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Thyroid Dysfunction and its Effect in Serum Lipids

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ABSTRACT

Background: Thyroid hormones are involved in regulation of lipid and lipoprotein metabolism; therefore, thyroid dysfunctions induce significant change in lipid levels. This study was conducted to study the prevalence of thyroid dysfunction and to observe the relationship between hypothyroidism and hyperthyroidism in lipid profile.

Methods: The study group comprised of 567 patients. 100 subjects with normal thyroid profile and no history of any chronic diseases were taken as control group. Serum free triiodothyroxine(fT3), free thyroxine(fT4), thyroid stimulating hormone(TSH), Total cholesterol, low density lipoprotein(LDL) cholesterol, high density lipoprotein(HDL) cholesterol and Triglycerides were estimated in these patients and the results were analyzed using SPSS 11.5.

Results: Out of 567 sera tested, 146 (25.75%) had thyroid dysfunction. Total cholesterol and LDL-cholesterol was significantly raised in hypothyroidism. However, there was no significant association among lipid levels in hyperthyroid and control group.

Conclusions: Lipid profile was significantly raised in hypothyroid patients thereby, indicating the need for monitoring of lipid levels in patients with thyroid dysfunction to avoid the risk of cardiovascular diseases.

Keywords: cardiovascular diseases, dyslipidemia, hyperthyroidism, hypothyroidism.

INTRODUCTION

Diseases of thyroid gland are amongst the most abundant endocrine disorder in the world second only to diabetes mellitus.[1] Thyroid diseases are primarily conditions that affect the amount of thyroid hormones being produced. Excess production leads to hyperthyroidism while diminished production leads to hypothyroidism.[2] Thyroid hormones are important modulator of intermediary metabolism. They affect synthesis, mobilization and degradation of lipids, although degradation is influenced more than synthesis. Consequently, thyroid dysfunction particularly hypothyroidism is associated with dyslipidemia which increase the risk of endothelial dysfunction, hypertension and cardiovascular diseases.[3]

Hypothyroidism, like obesity is one of the pathological conditions most frequently associated with disorders of lipid metabolism.[4] Overt hypothyroidism is characterized by hypercholesterolemia and a marked increase in LDL-cholesterol because of a decreased fractional clearance of LDL by a reduced number of LDL receptors in the liver. However the controversy persists regarding the lipids level in subclinical hypothyroidism and its clinical significance. Moreover it is likely to be a risk factor for atherosclerosis and coronary diseases.[3, 5]

Endocrine diseases are increasing globally but are growing more rapidly in Asia.[6] Iodine deficiency has

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been a major cause of morbidity in the past and at present, thyroid disorders other than iodine deficiency disorders in the form of thyroiditis, hypothyroidism or autoimmune thyroid dysfunctions are on rise. The WHO estimates that substantially greater than 190 million suffer from iodine deficiency disorders.[7] Nepal is an endemic area with regard to iodine deficiency and nutritional iodine deficiency are thought to be prevalent in all Himalayan, sub-Himalayan and Terai regions of Nepal.[8] The prevalence of thyroid disorder is very high in Nepal however, studies focusing on the association between thyroid function markers and lipids are sparse. So, this study aims to estimate the prevalence of thyroid dysfunction and the relationship between thyroid dysfunction and serum lipids.

METHODS

A cross-sectional study was conducted in National Public Health Laboratory, Teku from 25th October to 24th January 2010 among 567 patients with suspicion of thyroid disorders. Ethical approval was taken from the hospital. 100 patients with normal thyroid profile and no history of other chronic diseases were taken as control group. Detailed information of the patients was collected after informed consent with the help of pre-test proforma that included age, sex and family or personal history of chronic diseases.

After 12 hours overnight fasting, 6ml blood was collected by standard venipuncture method, and the serum was separated. fT3, fT4 a nd TSH were quantitatively estimated by Enzyme linked immunosorbent assay (ELISA) method while TC, HDL and TG were estimated by colorimetric method using kits and standard protocols of Human, Germany. Computer software program SPSS 11.5 was used for statistical analyses of different parameters.

RESULTS

Among the 567 patients suspected of thyroid disorders, 25.75% had thyroid dysfunction. Subclinical hypothyroidism was the most prevalent thyroid disorder overall (14.11%). There was a trend toward a higher prevalence of overt thyroid dysfunction in the age group less than 20 and that of subclinical thyroid dysfunctions in the age group 20-40. Gender wise, female had higher prevalence of all forms of thyroid dysfunctions.

Positive correlation was observed between TSH and TC (p=0.432), TSH and HDL (p=0.424) and TSH and LDL (p=0.472) in case of overt hypothyroidism and between TSH and TC (p=0.214) and TSH and LDL (p=0.277) in case of subclinical hypothyroidism (Table 1). The serum TC and LDL levels in hypothyroid individuals (both overt and subclinical) were significantly higher than euthyroid subjects (p<0.001) but the levels were comparable between hyperthyroid and euthyroid group (Table 2). The TC and LDL level increased progressively with the increasing TSH values (Table 3).

