

Original Research Article

Clinical profile and dyslipidemia in subclinical hypothyroidism

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Abstract

Background: Subclinical hypothyroidism (SH) is more frequent in areas of iodine sufficiency as compared to iodine-deficient areas. The burden of SH in India is expected to increase with increasing iodine sufficiency. Studies have shown conflicting results concerning not only the degree of lipid changes in SH but also the effect of thyroxine substitution therapy. The effects of thyroxine replacement on lipid levels are not completely understood. Indian studies on dyslipidemia in SH and the effect of thyroxine on lipid profile are currently lacking.

Aim of the study: To assess the lipid profile abnormalities in patients with subclinical hypothyroidism.

Materials and methods: The study was conducted in the year 2018, at Madha Medical College and Research Institute, Chennai. 96 patients were included in the study. Patients presenting to these op with vague complaints of obesity, a recent gain of weight, tiredness, coarse facial features, hair loss, dry skin, infertility, voice changes, memory disturbance, cognitive dysfunction, mood disorders, swelling of the neck, menstrual irregularities are selected. They are screened for subclinical hypothyroidism by doing fasting TFT comprising free T4, free T3, and TSH, and fasting lipid profile is also done for the patient. Among the 620 patients screened for subclinical hypothyroidism, 96 turned out to have the disease.

Results: In the majority of cases around 61% were having normal BMI ranging from 20 to 25 kg/m². Among the 96 cases, the mean TSH value was 12.3 mIU/l ranging between 5.8 and 25 mIU/l. 49% of cases were having TSH between 5.5 and 10mIU/l and 34% were having TSH between 10 to 20 mIU/l. Hypercholesterolemia was found in 40.6% of patients. Among 96% of patients, 39 cases had high total cholesterol values. Borderline high values were found in 18.8 % of patients. Mean cholesterol value of 213 mg/dl ranging from a minimum of 119 to 310 mg/dl. LDL was elevated in 42.7% of cases. Among 96 cases, 41 patients had elevated LDL levels of more than 160 mg/dl. Borderline high LDL values were found in 14.6%. The mean LDL value was 139 mg/dl ranging from a minimum of

76 to 290 mg/dl. Triglyceride was elevated in only 27.1%. Among 96 cases, only 26 cases had high triglyceride values. Mean triglyceride value of 121.3 mg/dl ranging from a minimum of 76 to 222 mg/dl. HDL values were found to be normal in 66.7% of cases. The mean HDL was 51.9 mg/dl ranging from a minimum of 33 to 70 mg/dl.

Conclusion: Those with lipid abnormalities, mostly benefit from treatment with thyroxine. So this study holds good in evaluating cases of lipid abnormalities in subclinical hypothyroidism. Appropriate follow-up of patients annually in untreated cases of subclinical hypothyroidism is essential for preventing the progression of the disease.

Key words

Body mass index, Blood pressure, Coronary heart disease, Fasting blood sugar, Dyslipidemia.

Introduction

The diagnosis of subclinical hypothyroidism is mostly biochemical as most of the patients have a serum thyroid-stimulating hormone above the normal reference range and serum-free and total thyroxine T₄ and T₃ are normal [1]. Most of the patients with subclinical hypothyroidism have few or no signs of thyroid dysfunction. The normal reference range of TSH was 0.45 – 4.5 mIU/l. The overall percentage range from 5 to 10% in a large screening population. The prevalence is 7 to 26% in studies conducted on the elderly. Since the hormone levels are normal there comes confusion between compensated hypothyroidism and euthyroid state [2]. Subclinical hypothyroidism is more common in women. Among patients with subclinical hypothyroidism, 80% have TSH of less than 10 mIU/l [3]. The most notable consequence of subclinical hypothyroidism is its high chance of transformation to true hypothyroidism. It is also associated with dyslipidemia and adverse cardiovascular risk profile. Now the recent practical approach of treatment of subclinical hypothyroidism is levothyroxine therapy for persons with serum TSH of more than 10 mIU/L and the therapy is individualized for patients with a TSH value of less than 10 mIU/L [4]. Subclinical hypothyroidism is a common endocrine problem with a 3 to 8% prevalence among the general population. Anti-thyroid antibodies are positive in 80% of patients with SCH. Before radioiodine therapy, external neck and head irradiation may cause a mild form of thyroid dysfunction. Transient elevation of TSH

