ORIGINAL ARTICLE GENERAL MEDICINE

Journal of Contemporary Medicine and Dentistry
www.jcmad.com

ISSN [P-2347-4513]
ISSN [O-2349-0799]
Year: 2021, Volume: 9
Issue: 1, p: 66 - 70

A Clinical Study of Dyslipidemia Associated with Subclinical Hypothyroidism

Gangum Venkatreddy
Assistant Professor, Department of General Medicine, Prathima Institute of Medical Sciences, Naganoor, Karimnagar.

Abstract

Background: *Thyroid dysfunctions invariably result in deranged lipid metabolism. It also significantly increases the number of other cardiovascular risk factors. The effects of subclinical hypothyroidism on lipid metabolism have not been determined. We in the current study tried to determine the etiological factors and lipid disorders in cases of subclinical hypothyroidism.* ***Methods:*** *This was a hospital-based cross-sectional study conducted in the OPD of General Medicine Department, Prathima Institute of Medical Sciences, Naganoor, Karimnagar. All adult patients with the biochemical criteria for subclinical hypothyroidism were included in the study. None of the patients were part of a routine screening program. Diagnosed cases of subclinical hypothyroidism patients who fulfilled the inclusion and exclusion criteria were included in the study. Inclusion criteria. All diagnosed cases of subclinical hypothyroidism (normal T_3, T_4 and fT4 with TSH more than 4.5μIU/mL).* ***Results****: Most common cause of subclinical hypothyroidism in our study was autoimmune thyroiditis, as suggested by the presence of thyroid peroxidase antibody, seen in N=25 cases (62.5%). N=32 cases (80%) were having TSH in the range of 10 to 20. N=5 patients (12.5%) had TSH between 5 and 10. N=3 cases (7.5%) were having TSH above 20. 25 cases (62.5%) had positive thyroid peroxidase antibody while 15 (37.5%) were negative for TPO Ab. There were significant elevations of Total cholesterol and LDL- cholesterol in cases of subclinical hypothyroidism as compared to controls, the levels of triglycerides were also found to be elevated however the values were not significant.* ***Conclusion****: Lipid abnormalities are seen in subclinical hypothyroidism patients in the form of significant elevation of total cholesterol and LDL while changes in HDL and triglycerides. These patients are expected to benefit from thyroxine which may also help in reverting the lipid abnormalities.*

Keywords*: Subclinical hypothyroidism, dyslipidemia, TSH, T_4, T_3*

Address for correspondence: Dr. Gangum Venkatreddy, H-no 3-1-334, City Hospital, Behind civil hospital, Karimnagar 505001. Email: drvenkatreddygangum@gmail.com

Date of Acceptance: 07/04/2021

Introduction

Hypothyroidism is a decrease in T_4 and T_3 with elevated TSH levels. When elevated TSH levels are associated with normal total or free T_4 and T_3 values it is called subclinical hypothyroidism. The prevalence is different in different geographic locations however, its overall prevalence has been reported from 6 – 8% in women and 3% in men. [1] The etiology of hypothyroidism and subclinical hypothyroidism are similar and some of the important causes include autoimmune thyroiditis (Hashimoto's thyroiditis) is found in a large number of such cases. In about 54% of cases of subclinical hypothyroidism high concentration of antithyroid microsomal or antithyroid peroxidase antibodies. [2] While the association between overt hypothyroidism and alteration in lipid profile is an undisputed fact, the situation is less clear when subclinical hypothyroidism is concerned. Subclinical hypothyroidism is involved in the aggravation of coronary risk factors and may increase coronary artery disease. Studies have found that cases of subclinical hypothyroidism tend to have higher

total cholesterol and LDL as compared to euthyroid. [3] Studies have also shown that cases of subclinical hypothyroidism have increased levels of CRP. [4] One of the important concerns is the progression of subclinical hypothyroidism to overt hypothyroidism during a time when left untreated. The risk is high if the TSH is more than 10 µIU/mL or the thyroid peroxidase antibody is positive. In the Whickham survey, the annual risk of women developing hypothyroidism was 4.3% per year if both elevated serum TSH and anti-thyroid antibodies were found, 2.6% with elevated TSH alone, and 2.1% per year with positive anti-thyroid antibodies alone. [5] This study mainly focuses on the lipid abnormalities and etiology of patients with subclinical hypothyroidism in our setting.

