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Research Article

ASSOCIATION BETWEEN TSH LEVELS & SERUM LIPID CONCENTRATION IN HYOTHYROID PATIENTS

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ABSTRACT

Objectives: Alteration in lipid profile constitutes an important risk factor for development of cardiovascular diseases. Thyroid status may affect lipid profile and the mechanism of this relationship is traditionally attributed to the influence of thyroid hormone. We have studied the association between TSH outside the reference range and concentrations of serum lipids in a hypothyroid patients and the role of BMI in modulating the association between TSH and lipid parameters.

Methods: Using general linear models, we calculated mean concentrations of total serum cholesterol, low-density lipoprotein (LDL) cholesterol, very low-density lipoprotein (VLDL) cholesterol, HDL cholesterol and triglycerides across categories of TSH.

Results: outside the reference range of TSH, there was a linear and significant (P value< 0.001) increase in total serum cholesterol, LDL cholesterol, VLDL cholesterol and triglycerides, and a linear decrease ((P value < 0.001) in HDL cholesterol with increasing TSH. The associations with triglycerides and HDL cholesterol were stronger among overweight than normal weight individuals.

Conclusions: we found that increasing level of TSH was associated with less favourable lipid concentrations. MI mediates the effect of thyroid function on lipid profile in hypothyroid patients.

INTRODUCTION

The association between thyroid diseases and serum cholesterol was firmly established following the classic article by Mason *et al*. on Christmas Day of 1930, which shedded light on the importance of thyroid function in cholesterol metabolism [1]. In 1951, Scow reported the accumulation of fat in the tissues of hypothyroid mouse models, as compared to controls, thereby giving support to the observations of von Noorden, in Vienna , that the thyroid gland plays a key role in the development of "fatty disease" [2]. Since then, hypothyroidism has been found to be associated with obesity and hypercholesterolemia, and the extent of the hypercholesterolemia usually being greater in primary than in secondary hypothyroidism due to the more severe condition of the primary hypothyroidism [3,4].

Alteration in lipid profile constitutes an important risk factor for development of premature atherosclerosis and cardiovascular disease which is major cause of morbidity and mortality in both developed and developing countries [5]. Various risk factor causing dyslipidaemia are age, eating habits, physical activities, stress, hereditary and thyroid function. Thyroid function plays an impressive role in regulating a wide array of metabolic parameters (6) .Hypothyroidism is often accompanied by alteration in serum lipid concentrations that are associated with increased risk of cardiovascular disease [7-9].Thyrotrophin (TSH) may also be associated with unfavourableserumlipids, especially if TSH is higher than 10 mU/l [10]. Further, thyroxine treatment of sub clinically hypothyroid individuals may reduce total serum cholesterol and low-density lipoprotein (LDL) cholesterol [11-13].

There is a lack of population-based studies of the association between TSH and serum lipid concentrations.

In this study of more than 300 patients from the general population were examined the association between TSH outside the reference range with total serum cholesterol, LDL cholesterol, VLDL cholesterol, HDL cholesterol and triglycerides.

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MATERIAL AND METHODS

The study was conducted in collaboration with department of Biochemistry, Government medical college, Jalgaon& VSM medical college, Sholapur to evaluate the lipid profile of hypothyroid patients and to find out relationship of dyslipidaemia with severity of hypothyroidism. Clinically and biochemically newly diagnosed hypothyroid patients of both sexes age 20 to 60 years, with no historyofthyroxine and hypolipidemic drugs in last three months were included in the study. Patients with chronic renal failure, diabetes mellitus, liver diseases, chronic diseases, pregnancy age less than 20 and more than 60 years were excluded. Hypothyroidism was diagnosed by clinical history, physical examinations and relevant laboratory investigations. Total 150 hypothyroid cases were included in the study and cases were further grouped on the basis of serum TSH concentrations into Group A (TSH level 4.0-6.0), Group B (TSH level 6.0-8.0) and Group C (TSH level >8.00).Specimen was collected in fasting condition, allowed to clot and serum was separated.TG and TC in serum samples were measured by enzymatic CHOD-POD Colorimetric method. HDL-C in serum was measured by phosphotungstic acid method. LDL-C and VLDL were measured by using the Friedewald's formula [10]. Serum TSH was measured by immuno-radiometric assay (IRMA).

