CORRELATION OF SUBCLINICAL THYROID DYSFUNCTION WITH DYSLIPIDEMIA

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Date Received:
August 03, 2016
Date Revised:
March 22, 2017
Date Accepted:
March 27, 2017

ABSTRACT

Objective: To determine the relationship between sub-clinical thyroid dysfunction (STD) and dyslipidemia.

Methodology: This cross sectional study was conducted in Pakistan Health Research Centre (PHRC), Khyber Medical College and Khyber Medical University, Hayatabad Peshawar, Pakistan in the year 2012-2013. Thirty patients of both genders and between 10-70 years of age, residing in Peshawar were studied. Lipid profiles were assessed for relationship with sub-clinical hypothyroidism (SCH-I) and sub-clinical hyperthyroidisms (SCH-II).

Results: Total cholesterol (TC) was 194.67 ±34.81 in (SCH-I) and 151.29 ±35.22 in (SCH-II); low density lipoprotein cholesterol (LDL-C) was 146.56 ±47.6 in (SCH-I) and 89.48 ±27.15 in (SCH-II); triglycerides (TG) were 91.89 ±33.62 in (SCH-I) and 125.62 ±68.98 in (SCH-II). Serum TC and LDL-C levels were significantly high in SCH-I (p values 0.033 & 0.029 respectively). Serum TC, LDL-C, VLDL-C and TG levels were negatively correlated with STD (r values -0.601, -0.533, -0.401 & -0.401 respectively).

Conclusions: Serum TC and LDL-C levels were high in SCH-I. Lipid profile was non-significant in SCH-II patients. Serum TC, LDL-C, VLDL-C and TG were negatively correlated with STD.

Key Words: Sub-clinical thyroid dysfunction, Sub-clinical hypothyroidism, Sub-clinical hyperthyroidism, Dyslipidemia, Overt hyperthyroidism

This article may be cited as: **Attaullah S, Haq BS. Association of subclinical hypothyroidism and subclinical hyperthyroidism with hypercholesterolemia. J Postgrad Med Inst 2017; 31(2): 142-6.**

INTRODUCTION

The condition of upset thyroid hormone levels is termed as sub-clinical thyroid dysfunction (STD). Sub-clinical hypothyroidism (SCH-I) is not an unusual disorder with a frequency of, approximately 5-10%, in the general population[1]. It seems that the elderly population is mainly predisposed to sub-clinical hyperthyroidism (SCH-II)[2]. The development of overt hypothyroidism or overt hyperthyroidism can be viewed as the final stage of autoimmune thyroid disease. The immediate prior stage is the subclinical phase when serum TSH is abnormal but serum fT_4 is still within the desired range[3].

Hypercholesterolemia is closely associated with SCH-I. Subclinical hypothyroid patients have high serum LDL-C and total cholesterol, than in euthyroid controls[4]. However HDL-C and TAG were in the normal range. Overt thyroid dysfunction is related to a variety of metabolic abnormalities like hypercholesterolemia[5]. Hypothyroidism is frequently associated with disorders of lipid metabolism[6]. Such patients were more prone to experience elevated levels of cholesterol and triglycerides[7,8]. Increase in TG levels may be due to lesser activity of LPL, whereas HDL-C is in the normal range.

Patients with subclinical hypothyroidism sometimes might have minor dysfunctions of serum lipid profile and heart diseases[9-11]. Incidence is 3-8%, in different age groups and generally more frequent in women. After crossing 60 years of age the incidence increases to 10% in both male and female[12,13].

Alterations in cardiac haemo-dynamics has been stated in some, but not other studies of subclinical hyperthyroidism[14]. Although the data relating to the raise of heart rate and the supra-ventricular arrhythmias in patients with subclinical hyperthyroidism are non-consistent. The present study was carried out to determine the relationship between sub-clinical thyroid dysfunction (STD) and dyslipidemia.

METHODOLOGY

The selected cases were studied at PHRC, Khyber Medical College and Khyber Medical University, Hayatabad Peshawar, Pakistan in the year 2012-2013.