Materials and Methods

This was a hospital-based cross-sectional study conducted in the OPD of General Medicine Department, Prathima Institute of Medical Sciences, Naganoor, Karimnagar. Institutional Ethical committee permission was obtained for the study. Written consent was obtained from all the participants of the study. All adult patients with the biochemical criteria for subclinical hypothyroidism were included in the study. None of the patients were part of a routine screening program. Diagnosed cases of subclinical hypothyroidism patients who fulfilled the inclusion and exclusion criteria were included in the study.

Inclusion criteria

1. All diagnosed cases of subclinical hypothyroidism (normal T_3, T_4 &, fT4
2. with TSH more than 4.5µIU/mL)

Exclusion criteria

1. Chronic renal failure, chronic liver disease
2. Primary adrenal failure
3. Severe nonthyroidal illness.
4. Patients who are on hypolipidemic drugs.
5. Known cases of diabetes mellitus.

Selection of controls

Controls were taken for comparing the lipid profile of the cases. Healthy euthyroid (normal T_3, T_4, TSH) population were taken as controls.

A total of n=40 cases of subclinical hypothyroidism and age and sex-matched controls were included in the study. The patients in the study group were evaluated with a detailed clinical history, examination, and relevant laboratory investigations. The diagnosis of subclinical hypothyroidism was made according to the diagnostic criteria mentioned above. The evaluation aimed to identify probable etiology and lipid abnormalities. Clinical data comprised of the history of past medical illness and surgery, history of drug intake, and examination. Laboratory data consisted of blood sugar, blood urea, serum creatinine, T_3, T_4, TSH, Ft_4, TPO antibody, and fasting lipid profile. Blood urea, sugar, and serum creatinine were estimated using an automated analyzer. T_3 and T_4 were measured by Competitive Chemi Luminescent Immuno Assay and TSH by Ultrasensitive Sandwich Chemi Luminescent Immuno Assay. Anti TPO antibody estimation was done in all cases by electrochemiluminescence assay. A value more than 34 IU/L is taken as positive. Fasting lipid profile was done with the autoanalyzer. Total cholesterol, Triglycerides, and HDL were estimated, and LDL was calculated by Friedwald's equation. [6] The information collected regarding all the selected cases was recorded in a Master Chart. Data analysis was done with the help of a computer using Graph pad prism 7 software**.** Using this software, range, frequencies, percentages, means, standard deviations, chi-square, and 'p' values were calculated. Kruskal Wallis chi-square test was used to test the significance of the difference between quantitative variables. A 'p' value less than 0.05 is taken to denote a significant relationship.

Results

Out of the n=40 cases in the study group, n=2 were males and n=38 were females. In the control group, n=40 cases were females. Based on the age group n=9 cases were found between 18 – 30 years. N=6 cases were found between 31 – 40 years. N=18 cases were found between 41-50 years and > 50 years n=7 cases were included in the study. The mean age of the study group was 42 years. A similar number of age-matched controls were also included in the study. N=26(65%) cases of the cases were having BMI in the range 20 –25 Kg/m^2 the mean BMI was 22.62 ± 1.66. In the control, the

mean BMI was 22.01 ± 1.63. N=6 cases had a history of hypertension and were on treatment. We also had four patients with Ischemic Heart Disease. Two cases had a history of thyroidectomy for multinodular goiter. Two cases were on treatment for hyperthyroidism with carbimazole.

Table 1: TSH distribution in study cases

TSH (uIU/mL)	No.	%
< 10	5	12.5
10 - 20	32	80
> 20	3	7.5

N=32 cases (80%) were having TSH in the range of 10 to 20. N=5 patients (12.5%) had TSH between 5 and 10. N=3 cases (7.5%) were having TSH above 20. 25 cases (62.5%) had positive thyroid peroxidase antibody while 15 (37.5%) were negative for TPO Ab.

Table 2: Thyroid Peroxidase Antibody

TPO Ab	No.	%
Positive(>34IU/L)	25	62.5
Negative	15	37.5

The most common cause of subclinical hypothyroidism in our study was autoimmune thyroiditis, as suggested by the presence of thyroid peroxidase antibody, seen in N=25 cases(62.5%). Other causes were posted thyroidectomy and drug-induced like antithyroid agent Carbimazole and antiarrhythmic agent Amiodarone.