Table 1. Pearson correlation coefficient between fT3, fT4, TSH and lipid profile.

		TC	HDL	LDL	TG
Overt hypothyroidism	fT3	-.056	.007	-.004	-.243
	fT4	-.360	-.085	-.387	.046
	TSH	.432*	.424*	.472*	-.304
Subclinical hypothyroidism	fT3	-.095	-.051	-.042	-.216
	fT4		.099	-.107	-.076
	TSH	-.111 .214**	.023	.277**	-.122
Overt hyperthyroidism	fT3	-.506	-.234	-.470	.354
	fT4	-.344	.261	-.422	.157
	TSH	.351	-.407	.361	.318
Subclinical hyperthyroidism	fT3	-.374	-.216	-.309	.086
	fT4	-.293	-.375	-.235	.231
	TSH	.213	.019	.274	-.217

**Correlation is significant at the 0.01 level (1-tailed).
*Correlation is significant at the 0.05 level (1-tailed).

Table 2. Comparison of mean lipid profiles between normal and thyroid dysfunction patients.

	Overt hypothyroid	Subclinical hypothyroid	Normal	Overt hyperthyroid	Subclinical hyperthyroid
TC mg/dl	213.05±63.80 P=0.000	202.88±50.74 P=0.000	159.51±27.13	146.33±25.67 P=0.159	162.87±39.35 P=0.656
HDL mg/dl	39.86±9.45 P=0.747	42.24±10.51 P=0.009	39.19±8.78	39.67±9.21 P=0.974	45.44±11.29 P=0.010
LDL mg/dl	136.14±60.75 P=0.000	123.62±47.25 P=0.000	89.56±29.70	79.89±25.41 P=0.342	91.81±39.46 P=0.782
TG mg/dl	177.81±61.01 P=0.069	184.02±85.70 P=0.000	147.86±71.10	121.78±31.68 P=0.277	117.50±48.50 P=0.099

P value indicates the significance of t-test

Table 3. Lipid profile in categorical TSH value.

TSH (μU/ml)	TC (mg/dl (mean±s.d.)	HDL (mg/dl) (mean±s.d.)	LDL (mg/dl) (mean±s.d.)	TG (mg/dl (mean±s.d.)
0.0-0.3	156.92±35.40	43.36±10.77	87.52±34.97	119.04±42.53
0.3-6.2	159.51±27.13	39.19±8.78	89.56±29.70	147.86±71.10
6.2-10.0	194.05±51.74	40.11±9.6	115.17±47.51	196.71±100.04
10.0-15.0	197.64±43.90	44.19±11.51	113.14±41.22	184.22±80.21
15.0-20.0	206.59±38.05	44.32±11.51	128.86±33.65	166.62±71.68
20.0-40.0	226.42±62.55	41.50±9.32	151.89±57.00	168.66±51.11
P value	0.000	0.498	0.000	0.000

P value indicates the significance of t-test.

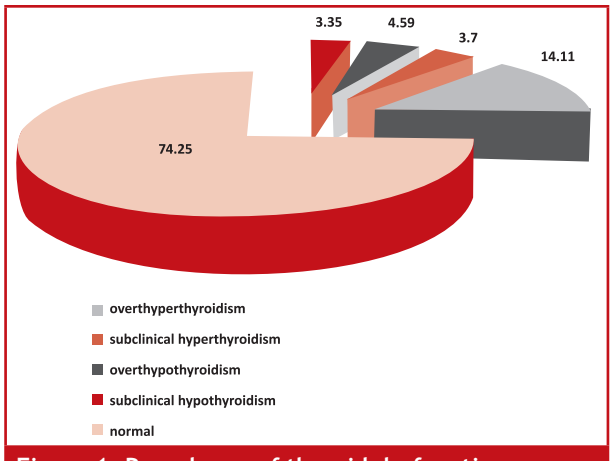

Figure 1. Prevalence of thyroid dysfunction.

DISCUSSION

Thyroid dysfunction, along with a higher prevalence of goiter, is a major public health problem in Nepalese population as Nepal lies in an endemic iodine deficiency area.[6] In this study, the prevalence of thyroid dysfunction, viz. overt hypothyroidism, subclinical hypothyroidism, overt hyperthyroidism and subclinical hyperthyroidism was 3.70%, 14.11%, 3.35% and 4.59% respectively. The prevalence of thyroid dysfunction in a population can produce different results according to the subgroups or diagnostic criteria chosen.[9] The prevalence of hypothyroidism in this study was slightly higher than in eastern Nepal (13.68%) while the prevalence of hyperthyroidism was lower than that reported by Jha et al (17.19%) and Baral et al (13.68%).[10,11] The difference in results may reflect the difference in methodology employed (total population screening or hospitalized patients). There are also geographic variations in the risk of thyroid disease between regions, which could reflect variety of environmental and/or genetic factors.[9]

