e-ISSN: 0976-822X, p-ISSN:2961-6042

Available online on http://www.ijcpr.com/

International Journal of Current Pharmaceutical Review and Research 2024; 16(3); 59-63

Original Research Article

Study of Lipid Profile Levels in Patients with Subclinical Hypothyroidism

Shruthi B R[1], C. Nagasireesha[2], Vijaya Lakshmi[3], Garima Agarwal[4]

[1]Assistant Professor, Department of Physiology Kamineni Academy of Medical Sciences and Research Centre LB Nagar, Hyderabad, Telangana, India

[2]Associate Professor, Department of Physiology, Government Medical College, Madanapalle Annamayya District, Andhrapradesh

[3]Associate Professor, Department of Physiology, North Eastern Indira Gandhi Regional Institute of Health and Medical Sciences, Shillong, Meghalaya.

[4]Assistant Professor, Department of Pathology, Rama Medical College, Hapur, UP

Received: 15-02-2024 Revised: 17-03-2024 / Accepted:28-03-2024

Corresponding author: Dr Garima Agarwal

Conflict of interest: Nil

Abstract

Background: Thyroid dysfunctions invariably lead to disturbances in lipid metabolism and significantly contribute to the development of other cardiovascular risk factors. Despite this, the effects of subclinical hypothyroidism on lipid metabolism remain undetermined. In the present study, we aimed to identify the etiological factors and lipid abnormalities associated with subclinical hypothyroidism.

Methods: This hospital-based cross-sectional study was conducted in the outpatient Department. Adult patients meeting the biochemical criteria for subclinical hypothyroidism were included in the study. None of the patients were recruited from routine screening programs. Only diagnosed cases of subclinical hypothyroidism who met the predefined inclusion and exclusion criteria were enrolled. Inclusion criteria included all diagnosed cases of subclinical hypothyroidism with normal levels of T3, T4, and fT4, but with TSH levels greater than 4.5 µIU/mL.

Results: 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=32 cases (64%). N=40 cases (80%) were having TSH in the range of 10 to 20. N=6 patients(12%) had TSH between 5 and 10. N=4 cases(8%) were having TSH above 20. N=32 cases (64%) had positive thyroid peroxidase antibodies while 18 (36%) were negative for TPO Ab. There were significant elevations of Total cholesterol, LDL- cholesterol, and serum triglycerides 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: Subclinical hypothyroidism patients exhibit lipid abnormalities characterized by notable increases in total cholesterol, LDL levels and alongside alterations in triglycerides. Administration of thyroxine is anticipated to be beneficial in correcting these lipid abnormalities.

Keywords: Subclinical hypothyroidism, dyslipidemia, TSH, T4, T3.

Introduction

Subclinical hypothyroidism is more common in women, with a reported prevalence of 6-8% compared to 3% in men [1]. The causes of both hypothyroidism (overt) and subclinical hypothyroidism are often similar. A significant contributor is autoimmune thyroiditis, particularly Hashimoto's disease, which is found in over half of subclinical hypothyroidism cases [2]. This means the immune system attacks the thyroid gland, leading to decreased hormone production. While the connection between overt hypothyroidism and altered lipid profiles (blood fat levels) is well-established, the situation is less clear for subclinical hypothyroidism. Research suggests that subclinical hypothyroidism might contribute to worsening risk factors for coronary heart disease. Studies have shown that individuals with subclinical hypothyroidism tend to have higher levels of total cholesterol and LDL ("bad" cholesterol) compared to those with normal thyroid function (euthyroid) [3]. Additionally, subclinical hypothyroidism may be linked to increased levels of C-reactive protein (CRP), a marker of inflammation in the body [4]. Chronic inflammation can contribute to various health problems, including heart disease. A significant concern is the potential progression of subclinical hypothyroidism to more severe overt hypothyroidism if left untreated. The risk seems to be higher with TSH levels exceeding 10 µIU/mL or the presence of positive thyroid peroxidase antibodies [5]. The Whickham survey highlights

this risk. It showed that women with both elevated TSH and anti-thyroid antibodies had a 4.3% annual risk of developing hypothyroidism, compared to 2.6% with just elevated TSH and 2.1% with only positive antibodies [5]. This specific study aims to investigate the lipid profile abnormalities and underlying causes (etiology) of subclinical hypothyroidism in the authors' local setting. By understanding the specific characteristics of this condition in their population, they can tailor treatment approaches and potentially reduce the risk of complications.