Patients of both genders between 10-70 years of age residing in Peshawar, visiting IRNUM were considered for the collection of data. A questionnaire, which incorporated information about gender, age, locality and clinical diagnosis etc. were collected. Ethical approval and consent of the patients were obtained. This study consisted of total 30 subjects, 9 of subclinical hypothyroidism (SCH-I) and 21 of subclinical hyperthyroidism (SCH-II). Patients having diseases like hypertension, DM and CHD, thyroidectomy and those taking thyroxin were excluded from this study.

Serum fT_3 and fT_4 were determined following the principle of labeled antibody, known as competition assay. Thyroid stimulating hormone was estimated by using radioimmune assay (RIA). Serum lipids were measured by applying enzymatic colorimetric method (CHOD-PAP and GPO-PAP), using commercially available kit provided by Roche Diagnostic by using semi automatic analyzer Merck 200[16,17]. The reagents used for HDL-C and LDL-C homogenous enzymatic calorimetric assay were obtained from Roche diagnostics US, using Cobs C – III analyzer that automatically calculates the analyst concentration of each sample. Wilson's formula has been used for the calculation of very low density lipoprotein cholesterol (VLDL-C)[18].

The Software SPSS version 16 was used for data analysis. The level of significance chosen was 0.05. The difference was considered as statistically significant if p-value was $\leq$0.05. Coefficient of correlation (r) was also calculated. The correlation value was calculated between two parameters i-e subclinical thyroid disorder and serum lipid profile. When the r – value was nearer to +1 the correlation was considered as strongly positive, and if the "r" was negative the correlation was also negative, however if "r" was 1 the correlation was considered as perfect correlation.

RESULTS

Out of total 30 subjects, 9 were of SCH-I and 21 were of SCH-II. Results in figure 1 showed both male and female subjects of sub-clinical hypothyroid and sub-clinical hyperthyroid cases distributed on the basis of age groups. A greater prevalence (70%) of sub-clinical hyperthyroidism is shown by the patients in the age group 21– 50 years. For sub-clinical hypothyroidism the prevalence was (30%) for the same age group.

The thyroid hormones were compared with sub clinical hypothyroid and sub-clinical hyperthyroid subjects. The association was found to be statistically significant only in case of thyroxin. Negative correlation of thyroid function tests with sub-clinical hypothyroidism and sub-clinical hyperthyroidism was observed, as shown in table 1.

Total cholesterol (TC) was 194.67 ±34.81 in (SCH-I) and 151.29 ±35.22 in (SCH-II); low density lipoprotein cholesterol (LDL-C) was 146.56 ±47.6 in (SCH-I) and 89.48 ±27.15 in (SCH-II); triglycerides (TG) were 91.89 ±33.62 in (SCH-I) and 125.62 ±68.98 in (SCH-II). Serum TC and LDL-C levels were significantly high in SCH-I (p values 0.033 & 0.029 respectively). In case of SCH-I significant differences were observed with lipid parameters i-e, TC and lipoproteins (low density) whereas, SCH-II has non-significant differences with all the lipid parameters (table 2).

Serum TC, LDL-C, VLDL-C and TG levels were negatively correlated with STD (r values-0.601, -0.533, -0.401 & -0.401 respectively).Only high density lipoprotein cholesterol had a positive relationship when compared with sub-clinical hypothyroidism and hyperthyroidism (table 3).

