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Estimation of Lipid Profile among Hypothyroidism Patients Attending OPD in a Tertiary Care Centre at Puducherry

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ABSTRACT

Background: In the general population, hypothyroidism both overt and subclinical is a common endocrine condition. Elevated total cholesterol, triglycerides, or low HDL levels are signs of dyslipidemia, which is a significant risk factor for cardiovascular diseases (CVD), especially coronary heart disease (CHD). Higher TC and TC/HDL ratios are associated with increased risk. The morbidity and mortality associated with CVD can be decreased by early dyslipidemia identification and treatment. In 1930, it was discovered that thyroid dysfunction and lipid abnormalities were related; hypothyroidism frequently resulted in high levels of TC and LDL-C. This study was carried out to quantify the frequency of hypothyroidism and evaluate the severity of related dyslipidemia among OPD patients, given the high prevalence of the condition in India.

Materials and Methods: In a Puducherry Tertiary Care Centre, 71 hypothyroid patients who were at least 18 years old participated in a planned cross-sectional study. The purpose of the study was to evaluate the lipid profiles of patients who visited the General Medicine Outpatient Department. Convenient sampling was used to choose participants, and a standardized questionnaire was used for interviews to gather clinical and sociodemographic information. Epi-info software version 7.2.2.6 was used for data analysis and blood investigations.

Results: In this study group, 19.7% had subclinical hypothyroidism and 80.3% had overt hypothyroidism, with hypercholesterolemia (16.9%), hypertriglyceridemia (23.9%), low HDL (100%), high LDL (38%), and high VLDL (70.4%) with HDL and VLDL abnormalities being most significant. A strong association between hypothyroidism and dyslipidemia was observed, highlighting increased risk. Diabetes and hypertension were the most common comorbidities, while CKD patients showed elevated lipid and thyroid parameters. Overweight and obese individuals had higher lipid (except TC) and thyroid (except FT3) levels. The study underscores the need for routine dyslipidemia screening in thyroid patients for effective integrated management.

INTRODUCTION

Both overt and subclinical forms of hypothyroidism are prevalent in the general population. Elevated serum levels of thyroid-stimulating hormone (TSH) and decreased levels of free peripheral thyroid hormone (TH) are indicative of overt hypothyriodism. A characteristic of subclinical hypothyriodism is normal free peripheral TH levels. Common symptoms and indicators of hypothyroidism include weight gain, exhaustion, constipation, dry skin, cold intolerance, hoarseness, goitre, depression, mental impairment, mild diastolic hypertension, narrowed pulse pressure, bradycardia, decreased appetite, or arthralgia. Patients may also be asymptomatic or in myxoedema coma.

Dyslipidemia is characterized by low HDL levels or a rise in plasma total cholesterol, triglycerides, or both. One well-known risk factor for cardiovascular disease (CVD) is dyslipidemia. The risk of atherosclerotic diseases, including coronary heart disease (CHD) increases with increasing plasma Total Cholesterol concentration, and in particular with increasing ratio of total cholesterol to High Density Lipoprotein (HDL) Cholesterol. Early diagnosis and management can significantly minimize the mortality and morbidity associated with Dyslipidemic Cardiovascular Diseases.

The relationship between Thyroid dysfunction and Dyslipidemia was first described in 1930. Since then, it has been increasingly clear that Hypothyroidism can cause lipid metabolism issues (1), primarily with elevated Total Cholesterol (TC) and LDL-C levels in the blood.(1) Elevated LDL-C levels can induce progressive lipid accumulation, plaque formation in the arteries, and an increased

risk of Cardiovascular Disease (CVD), which is the leading cause of death worldwide.

These lipid profile fluctuations are explained by Thyroid hormones regulation effect on the activity of key lipoprotein metabolic enzymes. By stimulating the 3-Hydroxy-3-Methylglutaryl Coenzyme A (HMG-CoA) reductase, which catalyzes the conversion of HMG-CoA to mevalonate, the first step in cholesterol biosynthesis, the thyroid hormone precisely calculates hepatic denovo cholesterol synthesis.(2) This results in a decrease in hypothyroidism and an increase in intracellular cholesterol levels in hyperthyroidism. The LDL receptors are also activated by thyroid hormones; Triiodothyronine (T3) can increase the expression of the LDL receptor gene because the promoter of the LDL receptor gene contains a Thyroid Hormone Responsive Element (TRE).(3) Additionally, the Cholesteryl Ester Transfer Protein (CETP), an enzyme that moves cholesteryl esters from HDL2 to Very Low Density Lipoprotein, is activated by thyroid hormones, low Density Lipoproteins (VLDL) and Triglycerides in the reverse direction.(4) Finally, Thyroid Hormones Activate Lipoprotein Lipase (LPL), which catabolizes Triglyceride-rich lipoproteins, and Hepatic Lipase (HL), which converts HDL2 to HDL3.(5)