values may occur after episodes of postpartum thyroiditis [4]. Due to the recent increasing prevalence of SCH and metabolic risk factors such as adverse cardiac function and hyperlipidemia, the American Thyroid Association has recommended the importance of screening by assessment of serum TSH values above the age of 35 years and followed up every 5 years later [5]. Because of the high likelihood of SCH to cause complications during pregnancy and brain development of the fetus, screening of pregnant women for subclinical hypothyroidism is suggested [6]. In the conclusions of the Wickham survey, the risk of acquiring hypothyroidism was 4.3% per year in women in a year, if both the levels serum TSH and anti-thyroid antibodies were found to be elevated, 2.6% chance in patients with elevated TSH alone, and 2.1% chance per year with positive anti-thyroid antibodies alone [7]. Huber and team concluded that high-risk factors for progression to overt hypothyroidism were baseline TSH >12 uIU/mL, reduced thyroid reserve, and positive for thyroid peroxidase antibody. So treatment of subclinical hypothyroidism holds good in various situations and prevention of conversion to overt hypothyroidism [8].

Materials and methods

The study was conducted in the year 2018, at Madha Medical College and Research Institute, Chennai. 96 patients were included in the study. Patients presenting to these OP with vague complaints of obesity, a recent gain of weight, tiredness, coarse facial features, hair loss, dry

skin, infertility, voice changes, memory disturbance, cognitive dysfunction, mood disorders, swelling of the neck, menstrual irregularities are selected. They are screened for subclinical hypothyroidism by doing fasting TFT comprising free T4, free T3, and TSH, and fasting lipid profile is also done for the patient. Among the 620 patients screened for subclinical hypothyroidism, 96 turned out to have the disease.

Inclusion criteria: All newly detected cases of subclinical hypothyroidism (normal t3, t4, free t4, and TSH > 5.5 mU/L).

Exclusion criteria: Patients aged twelve or less. Patients on thyroxine, Known cases of diabetes and hypertension, Chronic renal failure, chronic liver disease, Primary adrenal failure, Patients already on hypolipidemic drugs.

Clinical data comprised of thorough symptomatic analysis and physical examination and detailed history regarding past illness and drug intake. Laboratory analysis of blood urea, serum creatinine, TFT comprising of free T3, free T4, and TSH and fasting lipid profile. Thyroid function test was done using ELISA and lipid profile using the enzymatic kit method.

Statistical analysis

The collected data were analyzed with SPSS 16.0 version. To describe the data descriptive statistics, frequency analysis, percentage analysis were used for categorical variables and the mean and were used for continuous variables. To assess the relationship between the variables Pearson's Correlation was used. To find the significance in categorical data Chi-Square test was used. In both the above statistical tools the probability value .05 was considered as a significant level. Using this computer software, multiple variables like mean range percentages, standard deviation, chi-square, and p-value, etc. were used to test for the statistical significance of the study. A p-value of less than 0.05 denotes a significant relationship.

Results

Of the 96 cases, 88 cases (91.7%) were females and 8 cases (8.3%) were males. Among the 96 patients ranging from 11 years to 60 years with a maximum of 33% were between 46 to 55 years. The mean age was 41.3 years. Majority of cases around 61% were having normal BMI ranging from 20 to 25 kg/m². Among the 96 cases, the mean TSH value was 12.3 mIU/l ranging between 5.8 and 25 mIU/l. 49% of cases were having TSH between 5.5 and 10mIU/l and 34% were having TSH between 10 to 20 mIU/l. Hypercholesterolemia was found in 40.6% of patients. Among 96% of patients, 39 cases had high total cholesterol values. Borderline high values were found in 18.8 % of patients. Mean cholesterol value of 213 mg/dl ranging from a minimum of 119 to 310 mg/dl. LDL was elevated in 42.7% of cases. Among 96 cases, 41 patients had elevated LDL levels of more than 160 mg/dl. Borderline high LDL values were found in 14.6%. The mean LDL value was 139 mg/dl ranging from a minimum of 76 to 290 mg/dl. Triglyceride was elevated in only 27.1%. Among 96 cases, only 26 cases had high triglyceride values. Mean triglyceride value of 121.3 mg/dl ranging from a minimum of 76 to 222 mg/dl. HDL values were found to be normal in 66.7% of cases. The mean HDL was 51.9 mg/dl ranging from a minimum of 33 to 70 mg/dl.