The prevalence of overt hypothyroidism and overt hyperthyroidism was found to higher in the age group <20 while that of subclinical hypothyroidism and subclinical hyperthyroidism was found to be higher in the age group 20-40years which is in accordance with the findings by Baral et al.[10] Higher prevalence of thyroid dysfunction in the middle age and young may be attributed to stress and environmental pollutants.[12] Although most studies have reported higher prevalence of thyroid dysfunction in elderly, this study contradicted.[13-16] This could be due to lesser number of elderly patients being referred for the test. Further the clinical features of thyroid disorders tend to be non-specific and fewer in elderly compared to younger patients and the symptoms are often confused with normal aging process and coexisting diseases.[17] This results in greater number of elderly patients being undiagnosed.

In accordance with the results published by other studies, this study also found higher prevalence of thyroid dysfunctions in female.[13, 18, 19] Sisk reported that women are 5-8 times more likely to develop hypothyroidism and 8-10 times more likely to develop hyperthyroidism.[19] Women face a greater risk of developing thyroid diseases than men due to sex difference in the prevalence of autoimmune diseases.[20]

There was an association between hypothyroidism and TC>200, LDL>130 and TG>200mg/dl; 48.40% of hypothyroid patient had hypercholesterolemia and as compared with 3.57% in the control group (p=0.000) and 32.30% had hypertriglyceridemia compared with 15% in control (p=0.000). 40.99% had LDL>130mg/dl compared to 6.43% of control (p=0.000). Cabral et al found that 55.7% and 17.3% of hypothyroid individual had hypercholesterolemia and hypertriglyceridemia respectively and combination of hyper cholesterolemia and hypertrigyceridemia is present in about 40-70% of hypothyroid individuals.[21]

Although overt hypothyroidism has always been associated with hypercholesterolemia, there is much controversy in association of subclinical hypothyroidism and hypercholesterolemia.[22] In this study, all the parameters of lipid profile i.e., TC, HDL, LDL and TG were found to be increased in subclinical hypothyroidism and

the difference was statistically significant. Increase of total cholesterol and LDL can be attributed to the effect of thyroid hormone on expression of LDL receptors and CYP7A, a rate limiting enzyme in bile acid synthesis.[23] Decreased thyroid function not only increases the number of LDL particles but also promote LDL oxidability, thereby increasing the risk of atherosclerosis.[24]

HDL was increased in both overt and subclinical hypothyroidism however, the increase was significant only in case of subclinical hypothyroidism (p=0.009). Elevation in HDL cholesterol could be due to decreased activity of cholesteryl ester transfer protein and hepatic lipase.[25]

Triglyceride level also increased in both overt and subclinical hypothyroidism. The difference was statistically significant in case of subclinical hypothyroidism (p=0.000) but only marginally significant in case of overt hypothyroidism (p=0.069). The increase in triglyceride level in hypothyroidism is attributable to the decreased activity of lipoprotein lipase, which is responsible for the clearance of triglyceride rich lipoprotein.[26]

The mean TC, LDL and TG levels rose with a significant trend across grades of thyroid function as observed by Canaris et al.[13] It was notable in this study that the mean TC, LDL and TG of subjects with modest elevations of serum TSH (i.e. between 6.2-10mU/ml) were higher than that of the euthyroid group. While several studies have linked hyperlipidemia with cardiovascular morbidity, it is arguable whether this reflects a clinically significant difference.[27-29] Normalizing subclinical hypothyroidism may have a role in the treatment of hyperlipidemia and perhaps the prevention of cardiovascular morbidity but to what degree is unclear.[30]

The TC, LDL and TG levels were found to be decreased in overt hyperthyroidism while HDL level was increased. In subclinical hyperthyroidism, however, TC and LDL levels were slightly increased but not significant statistically. Despite the increased activity of HMG-CoA reductase, the cholesterol levels tend to increase in hyperthyroidism due to augmented excretion of cholesterol by bile together with enhanced receptor mediated catabolism of LDL particles.[23,24] Variations observed in TG levels could be due to the action of thyroid hormone on VLDL. Catabolism of VLDL is accelerated in hyperthyroidism which is probably related to changes in activity of lipoprotein lipase and/ or hepatic TG lipase.[31, 32]

CONCLUSIONS

Overall both overt and subclinical hypothyroidism is associated with abnormal lipoprotein levels which can lead to cardiovascular diseases. It has been observed that the abnormal lipid pattern is fully reversed to normal by treatment with thyroxine so screening of dyslipidemic patient for thyroid abnormalities is necessary along with prudent substitution therapy to counteract the cardiovascular risk from dyslipidemia.

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