 3 months.

Group-II: Euthyroid subjects - who attended routine health check, and whose serum TSH levels ranged from 0.27 to 4.2 μIU/ml with normal serum levels of T3 and T4. They were apparently healthy and aged 25 to 45 years. There were total 53 subjects out of which 30 were males and 23 were females.

All the study subjects were requested to fill a questionnaire on demographic details, food habits, habits of alcoholism and smoking, medications taken and any illness.

Exclusion criteria: Patients with clinically detected goiter, diabetes mellitus, hypertension, impaired glucose tolerance, and those taking lipid-lowering drugs and oral contraceptives were excluded from the study.

2. **Experimental design**: Observational case control study.
3. **Procedures employed**: Methods: Fasting venous blood samples were collected in plain vacutainers following aseptic precautions. The samples were centrifuged and sera were separated. Serum samples were assayed for T3, T4 and TSH by the chemiluminescence immunoassay using the reagent kits from Acculite. Procedure given in kit insert was followed. The assay used high affinity specific enzyme-conjugated and immobilized antibody in excess. The immobilization takes place at the surface of an opaque chemiluminescent reaction cell through the interaction of streptoavidin and exogenously added biotinylated monoclonal antibody coupled to the analyte of interest. Reaction between native antigen and antibodies, formation of soluble sandwich complex, and enzymatic conversion of substrate to product to generate light are the phenomena involved. The light generated is directly proportional to the concentration of antigen (hormone).

Estimation of lipids in serum: Estimation of lipids was done in Chem-7 semiautomated analyzer using reagent kits from CPC diagnostics. Total cholesterol was estimated by cholesterol oxidase-peroxidase method,[10] triglycerides were assayed by glycerol phosphate oxidase method.[11] Assay of HDL was based on precipitation of other lipoproteins using phosphotungstate-magnesium, and then estimation of HDL cholesterol in the supernatant by cholesterol oxidase-peroxidase method.[12] LDL-Cholesterol was calculated by the Friedwald's formula.[13]

Body weight was measured to the nearest of 0.1 kg using beam balance weighing scale. The subjects were advised to wear light clothes without shoes. Height was measured to the nearest of cm using height scale. The subjects were categorized based on body mass index (BMI) as follows.[4,9,14] Normal weight: 18.5 to 24.9 kg/m^2; Overweight : 25 to 29.9 kg/m^2; Obese : 25 to 29.9 kg/m^2.

4. **Statistical Analysis**: Statistical analysis was done using excel Microsoft corporation Redmond. Significance of difference in values between the groups was analyzed by Student's "t" test. P value of <0.005 was considered significant.

Results

Average age of Subclinical hypothyroid patients in females is 38.59±11.3 years and males is 48.4±8.08 years. The BMI (in Kg/m^2) of normal weight, overweight and obese subjects was 23.4 ± 1.88, 27.71 ± 1.63 and 35.5 ± 7.6 respectively. The serum lipid profile and values of TSH, T3 and T4 in hypothyroid patients Pre and post L-thyroxine therapy(Table 1).

Table 1: Pre and Post –Thyroxine therapy: Thyroid function tests and total cholesterol in study subjects

		Serum Total Cholesterol (mg/dl)	Serum TSH (□IU/ml)	Serum T3 (ng/ml)	Serum T4 (□g/dl)
Females	Pre -Throxine therapy(n=200)	245 ± 28.9	8.56 ±0.87	1.3 ± 0.25	7.3 ± 0.5
	Post -Throxine therapy(n=153)	182.5±24.68	3.94±3.24	1.6±0.7	7.78±1.82
Males	Pre -Throxine therapy (n=75)	255.8 ± 26.5	7.5 ± 0.77	1.5 ± 0.6	8.05 ± 0.78
	Post -Throxine therapy (n=59)	167±31.4	4.56±3.06	1.54±0.54	8.29±1.99

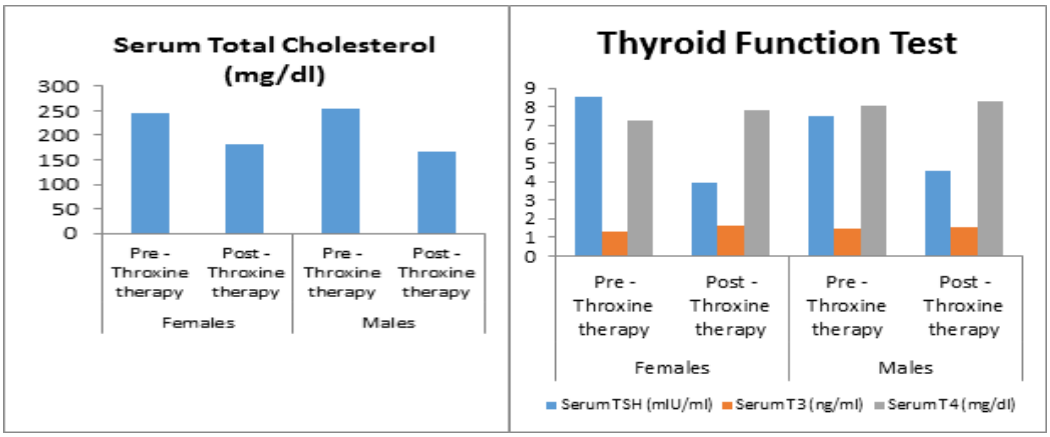

Fig. 1: Total cholesterol and Thyroid function test levels in pre and post thyroxine therapy