There exists a statistical correlation between rising TSH levels and increased BMI status. The correlation is not statistically significant with a p-value > 0.05 and x² value of 0.298 (**Table – 1**).

There exists a correlation between rising TSH levels and total cholesterol in patients with subclinical hypothyroidism. The relation was statistically significant with a p-value of 0.001 (**Table – 2**).

There exists a relation between rising TSH and LDL levels. The correlation was statistically significant with a p-value of 0.000 (**Table – 3**).

Table - 1: Correlation between TSH and BMI.

			TSH range			Total
			< 10	10 - 20	> 20	
BMI range	Lean	Count	12	11	1	24
		% within TSH range	25.5%	33.3%	6.3%	25.0%
	Non-Obese	Count	30	17	12	59
		% within TSH range	63.8%	51.5%	75.0%	61.5%
	Obese	Count	5	5	3	13
		% within TSH range	10.6%	15.2%	18.8%	13.5%
Total		Count	47	33	16	96
		% within TSH range	100.0%	100.0%	100.0%	100.0%

Table - 2: Correlation between TSH and total cholesterol.

Total cholesterol			TSH range			Total
			< 10	10 - 20	> 20	
TC range	Normal	Count	29	10	0	39
		% within TSH range	61.7%	30.3%	0.0%	40.6%
	Borderline	Count	11	7	0	18
		% within TSH range	23.4%	21.2%	0.0%	18.8%
	High	Count	7	16	16	39
		% within TSH range	14.9%	48.5%	100.0%	40.6%
Total		Count	47	33	16	96
		% within TSH range	100.0%	100.0%	100.0%	100.0%

Table - 3: Correlation between TSH and LDL.

LDL Range			TSH range			Total
			< 10	10 - 20	> 20	
LDL range	Normal	Count	27	13	1	41
		% within TSH range	57.4%	39.4%	6.3%	42.7%
	Borderline	Count	11	3	0	14
		% within TSH range	23.4%	9.1%	0.0%	14.6%
	High	Count	9	17	15	41
		% within TSH range	19.1%	51.5%	93.8%	42.7%
Total		Count	47	33	16	96
		% within TSH range	100.0%	100.0%	100.0%	100.0%

There exists a correlation between rising TSH values and a rise in serum triglyceride levels. The correlation was statistically significant with a p-value of 0.000 and χ^2 value of 0.000 (**Table – 4**).

There seems to exist some correlation between rising TSH and serum HDL levels (**Table – 5**).

Discussion

Subclinical hypothyroidism is an endocrine disorder, where the patients mostly have no or only a few symptoms and signs for diagnosis, and the diagnosis is made from elevated serum thyroid stimulating hormone and the serum-free T4 and free T3 levels are within the reference range. The diagnosis of subclinical hypothyroidism is important in society, as the patient does not display any signs and symptoms consistent with thyroid dysfunction. So this

necessitates, early diagnosis and management of subclinical hypothyroidism as they may transform to true hypothyroidism [9]. The rate of conversion of subclinical hypothyroidism to overt is around 2 to 5% per year. Though subclinical hypothyroidism is asymptomatic, the consequences of subclinical hypothyroidism warrant further evaluation and treatment. "In this study, I screened patients for subclinical

hypothyroidism and evaluation of dyslipidemia in these patients. Among 96 cases of subclinical hypothyroidism, 33% of them were found to be between the age group of 46 to 55 years." The mean age of presentation was found to be 41.3 years, ranging from a minimum of 11 years to a maximum of 60 years. This prevalence rate increases as age increases [10].

Table - 4: Correlation between TSH and triglyceride.

TSH range		TSH range			Total
		< 10	10 - 20	> 20	
Normal	Count	43	24	3	70
	% within TSH range	91.5%	72.7%	18.8%	72.9%
Borderline	Count	4	6	6	16
	% within TSH range	8.5%	18.2%	37.5%	16.7%
High	Count	0	3	7	10
	% within TSH range	0.0%	9.1%	43.8%	10.4%
Total	Count	47	33	16	96
	% within TSH range	100.0%	100.0%	100.0%	100.0%

Table - 5: Correlation between TSH and HDL.