Statistical Analysis

We studied the associations between TSH and serum lipid levels and calculated geometric means of each lipid for three categories of TSH 4.0, 7.1 to 9.9 and 10.0 mU/l and higher), with the corresponding 95% confidence intervals (CI). Statistical significance was assessed by P values for trend and correlation coefficient. We further explored whether the association between TSH and lipid levels differed between overweight and normal weight individuals, using body mass index (BMI; weight divided by the squared value of height) of 25.0 kg/m2 as cut-off. In a separate analysis, we included TSH outside the reference range and studied associations with serum lipids.

RESULTS

Table 1 shows the association between TSH within the reference range and concentrations of serum lipids. In both men and women, there was a consistent and significant increase in concentrations of total serum cholesterol, LDL cholesterol, VLDL cholesterol and triglycerides, with increasing concentration of TSH outside the reference range. There was also a consistent reduction in HDL cholesterol with increasing TSH. These estimates were adjusted for age, smoking status and time since last meal. Additional adjustment for daily use of medication, month of serum collection and prevalence of diabetes mellitus, angina pectoris, myocardial infarction or stroke did not substantially influence these associations. The linearity of the associations of TSH with TG and HDL cholesterol is illustrated in Figs 1 and 2 respectively.

We explored whether the associations between TSH and serum lipids differed between overweight (BMI 25.0 kg/m2 or higher) and normal weight (BMI lower than 25.0 kg/m2) individuals. For total serum cholesterol, LDL cholesterol and VLDLcholesterol, the results were similar between the groups. The positive association related to triglycerides was stronger among the overweight, and the negative association between TSH and HDL cholesterol was observed only among overweight people (P Value Table 2) elevated, when compared with those who were within the reference range of TSH (P value for triglycerides<0.001 for the other lipids).

Table 1 Geometric mean of serum lipids (mgl/dl) according to categories of thyroid stimulating hormone (TSH) outide the reference range, in men and women.

no	TSH (mU/l)	N	TC(mgl/dl)	LDL (mgl/dl)	VLDL (mgl/dl)	HDL(mgl/dl)	TG(mgl/dl)
1	Male						
2	4-6.9	50	161.28+15.77	86.28+10.91	30.40+6.66	41.47+7.42	153.97+24.06
3	7-9.9	50	170.31+15.64	89.60+12.81	30.80+3.95	39.42+4.78	161.04+20.36
4	>10	50	188.42+14.39	98.91+11.66	34.68+3.35	35.85+9.45	169.22+23.05
	P Value		<0.001	<0.001	<0.001	<0.001	<0.001
5	Female						
6	4-6.9	50	168.91+15.00	91.03+10.79	31.93+6.82	37.48+9.21	163.22+31.88
7	7-9.9	50	180.47+8.64	98.72+17.30	32.67+5.18	35.78+5.76	169.81+24.48
8	>10	50	190.81+12.16	109.47+18.85	35.89+6.90	33.81+5.42	183.84+24.59
	P Value		<0.001	<0.001	<0.001	<0.001	<0.001

Table 2 Geometric mean of HDL cholesterol and triglycerides (mg/dl) according to categories of thyroid stimulating hormone (TSH) outside the reference range, by sex and body mass index (BMI).

No		Male		Female	
1	BMI	<25	>25	<25	>25
2		HDL(mgl/dl)			
3	TSH(mU/l)				
4	4-6.9	42.45+6.96	40.59+7.87	38.80+7.03	36.63+5.28
5	7-9.9	40.33+4.53	38.62+4.95	37.47+5.65	34.73+5.66
6	>10	38.95+9.75	31.73+7.48	34.96+5.64	32.69+5.63
	P value	0.324	<0.001	0.075	<0.001
		TG-C(mgl/dl)			
8	TSH (mU/l)				
9	4-6.9	149.00+29.62	158.50+25.73	154.20+21.11	167.97+34.97
10	7-9.9	153.76+13.31	167.41+23.42	165.85+26.50	172.26+23.21
11	>10	168.35+20.51	170.40+26.77	179.93+27.25	187.63+21.44
	P value	0.310	<0.001	0.20	<0.001