The serum total cholesterol and TSH levels decreased significantly after thyroxine treatment. There was no significant difference among T3 and T4 levels.

Male hypothyroid subjects showed significantly lower serum triglycerides, post thyroxine therapy, when compared to euthyroid males (P <0.001). Other lipid profile parameters did not differ significantly between euthyroid subjects and hypothyroid males post-thyroxine therapy. In females, hypothyroid subjects post-thyroxine treatment showed significant difference with euthyroid controls only with respect to triglycerides and LDL-cholesterol (Table 2). With respect to other lipid profile parameters and TSH the values did not differ significantly between the two groups(P <0.001).

Table 2: Comparison of TSH and Lipid Profile of Euthyroid controls and Post Thyroxine Therapy Subjects among normal BMI males and females

Groups	Total Cholesterol (mg/dl)	Triglycerides (mg/dl)	HDL-Cholesterol (mg/dl)	VLDL (mg/dl)	LDL-Cholesterol (mg/dl)	TSH (µIU/ml)
Euthyroid control Males (n=30)	180.7 ± 34.8	161.5 ± 73.1	44.2 ± 9.7	33.1 ±14.94	156.3 ± 37.9	2.42 ± 0.71
Post-Thyroxine Therapy, Normal BMI males (n=19)	174.9 ± 31.3 NS	133.54 ± 13.7 S	48.46 ± 7.8 NS	26.6 ± 6.7 S	147.21 ± 29.7 NS	2.35 ±0.61 NS
Euthyroid control Females (n=23)	168.4 ± 22.02	153.5 ± 49.7	48.9 ± 9.7	31.3 ±10.6	147.21 ± 29.7	2.35 ± 0.61
Post-Thyroxine Therapy, Normal BMI Females (n=25)	174.4 ± 21.96 NS	109.3 ± 22.4 S	51.06 ± 5.55 NS	21.71 ± 4.75 S	100.38 ± 24.5 S	2.85 ±2.15 NS

NS- Not Significant; S – Significant.

Obese male and normal weight hypothyroid subjects (post-thyroxine) differed significantly with respect to LDL-cholesterol, and total cholesterol (significantly higher levels in obese; P <0.001). The obese and overweight groups differed significantly with respect to LDL-cholesterol (higher in obese). There was no significant difference between normal weight and overweight males (post-thyroxine, sub clinical hypothyroidism) with respect to any lipid profile parameters and TSH. In female hypothyroid subjects post-thyroxine treatment, LDL-cholesterol and triglycerides were significantly higher in overweight and obese when compared to normal weight females. The most pronounced increase was seen in obese females. (Table 3).

Table 3: Effect of BMI on Lipid Profile and TSH in Post LT4 therapy Male and Female Subjects

	Males			Females		
	Normal BMI	**Over weight**	**Obese**	**Normal BMI**	**Over weight**	**Obese**
Total Cholesterol (mg/dl)	174.9 ± 31.3	173.6 ± 29.6 ^{NS}	156.4 ± 33.3 **, ^{NS2}	174.0 ± 21.96	186.45 ± 22.59*	186.89 ± 29.5
Triglycerides (mg/dl)	133.54 ± 13.7	139.8 ± 35.25 ^{NS}	147. 39 ± 49.3 $^{NS1, NS2}$	109.3 ± 22.4	128.85 ± 45.37 *	184.11 ± 27.39 **,***
HDL-Cholesterol (mg/dl)	48.46 ± 7.8	50.21 ± 6.66 ^{NS}	49.45 ± 11.49 $^{NS1, NS2}$	51.06 ± 5.63	47.25 ± 7.22 ^{NS}	49.4 ± 6.5$^{NS1, NS2}$
VLDL-Cholesterol (mg/dl)	26.6 ± 6.7	27.7 ± 7.12 ^{NS}	29.10 ± 11.69 $^{NS1, NS2}$	21.71 ± 4.75	25.14 ± 5.79 ^{NS}	36.56 ±4.5 **,***
LDL-Cholesterol (mg/dl)	96.4 ± 22.93	95.59 ± 30.85 ^{NS}	135.34 ± 26.6**,***	100.3 ± 24.5	114.7 ± 27.5 *	173.97 ± 21.1**,***
TSH (µIU/ml)	3.82 ± 2.51	5.3 ± 3.81 ^{NS}	4.52 ± 2.82 $^{NS1, NS2}$	3.85 ± 2.15	4.6 ± 4.3 ^{NS}	3.3 ± 3.28$^{NS1, NS2}$