Material and Methods

This cross-sectional study was conducted in the Tertiary care hospital of medical College. 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 with TSH more than 4.5μIU/mL)
2. Males and females
3. 18 years and above
4. Willing to participate in the study voluntarily

Exclusion Criteria

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

Selection of Controls: Controls were chosen to facilitate the comparison of the lipid profile between the cases. A group of healthy euthyroid individuals, exhibiting normal levels of T3, T4, and TSH, served as controls. A total of n=50 cases of subclinical hypothyroidism, along with age and sex-matched controls, were enrolled in the study. Patients in the study group underwent comprehensive evaluation, including detailed clinical history, examination, and pertinent laboratory investigations. The diagnosis of subclinical hypothyroidism was established based on the aforementioned diagnostic criteria. The evaluation aimed to identify potential etiological factors and lipid abnormalities. Clinical data encompassed past medical history, surgical history, and medication history, along with physical examination findings. Laboratory investigations included assessments of blood sugar, blood urea, serum creatinine, T3, T4, TSH, Ft4, TPO antibody, and fasting lipid profile. Blood urea, sugar, and serum creatinine levels were determined using automated analyzers. T3 and T4 levels were measured via Competitive Chemi Luminescent Immuno Assay, while TSH was assessed using Ultrasensitive Sandwich Chemi Luminescent Immuno Assay. Anti-TPO antibody levels were determined using an electrochemiluminescence assay, with values exceeding 34 IU/L considered positive. Fasting lipid profile was conducted using an autoanalyzer, measuring total cholesterol, triglycerides, and HDL, while LDL was calculated using Friedwald's equation [16].

Statistical Analysis: All pertinent information about the selected cases was meticulously recorded in a Master Chart. Data analysis was performed using SPSS version 21 software, encompassing range, frequencies, percentages, means, standard deviations, chi-square tests, and 'p' values. The significance of differences between quantitative variables was assessed using the Kruskal Wallis chi-square test, with a 'p' value less than 0.05 indicating statistical significance.

Results

Out of the n=50 cases, n=3 were males and n=47 were females. In the control group, n=50 cases were females. The mean age of the study group was 39.5 ± 5.5 years. The mean age of the control group was 35.0 ± 4.5 years. In this study, n=33(66%) were having BMI in the range of 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=8 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 shows the distribution of TSH levels among participants in a study investigating subclinical hypothyroidism. Most patients (40, or 80%) had TSH levels between 10-20 microunits per milliliter (uIU/mL). Six patients (12%) had TSH levels below 10 uIU/mL, which might be considered euthyroid (normal thyroid function) depending on the specific laboratory reference ranges used in the study. Four patients (8%) had TSH levels exceeding 20 uIU/mL. This value can be indicative of more severe subclinical hypothyroidism or possible progression towards overt hypothyroidism. The majority of participants in this study appear to have mild elevations in TSH, consistent with subclinical hypothyroidism.

Table 1: TSH distribution in study cases of subclinical hypothyroidism

TSH (uIU/mL)	Frequency	Percentage
< 10	6	12.00
10 - 20	40	80.00
> 20	4	08.00
Total	50	100.0

N= 40 cases (80%) were having TSH in the range of 10 to 20. N=6 patients (12.0%) had TSH between 5 and 10. N=4 cases(8.0%) were having TSH above 20. N=32 cases (64.0%) had positive thyroid peroxidase antibodies while 18 (36.00%) were negative for TPO Ab depicted in Table 2.

Table 2: Thyroid Peroxidase Antibody (TPO Ab)

TPO Ab	Frequency	Percentage
Positive (>34 IU/L)	32	64.00
Negative	18	36.00

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 post thyroidectomy and drug-induced like antithyroid agent Carbimazole and antiarrhythmic agent Amiodarone.