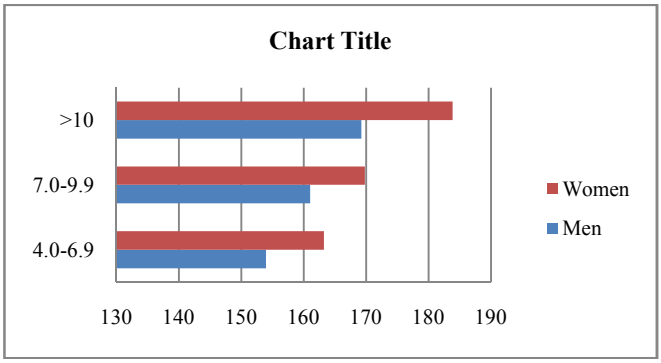

Figure 1 Geometric mean of TG by categories of TSH outside the reference range in men and women

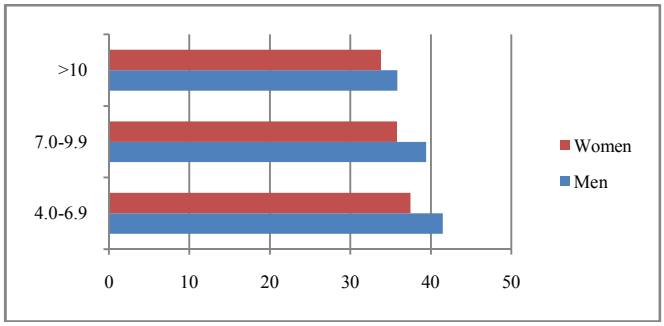

Figure 2 Geometric mean of HDL cholesterol by categories of TSH outside the reference range in men and women

DISCUSSION

Thyroid dysfunction has been shown to be associated with a common feature iedyslipidaemia[14]. Compared to normal controls, the Patients with overt hypothyroidism exhibit significantly higher TC, LDL-C and TG [15, 16].The thyroid hormone supplementation reverses the increased lipid level [17]. In subjects with subclinical hypothyroidism, significant increase in the levels of TC, LDL-C, TC/HDL ratio has been also observed compared to euthyroid subjects [18]. Contrarily, hyperthyroid patients exhibit lower level of TC, HDL-C and LDL-C [19].

This is a small population-based study, which allows an opportunity to study the association between TSH and concentrations of serum lipids in hypothyroid patients. Total serum cholesterol, LDL cholesterol, VLDL cholesterol and triglycerides were found to increase consistently with increasing TSH and that HDL decreased consistently. These associations displayed remarkably linear trends, with no indication for any threshold effects.

Our data appear to confirm the results of some of the studies of TSH among people with no apparent thyroid dysfunction. These studies showed positive associations with total serum cholesterol, LDLcholesterol, VLDL and triglycerides, and a negative association with HDL cholesterol [20, 21, 22].

There appears to be a concurrence that large number of people with TSH in the upper part of the reference range is likely to exhibit early signs of thyroid dysfunction [23]. 20 years of follow-up of the Whickham study indicated that the patients with TSH higher than 2mU/l was associated with increased risk of hypothyroidism [24].Earlier studies among euthyroid people have shown that the prevalence of thyroid peroxidase antibodies, indicating autoimmune thyroid disease, increases with increasing level of TSH [21, 23, 25]. In our study, there was a linear increase in serum lipids, with no apparent increase in the uppermost part of the reference range. However, we cannot exclude the probability of TSH more strongly related with serum lipids in patients with subtle signs of autoimmune thyroid disease.

Studies of thyroid dysfunction and its relation with metabolism may provide some understanding of mechanisms that could underlie the consistent associations in our study. Thus, high total serum cholesterol and LDL cholesterol may be caused by fewer cell-surface receptors for LDL, resulting in reduced LDL catabolism [2]. For triglycerides, reduced activity of lipoprotein lipase [26, 27] or impaired clearance of lipoproteins dependent on LDL receptor function [28], may result in higher levels. Linear positive association between outside the reference range and concentrations of total serum cholesterol, LDL cholesterol, VLDL Cholesterol and triglycerides, and a linear negative association with HDL cholesterols as seen from above data. Thus, patients with TSH levels indicating clinically normal thyroid function may have long-term harmful effects on cardiovascular system through the association with serum lipids. However, the firmness of the associations were relatively moderate, and their clinical significance remains to be determined in future studies of variations in normal thyroid function related to risk of cardiovascular disease.

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