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AN ASSOCIATIVE INVESTIGATION BETWEEN TSH AND SERUM LIPID CONCENTRATIONS IN THE POPULATION OF BHOPAL, INDIA

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ABSTRACT

The association between TSH and serum lipids in people with no apparent thyroid dysfunction is less understood. We have investigated the association between normal thyroid function, defined as TSH within the reference range and serum lipids concentrations. Cross-sectional, population based study with 1785 individuals without known thyroid dysfunction. We calculated mean concentrations of total serum cholesterol, low-density lipoprotein (LDL) cholesterol, non-high-density lipoprotein (HDL) cholesterol, HDL cholesterol and triglycerides across categories of TSH, using general linear models. Within the reference range of TSH, there was a linear and significant (*P* for trend <0.001) increase in total serum cholesterol, LDL cholesterol, non-HDL cholesterol and triglycerides, and linear decrease (*P* for trend <0.001) in HDL cholesterol with increasing TSH. Within the range of TSH that is considered clinically normal, we observed that increasing level of TSH was associated with less favorable lipid concentrations. The association with serum lipids was linear across the entire reference range of TSH.

INTRODUCTION: A hormone produced by the pituitary gland at the base of the brain in response to signals from the hypothalamus gland in the brain. Thyroid stimulating hormone (TSH) promotes the growth of the thyroid gland in the neck and stimulates it to produce more thyroid hormones. When there is an excessive amount of thyroid hormones, the pituitary gland stops producing TSH, reducing thyroid hormone production. This mechanism maintains a relatively constant level of thyroid hormones circulating in the blood.

TSH is a peptide hormone synthesized and secreted by thyrotrope cells in the anterior pituitary gland, which regulates the endocrine function of the thyroid gland. Hypothyroidism is a common endocrine disorder resulting from deficiency of thyroid hormone. It usually is a primary process in which the thyroid gland produces insufficient amounts of thyroid hormone. It can also be secondary- that is, lack of thyroid hormone secretion due to inadequate secretion of either thyrotropin (ie, thyroid-stimulating hormone [TSH]) from the pituitary gland or thyrotropin-releasing hormone (TRH) from the hypothalamus (secondary or tertiary hypothyroidism). The patient's presentation may vary from asymptomatic to, rarely, coma with multisystem organ failure (myxedema coma). The most common cause for hypothyroidism is autoimmune thyroid disease (Hashimoto thyroiditis).

Subclinical hypothyroidism, also referred to as mild hypothyroidism, is defined as normal serum free T4 levels with slightly high serum TSH concentration, may also be associated with unfavourable serum lipids, especially if TSH is higher than 10mU/l [1]. Further, thyroxine treatment of sub-clinically hypothyroid individuals may reduce total serum cholesterol and low

density lipoprotein (LDL) cholesterol [2-4]. Some studies have shown that serum lipids may also be altered within the range of thyroid function that is considered clinically normal. Evidence from the study suggests that total serum cholesterol and triglycerides increased consistently with increasing TSH and that HDL decreased consistently [5]. These associations displayed remarkably linear trends, with no indication for any threshold effects.

There is a lack of population-based studies of the association between TSH and serum lipid concentrations in India. In the present study 2000 individuals from the general population, we therefore examined the association between TSH within the reference range and total serum cholesterol, LDL cholesterol, non-HDL cholesterol, HDL cholesterol and triglycerides. We also investigate the association with lipid levels for TSH outside the reference range.

MATERIALS AND METHODS:

Subjects and Methods: A non fasting venous serum samples were drawn from each individual. Total serum cholesterol, HDL cholesterol and triglycerides were measured shortly after serum collection. Analysis of TSH was carried out in subsamples of population, including all women above 40 years of age and 50% of men above 40 years of age. In addition, TSH was measured in 5% random samples of men and women 20-40 years of age.

Laboratory Measurements: Serum concentrations of thyroid stimulating hormone (TSH) and free thyroxine were analyzed at the Department of Microbiology, Barkatullah University, Bhopal, using ELISCAN ELISA kit. A euthyroid adult population has been studied and generalized range was defined as 0.50-5.0 mU/l.

Serum lipids were analyzed by ELISA reader (Lisa plus, Germany), applying reagents from Himedia Laboratories, Mumbai. Total serum cholesterol and LDL cholesterol were measured by an enzymatic esterase method, and HDL cholesterol was measured after precipitation with phosphotungstate and magnesium ions. Triglycerides were also measured with an enzymatic colorimetric method.