			TSH range			Total
			< 10	10 - 20	> 20	
HDL range	Abnormal	Count	6	14	12	32
		% within TSH range	12.8%	42.4%	75.0%	33.3%
	Normal	Count	41	19	4	64
		% within TSH range	87.2%	57.6%	25.0%	66.7%
Total	Count	47	33	16	96	
	% within TSH range	100.0%	100.0%	100.0%	100.0%	

The BMI distribution among subclinical hypothyroidism does not correlate with serum TSH levels. Among 96 patients with subclinical hypothyroidism, 61.5% of patients had a normal BMI between 20 and 25 kg/m² and 13.5% of patients had BMI beyond 25 kg/m² [11]. Regarding the sex distribution of patients, it was evident that the prevalence of subclinical hypothyroidism is more common among women. Among 96 cases of subclinical hypothyroidism, only 8 cases were men. On analyzing TSH distribution, it was found that among 96 cases, the mean TSH value was 12.3 mIU/l. The TSH values range from a minimum of 5.8 mIU/l to a maximum of 25mIU/l. 34% of the cases had TSH

values between 10 and 20 mIU/l [12-15]. On analyzing the lipid profile abnormalities, patients were subjected to fasting lipid profile comprising serum total cholesterol, serum triglyceride, serum HDL, and serum LDL. The reference range of serum lipid profile. Hypercholesterolemia was found in 40.6% of patients [13]. Among 96% of patients, 39 cases had high total cholesterol values. Borderline high values were found in 18.8% of patients. Mean cholesterol value of 213 mg/dl ranging from a minimum of 119 to 310 mg/dl. LDL was elevated in 42.7% of cases. Among 96 cases, 41 patients had elevated LDL levels of more than 160 mg/dl. Borderline high LDL values were found in 14.6%. The mean LDL

value was 139 mg/dl ranging from a minimum of 76 to 290 mg/dl. Triglyceride was elevated in only 27.1% [14]. Among 96 cases, only 26 cases had high triglyceride values. Mean triglyceride value of 121.3 mg/dl ranging from a minimum of 76 to 222 mg/dl. HDL values were found to be normal in 66.7% of cases. The mean HDL was 51.9 mg/dl ranging from a minimum of 33 to 70 mg/dl [15]. A study conducted in north India comprising 100 patients, in the age group of 15 to 60 years having subclinical hypothyroidism were screened for lipid abnormalities. They were found to have significant elevations in triglyceride and VLDL levels and nominal increases in cholesterol and LDL levels. There is no established evidence for the lowering of serum lipid profile with replacement therapy [16]. The meta-analysis conducted comprising 13 studies showed a significant reduction in total cholesterol by 8 to 15 mg/dl and LDL by 10 mg/dl with thyroxine therapy. The triglyceride and HDL showed no significant changes [17]. The changes noted in lipid abnormalities depend on multiple variables like age, race, sex, and pretreatment lipid values. Because of lipid abnormalities and their association with cardiovascular abnormalities, it is important to investigate the effect of the hormone on lipid profile in hypothyroidism [18]. Among 96 patients, 39 patients had high total cholesterol values and 18 cases were having borderline high total cholesterol values. It is important to note that among the 39 cases with high cholesterol values, 16 patients were having TSH between 10 to 20 mIU/l and 16 of them were having TSH >20 mIU/l. Similarly among the 96 cases, 41 patients had high serum LDL levels and 14 had borderline high LDL levels .among those 41 patients 17 of them were having TSH between 10 to 20 mIU/l, and 15 of them were having TSH > 20 mIU/l. so TSH levels have a significant correlation with total cholesterol and LDL levels. As the TSH level increases, the serum total cholesterol and LDL also increases [19].

Conclusion

Increased prevalence of subclinical hypothyroidism among females. Increased prevalence of subclinical hypothyroidism beyond the age group of 50 years. 34 % of patients have TSH levels between 10 to 20 mIU/l. Significant elevations in total cholesterol and serum LDL in subclinical hypothyroidism. Association of TSH with total cholesterol and LDL elevations. No much significant changes in triglycerides and HDL levels. Consensus on the treatment of subclinical hypothyroidism varies among different physicians on keeping in mind the adverse lipid abnormalities and the cardiovascular abnormalities. So it is advisable to initiate treatment in subclinical hypothyroidism patients with long term TSH more than 10 mIU/l. Those with lipid abnormalities mostly benefits from treatment with thyroxine. So this study holds good in evaluating cases of lipid abnormalities in subclinical hypothyroidism. Appropriate follow of patients annually in untreated cases of subclinical hypothyroidism is essential for preventing the progression of the disease.

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