Table 3: Comparison of total cholesterol values

Study cases (Subclinical hypothyroidism)	*Control cases (Euthyroid)*		*Total Cholesterol (mg/dl)*	
	No.	*%*	*No.*	*%*
Normal (< 200)	16	40	38	95
Borderline (201-239)	8	20	2	5
High (> 240)	16	40	-	-
Total	40	100	40	100
Range Mean S.D.	107-335 213.3 59.6		132-220 165.8 19.4	
p- value	0.0001*			

* significant

LDL was elevated in 52.5% of cases of the subclinical hypothyroid group. 47.5% of cases had LDL more than 160mg/dl. The mean LDL in study cases was 138.6 mg/dl and 109.4 mg/dl in the control group. The difference was statistically significant. (Table 4).

Hypercholesterolemia was present in 60% of subclinical hypothyroidism patients. The mean total cholesterol was 213.3 mg/dl in study cases and 165.8 mg/dl in the control population. The difference was statistically significant. (Table 3).

Table 4: comparison of low-density lipoprotein values

Study cases (Subclinical hypothyroidism)	*Control cases (Euthyroid)*		*LDL (mg/dl)*	
	No.	*%*	*No.*	*%*
Normal (< 130)	19	47.5	38	95
Borderline (131-159)	2	5	2	5
High (> 160)	19	47.5	-	-
Total	40	100	40	100
Range Mean S.D.	49-238 138.6 48.7		74-150 109.4 18.1	
p- value	0.005*			

* significant

Table 5: comparison of low-density lipoprotein values

Study cases (Subclinical hypothyroidism)	*Control cases (Euthyroid)*		*LDL (mg/dl)*	
	No.	*%*	*No.*	*%*
Normal (< 150)	29	72.5	38	95
Borderline (151-199)	6	15	1	2.5
High (> 200)	5	12.5	1	2.5
Total	40	100	40	100
Range Mean S.D.	49-238 138.6 48.7		74-150 109.4 18.1	
p-value	0.4853			

72.5% of the study cases were having triglycerides less than 150 mg/dl. The mean triglyceride level in the subclinical hypothyroid group was 143.6 mg/dl and 126.4 mg/dl in the control group. The difference was not statistically significant (Table 5).

Discussion

This study was done to find out the probable etiologies and lipid abnormalities in patients with subclinical hypothyroidism, who presented to our institute. Among the n=40 patients studied, the mean age was 42 years, range being 18 to 62 years. The majority of the patients (62.5%) were in the age group 41 – 62 years. Studies have shown that the incidence of subclinical hypothyroidism increases with age. [7, 8] The Colorado Thyroid Disease Prevalence Study had demonstrated an increase in serum TSH with age. [9] We had only n=7 patients (17.5%) above the age group 50 years. This difference may be since those studies were community-based screening studies done on a large population. Therefore, screening in the elderly population may be needed to detect more

cases as larger studies have shown that the majority of the patients are asymptomatic. In our study also majority were females (95%). A study on dyslipidemia in subclinical hypothyroidism by Bandyopadhyay et al; [10] reported that 78% of their cases were females. Our study evaluated the causes for subclinical hypothyroidism. The most important etiology found was autoimmune thyroiditis. Other causes were posted thyroidectomy and drug-induced like antithyroid agent Carbimazole and antiarrhythmic like Amiodarone. No definite cause was found in n=10 cases (25%). Autoimmune thyroiditis was diagnosed by doing an anti-TPO assay 62.5% of patients had positive thyroid peroxidase antibody test. This result was like the study by Shruti Mohanty et al; [11] reported n=45 out of n=61 subclinical hypothyroid cases had TPO antibodies suggesting autoimmune thyroiditis as the cause. Published literature states that the most common cause of subclinical hypothyroidism is autoimmune thyroiditis (Hashimoto's disease). [12] Progression to overt hypothyroidism is reported to vary from 3 to 20%, the risks being greater in those patients with TSH more than 10 μIU/mL or thyroid antibodies (or both). Hence it is recommended that anti- TPO measurement should be an integral part of the investigation in subclinical hypothyroidism. In this study, there was found to be a significant increase in the total cholesterol and LDL levels in study cases when compared with euthyroid controls, but the variations in HDL and triglycerides were not significant. This result was similar to the observations made in The Colorado Thyroid Prevalence Study in which among 25,862 participants in a statewide health fair in Colorado, fasting total cholesterol, triglyceride, and LDL-C levels were significantly greater in individuals with diminished thyroid function, with higher levels in sub-clinically hypothyroid subjects than in euthyroid subjects. [9] Compare to other studies in our study there is a trend towards increased triglycerides in cases with subclinical hypothyroidism compared with controls but this is statistically not significant (15% vs 2.5% for borderline and 12.5 % vs 2.5 % for high triglycerides, with a p-value of 0.4853). Another study by Guptha A et al. [13] demonstrated a significant elevation in serum cholesterol in subclinical hypothyroid cases when compared with euthyroid controls. There is a significant elevation of total cholesterol, LDL-C, apolipoprotein B, and apolipoprotein A in subclinical hypothyroidism patients compared with euthyroid. [14] They also demonstrated that changes in triglycerides and HDL-C were not significant. [14] These results were similar to those of our study. In conclusion lipid abnormalities are relatively common in subclinical hypothyroidism. Several randomized controlled trials have shown that treatment of subclinical hypothyroidism with thyroxine may have a favorable effect on the lipid profile by decreasing total cholesterol and LDL-C. These observations reinforce the need to screen for thyroid dysfunction in people with dyslipidemia, as this may be a reversible cause, amenable to thyroxine replacement.