LDL cholesterol was calculated using the Friedwald formula: LDL cholesterol=total serum cholesterol–HDL cholesterol- one- fifth of the triglyceride concentration [6]. The non-fasting state of the serum samples suggests that concentrations of triglycerides and LDL cholesterol were not accurately measured. Therefore, we calculated non-HDL cholesterol as the difference between total serum cholesterol and HDL cholesterol. Non-HDL cholesterol incorporates not only LDL cholesterol but also the cholesterol content of other atherogenic lipoproteins [7].

Statistical Analysis: Among the 2000 individuals who were selected for TSH analysis, we excluded 215 from this study, leaving 1785 individuals for analysis. Reasons for exclusion were invalid TSH or lipid measurements. We studied the associations between TSH and serum lipid levels using general linear models where lipid concentrations log transformed due to non-normal distribution. We calculated geometric means of each lipid for six categories of TSH within the reference range of 0.5-5.0 mU/l, in men and women. Using TSH as a continuous variable, we estimated partial-regression coefficients, from which we calculated the percentage change in serum lipid levels per mU/l increase in TSH. Statistical significance was assessed by *P* value for trend.

RESULTS AND DISCUSSION:

Table 1 shows the association between TSH within the reference range and serum lipid concentrations, in men and women. There was a consistent and significant increased in total serum cholesterol, LDL cholesterol, non-HDL cholesterol and triglycerides concentrations, with increase concentrations of TSH (reference range, 0.5-5.0 mUl/l).

With increasing TSH, there was also a consistent reduction in HDL cholesterol. The linearity of the association of TSH with non-HDL cholesterol, HDL cholesterol and triglycerides is illustrated in **Figs. 1, 2** and **3** respectively. This investigation provides a unique opportunity to study the association between TSH and serum lipids concentrations within the reference range of TSH.

TABLE 1: GEOMETRIC MEAN OF SERUM LIPIDS (mmol/l) ACCORDING TO CATEGORIES OF THYROID STIMULATING HORMONE (TSH) WITHIN THE THE REFERENCE RANGE (0.50-5.0 mU/l), IN MEN AND WOMEN

TSH (mU/l)	*N*	Total serum cholesterol	LDL cholesterol	Non-HDL Cholesterol	HDL cholesterol	Tryglycerides
Men						
0.5-0.99	110	5.75	4.14	4.44	1.23	1.44
1.00-1.4	153	5.82	4.18	4.48	1.22	1.46
1.5-1.9	120	5.86	4.22	4.54	1.22	1.48
2.0-2.4	85	5.90	4.26	4.62	1.20	1.54
2.5-2.9	68	5.92	4.28	4.68	1.19	1.66
3.0-3.5	42	5.96	4.32	4.74	1.16	1.68
3.6-4.0	38	6.02	4.34	4.76	1.14	1.70
4.1-4.5	22	6.08	4.38	4.82	1.12	1.74
4.6-5.0	18	6.14	4.40	4.84	1.10	1.76
% Change (95% CI)	--	5.9(5.8-6.0)	4.2(4.2-4.3)	4.6(4.5-4.7)	1.1(1.1-1.2)	1.6(1.5-1.7)
P for trend		<0.001	<0.001	<0.001	<0.001	<0.001
Women						
0.5-0.99	154	5.90	4.06	4.34	1.46	1.32
1.00-1.4	248	5.95	4.08	4.36	1.46	1.34
1.5-1.9	225	6.02	4.10	4.36	1.45	1.34
2.0-2.4	202	6.02	4.14	4.42	1.42	1.38
2.5-2.9	118	6.04	4.16	4.48	1.42	1.36
3.0-3.5	80	6.06	4.20	4.52	1.40	1.45
3.6-4.0	42	6.08	4.22	4.54	1.38	1.45
4.1-4.5	32	7.02	4.22	4.56	1.34	1.48
4.6-5.0	28	7.04	4.24	4.60	1.32	1.50
% Change (95% CI)		6.2(5.8-6.5)	4.1(4.1-4.2)	4.4(4.3-4.5)	1.4(1.3-1.4)	1.4(1.3-1.4)
P for trend		<0.001	<0.001	<0.001	<0.001	<0.001

% Change, percentage change in serum lipids per mU/l increase in TSH. LDL cholesterol was calculated only if serum triglycerides concentrations were lower than 4.5mmol/l.