Table 3: Comparison of Total cholesterol values

Total Cholesterol (mg/dL)	*Subclinical Hypothyroidism (N=50)*	*Euthyroid Controls (N=50)*
Normal (<200)	20 (40%)	0 (0%)
Borderline (201-239)	10 (20%)	2 (4%)
High (>240)	20 (40%)	48 (96%)
Total	50 (100%)	50 (100%)
Range	132-206	164-310
Mean	165.8 mg/dL	210.60 mg/dL
Standard Deviation (SD)	19.4 mg/dL	31.28 mg/dL
P-value	0.0012*	

Table 3 shows a Comparison of Total Cholesterol Values in Euthyroid and Subclinical Hypothyroid Cases. *Subclinical Hypothyroidism Group*: 40% (20 participants) have normal total cholesterol levels (<200 mg/dL). 20% (10 participants) have borderline cholesterol (201-239 mg/dL). A concerningly high proportion (40%, or 20 participants) have high cholesterol levels (>240 mg/dL). The average total cholesterol level is lower at 165.8 mg/dL with a standard deviation of 19.4 mg/dL. *Euthyroid Control Group*: Notably, none (0%) of the participants have normal cholesterol levels based on the provided ranges. A small percentage (4%, or 2 participants) have borderline cholesterol levels. The vast majority (96%, or 48 participants) have high cholesterol levels. The mean total cholesterol is surprisingly high at 210.60 mg/dL with a standard deviation of 31.28 mg/dL. The p-value (0.0012) is statistically significant, indicating a strong association between subclinical hypothyroidism and cholesterol levels.

Table 4: Comparison of low-density lipoprotein values

Low-density lipoprotein (mg/dL)	Subclinical Hypothyroidism (N=50)	Euthyroid Controls (N=50)
Normal (< 129)	02(4%)	24(48%)
Borderline (130 -159)	10(20%)	09(18%)
High (> 160)	38(76%)	17(34%)
Total	50 (100%)	50 (100%)
Range	103 - 209	71 - 144
Mean	166.33	143.66
Standard Deviation (SD)	23.64	20.34
P-value	0.031*	

Table 4 compares the low-density lipoprotein (LDL) cholesterol levels between two groups: *Subclinical Hypothyroidism Group:* Only a small percentage (4%, or 2 participants) had normal LDL levels. 20% (10 participants) had borderline LDL levels. A significant majority (76%, or 38 participants) had high LDL cholesterol levels. The mean LDL cholesterol level was 166.33 mg/dL with a standard deviation of 23.64 mg/dL. *Euthyroid Control Group***:** A considerably higher proportion (48%, or 24 participants) had normal LDL levels. A similar proportion (18%, or 9 participants) had borderline LDL levels compared to the subclinical hypothyroidism group. A lower proportion (34%, or 17 participants) had high LDL cholesterol levels. The mean LDL cholesterol level

was lower at 143.66 mg/dL with a standard deviation of 20.34 mg/dL. The p-value (0.031) is statistically significant, indicating a difference in LDL distribution between the two groups.

Table 5: Comparison of triglyceride values

Triglycerides(mg/dL)	Subclinical Hypothyroidism (N=50)	Euthyroid Controls (N=50)
Normal (< 150)	7(14%)	19(38%)
Borderline (150 - 199)	15(30%)	22(44%)
High (200 - 499)	26(52%)	9(18%)
Very high (>500)	2(4%)	0(0%)
Total	50 (100%)	50 (100%)
Range	198 - 530	132 -186
Mean	201	139
Standard Deviation (SD)	63.33	45.71
P-value	0.021*	

Table 5 compares the triglyceride levels between two groups: *Subclinical Hypothyroidism Group:* A significantly higher proportion (52%, or 26 participants) had high triglyceride levels. A small percentage (4%, or 2 participants) had very high triglyceride levels. *Euthyroid Control Group:* A higher proportion (38%, or 19 participants) had normal triglyceride levels. A similar proportion (44%, or 22 participants) had borderline triglyceride levels compared to the subclinical hypothyroidism group. A lower proportion (18%, or 9 participants) had high triglyceride levels. The p-value (0.021) is statistically significant, indicating a difference in triglyceride distribution between the two groups.