Figure 1: Frequency values of SCH-I and SCH-II

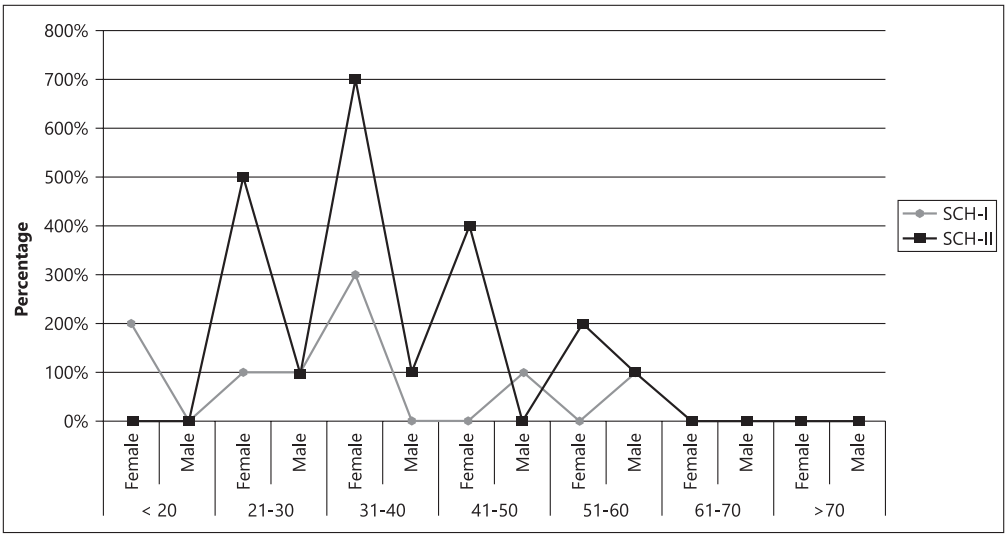

Table 1: Comparison of TFTs with SCH-I & SCH-II

Laboratory Results n=30	SCH-I (n=09)			SCH-II (n=21)				
	Min	Max	Mean± SD	Min	Max	Mean ± SD	r	P value
T3(pmol/L)	2.60	5.10	4.10± 0.91	3.10	5.90	4.26 ± 0.85	-0.437▲	0.506▲
T4(pmol/L)	11.20	19.00	13.76± 2.65	13.70	23.00	18.74 ± 3.09	-0.591▲	0.002*
TSH(uIU/ml)	51.0	51.0	51.0	0.001	0.001	0.001	NA	NA

P* significant
P▲ non-significant
r ▲ negative correlation

Table 2: Comparison of lipid profile with SCH-I & SCH-II

Laboratory Results n=30		SCH-I (n=09)					SCH-II (n=21)				
		Min	Max	Mean	SD	P value	Min	Max	Mean	SD	P value
Lipid Profile	TC	137.0	240.0	194.67	34.81	0.033*	70.0	211.0	151.29	35.227	0.452▲
	HDL-C	17.0	67.0	40.49	14.74	0.723▲	12.0	61.20	37.76	15.15	0.663▲
	LDL-C	83.0	217.0	146.56	47.6	0.029*	39.0	132.00	89.48	27.15	0.653▲
	VLDL-C	5.2	27.8	18.38	6.72	0.633▲	5.6	55.0	25.12	13.79	0.777▲
	TG	26.0	139.0	91.89	33.62	0.712▲	28.0	275.0	125.62	68.98	0.777▲

p ** highly significant
p* significant
p▲ non-significant

Table 3: Correlations of lipid profile with SCH-I & SCH-II

Laboratory Results n=30		SCH-I (n=09)				SCH-II (n=21)				
		Min	Max	Mean	SD	Min	Max	Mean	SD	r
Lipid Profile	TC	137.0	240.0	194.67	34.81	70.0	211.0	151.29	35.227	-0.601▲
	HDL-C	17. 0	67.0	40.49	14.74	12.00	61.20	37.76	15.15	0.735*
	LDL-C	83. 0	217.0	146.56	47.6	39.00	132.00	89.48	27.15	-0.533▲
	VLDL-C	5. 2	27. 8	18.38	6.72	5. 6	55.0	25.12	13.79	-0.141▲
	TG	26. 0	139.0	91.89	33.62	28.0	275.0	125.62	68.98	-0.141▲

r *** perfect correlation
r ** strong correlation
r * positive correlation
r▲ negative correlation

DISCUSSION

This study found that sub-clinical thyroid dysfunctions were more frequent in the age group of 21-50 years. Gender wise, female had higher prevalence of SCH-I (30%) and SCH-II (70%) thyroid dysfunctions. This is in accordance with a study stated that, women face a greater risk of developing thyroid diseases than men due to difference in the prevalence of autoimmune diseases[21].