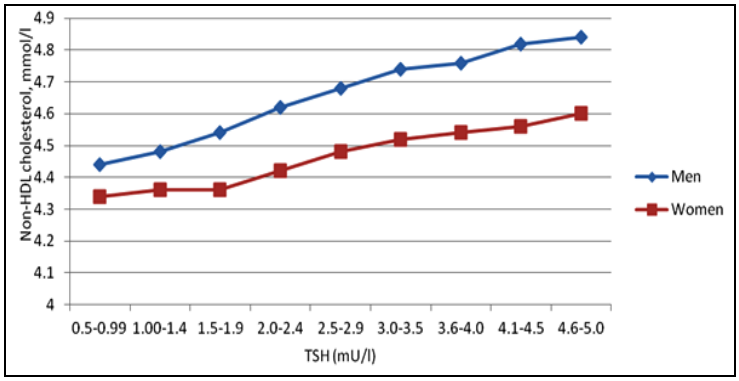

FIG. 1: GEOMETRIC MEAN OF NON-HDL CHOLESTEROL BY CATEGORIES OF TSH WITHIN THE REFERENCE RANGE (0.50-5.0 mU/l), IN MEN (*n* = 656) AND WOMEN (*n* = 1129)

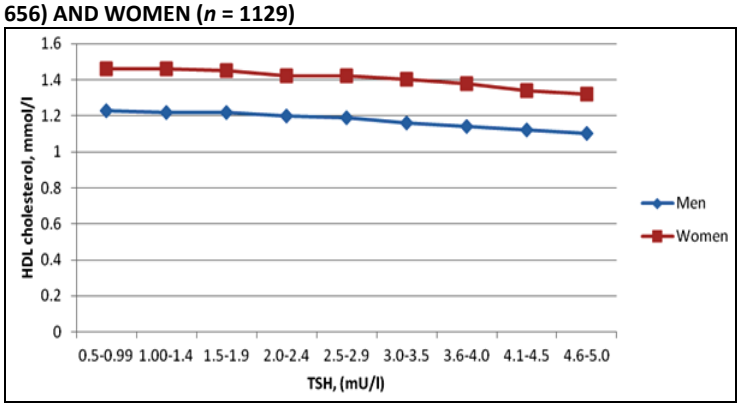

FIG. 2. GEOMETRIC MEAN OF NON-HDL CHOLESTEROL BY CATEGORIES OF TSH WITHIN THE REFERENCE RANGE (0.50-5.0 mU/l), in men (*n* = 656) AND WOMEN (*n* = 1129)

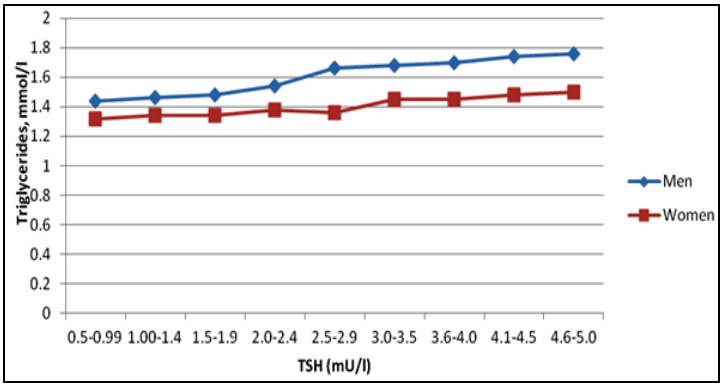

FIG. 3. GEOMETRIC MEAN OF TRIGLYCERIDES BY CATEGORIES OF TSH WITHIN THE REFERENCE RANGE (0.50-5.0 mU/l), IN MEN (*n* = 656) AND WOMEN (*n* = 1129)

We observed that total serum cholesterol, LDL cholesterol, non-HDL cholesterol and triglycerides increased consistently with increasing TSH and that HDL decreased consistently. These associations displayed remarkably linear trends, with no indication of threshold effects. Our study also substantiates the previous findings of Asvold *et al* [5]. Mild elevations of TSH are associated with changes in lipid profile significant enough to raise the cardiovascular risk [7]. Hypothyroidism results in a small increase in LDL cholesterol and decrease in HDL cholesterol that

enhances the risk for development of atherosclerosis and coronary artery disease, there is no clear evidence that hypothyroidism causes clinical heart disease [8].

CONCLUSION: In the present study, we concluded that positive association between TSH in the reference range and concentrations of total serum cholesterol, LDL cholesterol, non-HDL cholesterol and triglycerides, and a linear negative association with HDL cholesterol. TSH levels indicating that clinical normal thyroid function may have long term harmful effects on cardiovascular health by the association with serum lipids.

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