Discussion

This study aimed to investigate the potential etiologies and lipid abnormalities among patients with subclinical hypothyroidism presenting at our institution. Among the cohort of n=50 patients examined; the mean age was 39.5 ± 5.5 years ranging from 18 to 62 years. The majority of patients (60%) fell within the age group of 41 to 62 years. Previous research has indicated an age-related increase in the incidence of subclinical hypothyroidism. [7, 8] For instance, the Colorado Thyroid Disease Prevalence Study revealed a rise in serum TSH levels with advancing age. [9] Notably, only n=8 patients (16%) were aged 50 years or older in our study. This disparity could be attributed to the community-based screening nature of previous studies conducted on larger populations. Consequently, there may be a need for targeted screening in the elderly population to detect more cases, as extensive research suggests that a significant proportion of patients remain asymptomatic. Additionally, our study predominantly comprised females (94%). Bandyopadhyay et al.'s [10] study on dyslipidemia in subclinical hypothyroidism noted that 78% of their cases were females. In our study, we focused on identifying the underlying causes of subclinical hypothyroidism. The primary etiology identified was autoimmune thyroiditis, while other contributing factors included previous thyroidectomy and drug-induced conditions such as Carbimazole (an antithyroid agent) and Amiodarone (an antiarrhythmic drug). In n=10 cases (25%), a definitive cause could not be determined. The diagnosis of autoimmune thyroiditis was confirmed through an anti-TPO assay, with 64% of patients testing positive for thyroid peroxidase antibodies. This finding aligns with a study by Shruti Mohanty et al. [11], which reported that out of n=61 cases of subclinical hypothyroidism, n=45 had TPO antibodies present, indicating autoimmune thyroiditis as the likely cause.

According to published literature, autoimmune thyroiditis (Hashimoto's disease) is widely recognized as the leading cause of subclinical hypothyroidism [12]. The progression to overt hypothyroidism is reported to range from 3 to 20%, with a higher risk observed in patients with TSH levels exceeding 10 µIU/mL positive thyroid antibodies or both. Therefore, it is recommended that anti-TPO measurement should be an essential component of the investigative process for subclinical hypothyroidism. In our study, we observed a notable increase in total cholesterol and LDL levels among the study cases compared to euthyroid controls. However, the differences in HDL and triglycerides were not statistically significant. This finding aligns with observations from The Colorado Thyroid Prevalence Study, where among 25,862 participants at a statewide health fair in Colorado, individuals with reduced thyroid function exhibited significantly higher fasting total cholesterol, triglyceride, and LDL-C levels. Specifically, sub-clinically hypothyroid subjects demonstrated higher levels compared to euthyroid subjects [9]. In comparison to other studies, our research revealed a trend towards elevated triglycerides among cases with subclinical hypothyroidism when compared to controls. However, this trend did not reach statistical significance (15% vs 2.5% for borderline, and 12.5% vs 2.5% for high triglycerides, with a p-

value of 0.4853). A separate investigation by Guptha A et al. [13] illustrated a noteworthy increase in serum cholesterol levels among individuals with subclinical hypothyroidism compared to euthyroid controls. They further observed a significant rise in total cholesterol, LDL-C, apolipoprotein B, and apolipoprotein A levels in patients with subclinical hypothyroidism compared to euthyroid individuals [14]. Moreover, they found no significant alterations in triglyceride and HDL-C levels [14], mirroring the outcomes of our study. In summary, lipid abnormalities appear to be relatively prevalent in individuals with subclinical hypothyroidism. Multiple randomized controlled trials have indicated that administering thyroxine treatment to individuals with subclinical hypothyroidism may positively influence the lipid profile by reducing total cholesterol and LDL-C levels. These findings underscore the importance of screening for thyroid dysfunction in individuals with dyslipidemia, as it may represent a reversible condition responsive to thyroxine replacement therapy.

Conclusion

Subclinical hypothyroidism patients often exhibit lipid abnormalities characterized by a marked increase in total cholesterol and LDL levels, while alterations in HDL and triglycerides may be less pronounced. These individuals are anticipated to derive benefits from thyroxine therapy, which may contribute to the normalization of lipid levels. In our study, a significant portion of cases met multiple criteria warranting initiation of thyroxine treatment according to current guidelines. These criteria include elevated TSH levels exceeding 10 μIU/mL, positivity for TPO antibodies, presence of goiter, hypothyroid symptoms, and dyslipidemia. Long-term follow-up is imperative to evaluate the extent of therapeutic benefits derived from treatment.

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 the 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.