The current study demonstrated that there was a significant increase in the mean difference of total cholesterol and LDL cholesterol for subclinical hypothyroid when compared with euthyroid group. The increase in serum TC and LDL-C levels may be due to inactive life style, defective metabolism like hypothyroidism and hyperthyroidism, severe stress and socioeconomic conditions. Gender and genetics may also be the contributory factors for this dysfunction. HDL-C concentration is usu-

ally normal or even elevated which is in agreement with the results given by Hueston[19]. In SCH-I, the occurrence of dyslipidemias is controversial. Some reported elevated TC, TG and LDL-C, others did not find any significant difference in serum lipid levels. However, a significant correlation was observed between T_4 and TSH with TC and TAG as independent parameters. This probably explains the unaltered TC and TAG in some studies and the elevated levels in others, as the increased LDL is being masked by the diminished LDL fraction. It was reported in 2007 that there was no significant difference for SCH-I in lipid levels when compared to controls[20].

Elevated TC level in hypothyroidism and SCH-I can be a significant risk factor causing CVD. It is therefore, substantial to screen for TC level in such patients, in order to prevent from associated CVD[22]. Thyroid hormones are the principal regulators of energy balance. Their role in obesity has been the focus of various scientific studies. The unfavorable effects of high levels of serum TSH on the lipid metabolism have been reported and follow-up studies have shown an increase in the risk of atherosclerosis and cardiovascular events in sub-clinical hypothyroid subjects. Such variations are probably caused by a number of environmental factors in hilly areas of Rawalpindi, of which, iodine intake level seems to be of prime importance[23]. In another cross-sectional study it was reported that there is no association of lipids with SCH-I[24].

No association was established between lipid parameters and SCH-I, as studied in South India, by Raman et al.[25] Another research suggested a positive correlation of TSH with TC and LDL and a negative correlation with HDL. Whereas free T_3 and T_4 were negatively co-related with TC and LDL, while no relationship between TG and TFTs was established[26].

On the other hand, sub-clinical hyperthyroidism is accompanied by a decrease in serum levels of total, LDL and HDL cholesterol[27]. In SCH-II a decreased prevalence of lipid profile abnormalities is observed. Moreover, no difference in LDL-C, decrease in HDL-C and no change in TG has been observed. Previous evaluations differ in their suppositions and recommendations, often a consequence of troubles in understanding inadequate and conflicting data. Due to this uncertainty, clinicians still desire knowledgeable assistance for the diagnosis and management of sub-clinical thyroid diseases[28].

Clinical hyperthyroidism has been associated with systolic hypertension, increased pulse pressure, and possibly hyperhomocysteinemia. Additionally, patients with overt hyperthyroidism have an increased risk of thrombosis[29]. However, the association of SCH-II with CHD risk and cardiovascular mortality is not clear. Ochs et al[30] found a possible association, while the meta-analysis by Singh et al[31] found no significant association. Jeong et al[32] in a study of 382 patients with ischemic stroke found no difference in the prevalence of SCH-II (1, 6%) in comparison to the general population.

CONCLUSION

Serum TC and LDL-C levels were high in sub-clinical hypothyroidism (SCH-I). Lipid profile was non-significant in sub-clinical hyperthyroidisms (SCH-II) patients. Serum TC, LDL-C, VLDL-C and TG were negatively correlated with sub-clinical thyroid dysfunction (STD).

RECOMMENDATIONS

Higher serum TC, LDL-C, levels increases the risk of CHD therefore, the cardiovascular status of STD, patients should be monitored carefully. Large population based studies are needed to generalize these findings and to ascertain the therapeutic guidelines for executing lipid lowering agents in subclinical hypothyroidism.

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CONTRIBUTORS

SA conceived the idea, planned the study, and drafted the manuscript. BSH helped acquisition of data, drafted the manuscript and did statistical analysis. All authors contributed significantly to the submitted manuscript.