^{NS1} No significant difference in values (when overweight group is compared with normal BMI group)
** Significant difference in values (when obese group is compared with normal BMI group)
^{NS2} No significant difference in values (when Obese group is compared with normal BMI group)
*** Significant difference in values (when obese group is compared with overweight group)

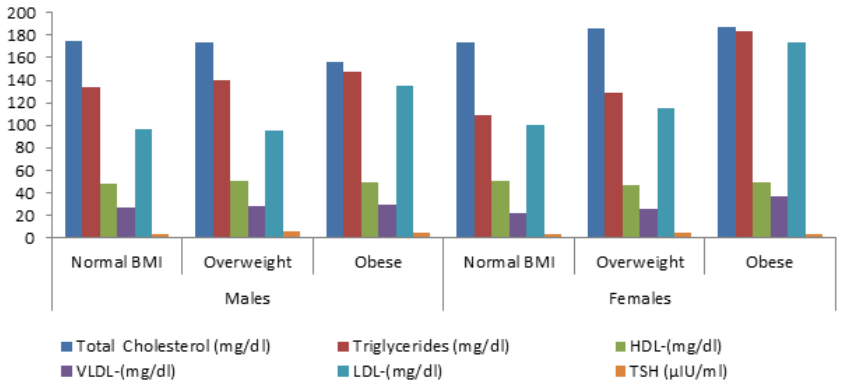

Fig. 2: Comparison of lipid profile and TSH in normal BMI, overweight and obese in male and female post hypothyroid subjects

Discussion

Effect of thyroxine therapy on thyroid hormone profile and lipid profile is evident from significant decrease in serum TSH and serum total cholesterol levels. These findings are in concordance with the previous studies.[1,15] In this study, patients with subclinical hypothyroidism but with hypercholesterolemia, were put on L-thyroxine therapy for a period of 90 days. These subjects had normal BMI. Euthyroid subjects with normal BMI and from the same population, served as controls in this study.

L-thyroxine decreased the levels of serum TSH, and the levels were statistically not significant when compared to euthyroid controls. The levels of total cholesterol decreased significantly on treatment with L—thyroxine. In this study we also observed that serum levels of triglycerides, LDL-cholesterol and VLDL-cholesterol were significantly lower in post-thyroxine subjects when compared to euthyroid controls. Previous studies have reported significant changes in serum lipid profile in hypothyroidism patients on thyroxine therapy. Studies by Monzani et al.[16] and Gluvic et al.[15] reported significant decrease in total cholesterol and LDL-cholesterol on L-thyroxine replacement therapy in subclinical hypothyroidism patients.[16] Researchers have suggested that degree of change depends on the pre-treatment levels of total cholesterol and degree of thyroid dysfunction.[1,15,16]

There are contradicting reports on changes in HDL-cholesterol level in subclinical hypothyroidism patients on thyroxine treatment. There are reports of decreased, increased or unaltered HDL-cholesterol levels on treatment with L-thyroxine treatment.[1,15-17] In the present study, serum HDL-cholesterol levels were significantly higher in males, and comparable in females when compared to respective euthyroid controls. The response of HDL-cholesterol in thyroid substitution remains obscure.

In the present study, we categorized the subjects as normal weight, overweight and obese based on BMI.

Among the post-thyroxine, female, subclinical hypothyroidism patients, overweight females had significantly higher Total cholesterol, triglycerides and LDL-cholesterol when compared to normal weight females. In these subjects, obese females had significantly higher triglycerides and LDL-cholesterol levels than the normal weight females. In male post-thyroxine subclinical hypothyroidism patients, triglycerides and LDL-cholesterol were significantly higher in obese compared to normal weight. All other parameters were comparable in normal weight, overweight and obese groups. Gluvic et al. reported a significant decrease in BMI in subclinical hypothyroidism patients post-levothyroxine therapy.[15]

Previous studies have shown positive association between BMI and TSH.[1,3,14] In the present study we did not find any significant difference in TSH among the normal weight, overweight and obese subclinical hypothyroidism patients. Studies have suggested that the decrease in serum TSH due to levothyroxine treatment could be mediated by leptin.[3,4,5]

Conclusions

Subjects with subclinical hypothyroidism showed significant improvement in dyslipidemia and thyroid hormones on treatment with L-thyroxine. Further studies with larger sample size, with detailed assessment of lipid profile are required. Assessing the lipid profile of subclinical hypothyroidism patients could help in preventing lipid abnormalities.

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