Conclusion

Lipid abnormalities are seen in subclinical hypothyroidism patients in the form of significant elevation of total cholesterol and LDL while changes in HDL and triglycerides. These patients are expected to benefit from thyroxine which may also help in reverting the lipid abnormalities. The majority of cases in our study had multiple indications for starting treatment with thyroxine as per the current recommendations TSH more than 10 μIU/mL, TPO Antibody positivity, Goiter, hypothyroid symptoms, and dyslipidemia. Long-term Follow up is needed to assess the extent of the benefit of treatment.

Conflict of Interest: *None declared*
Source of Support: *Nil*
Ethical Permission: *Obtained*

References

1. Fauci, Braunwald, Kasper, Hauser, Longo, Jameson, et al. Disorders of the thyroid gland. In: J.Larry Jameson, Anthony P. Weetman (Eds). Harrison's Principles of Internal Medicine. 17th Edn The Mc Graw Hill companies USA. 2008; 2224-46.
2. Hamburger JI, Meier DA, Szpunar WE. Factitious elevation of thyrotropin in euthyroid patients. NEJM. 1985; 313:267.
3. Pucci E, Chiovato L, Pinchera A. Thyroid and lipid metabolism. Int J Obes Relat Metab Disord. 2000;24(Suppl 2): S109–12.

4. Vanderpump M, Tunbridge M, French J, Appleton D, Bates D, Clark F, et al. The incidence of thyroid disorders in the community: a twenty-year follow-up of the Whickham survey. Clin Endocrinol. 1995; 43:55-68.
5. CV Rizos, MS Elisaf, EN Liberopoulos. Effects of thyroid dysfunction on lipid profile. Open Cardiovasc Med J. 2011; 5:76-84.
6. Friedewald WT, Levy RI, Fredrickson DS. Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. Clin Chem. 1972;18(6):499–502.
7. Duntas LH. Thyroid disease and lipids. Thyroid. 2002; 12:287–93.
8. Gesing, A., Lewiński, A. Karbownik-Lewińska, M. The thyroid gland and the process of aging; what is new? Thyroid *Res* 2012; 5:16.
9. Canaris GJ, Manowitz NR, Mayor G, Ridgway EC. The Colorado thyroid disease prevalence study. Arch Intern Med. 2000; 160:526–34.
10. Bandyopadhyay, SanjoyK, Basu A.K, PAL Sali K, et al. A study on dyslipidemia in subclinical hypothyroidism, Journal of the Indian Medical Association. 2006; 104:11: 622-26.
11. Shruti Mohanty, W Amruthlal, GC Reddy, G Kusumanjali, AS Kanagasabapathy, Pragna Rao. Diagnostic strategies for subclinical hypothyroidism**.** Indian Journal of Clinical Biochemistry. 2008:23:3:279-282.
12. Rotondi M, Luca de Martinis, F Coperchini, P Pignatti, et al. Serum negative autoimmune thyroiditis displays a milder clinical picture compared with classic Hashimoto's thyroiditis. Eur J Endocrinol 2014; 171:31-36.
13. Gupta A, Sinha R S. Echocardiographic changes and alterations in lipid profile in cases of subclinical and overt hypothyroidism. Journal Asso of Physicians India. 1996;44(8):546, 551-53.
14. Z Efstathiadou, S Bitsis, HJ Milionis Lipid profile in subclinical hypothyroidism. Is L-Thyroxine substitution beneficial? European Journal of Endocrinology. 2001; 145:6:705-710.