The prevalence of self-reported Goiter or Thyroid disorder was 2.2% in the National Family Health Survey IV(NFHS IV) (2015-2016), and 2.9% in the NFHS-V (2019-2021). According to the NFHS IV (2015-2016), the self-reported prevalence of Goiter or Thyroid disorder among people aged 15 - 49 was approximately 2% in women and less than 1% in men. In addition, the reported prevalence increased with age in women (15-19 years: 0.7%; 20-34 years: 1.8%; 35-49 years: 3.4%).(6) According to earlier research, the prevalence of subclinical hypothyroidism (about 11.1%) and overt hypothyroidism (about 4.3%) among hypercholesterolemic patients is higher than in the general population. Serum TSH levels above 10 mLU/L and overt and subclinical hypothyroidism were associated with a higher risk of cardiovascular disease and death.(7) According to these results, TH and TSH are important risk factors for disorders related to lipid metabolism. T4 replacement enhances heart function and it returns cholesterol levels to baseline regardless of TSH or TC concentrations. (8,9,10) Additionally, blood lipid profiles in overt hypothyroidism are more significantly affected by T4 therapy than in subclinical hypothyroidism.(11) Given the significant incidence of hypothyroidism in India, it was vital to determine its prevalence and severity of Dyslipidemia in patients with Hypothyroidism.

AIM AND OBJECTIVES

Estimation of lipid profile among Hypothyroidism patients attending OPD and IPD in a Tertiary Care Centre at Puducherry.

- To study the prevalence of Dyslipidemia among Hypothyroidism patients.
- To study the severity of Dyslipidemia in patients with Hypothyroidism.

MATERIAL AND METHODS

This prospective cross-sectional investigation was carried out in a Puducherry tertiary care hospital. Hypothyroid patients who were 18 years of age or older and who visited the General Medicine OPD over the 18-month period from October 28, 2022, to April 28, 2024, were included in the study. With Z = 1.96 at 95% CI, p = 8.85% (prevalence of hypothyroidism), q = 1–p = 0.9115, and acceptable error e = 7%, the sample size was set at 64 using the formula $n = Z^2pq/e^2$. The ultimate sample size was 71 after a 10% non-response rate was taken into consideration. Convenient sampling was used to choose the participants.

Patients attending the OPD who were 18 years of age or older and had a known diagnosis of hypothyroidism met the inclusion criteria. Pregnant women and individuals currently receiving treatment for dyslipidemia were excluded. A standardized questionnaire was used to interview eligible patients and gather clinical and sociodemographic information after they were selected based on clinical examination.

Each participant had a 5 ml fasting venous blood sample taken for biochemical analysis. Lipid profile testing comprised LDL, HDL, VLDL, TC, TG, and TSH, whereas thyroid profile tests included Free T3, Free T4, and TSH. A weighing scale and stadiometer were used to determine the body mass index (BMI), which was then classified using the Asian-Pacific system. The length of hypothyroidism and concomitant conditions such diabetes, hypertension, CAD, CKD, COPD, and CVA were also noted during the clinical evaluation. Every investigation was carried out at the biochemistry lab. TSH <10 indicates subclinical hypothyroidism, while ≥10 indicates overt hypothyroidism. The following lipid profile cut-off values are used for analysis (Rifai, 2017).(12)

STATISTICAL ANALYSIS

Epi Info Software Version 7.2.2.6 was used to analyze the data after it was entered into an MS Excel spreadsheet. Means and standard deviations were used to represent continuous data, whereas frequencies and percentages were used to represent categorical variables. The t-test, ANOVA, Chi-square, and correlation tests were used to determine the relationships between the variables, and a p-value of less than 0.05 was considered a statistically significant relationship.

RESULTS

BASELINE DEMOGRAPHIC PROFILE AND BMI OF STUDY PARTICIPANTS

Of the 71 participants in this study (43.7%), 31–40 years old followed by those over 50 (22.5%). The age distribution was 43.0±13.0 years. Women made up the majority of the subjects in this study (97.2%). The vast majority of participants in this survey (76.1%) were unemployed. The vast majority of the participants in this survey (77.5%) lived in cities. Of the 71 participants in the current study, 67.6% were obese, followed by overweight (15.5%) and normal (15.5%) according to the Asian-Pacific BMI definition. A mean BMI of 27.2±4.52 kg/m2 was found. (Table 1)

HYPOTHYROIDISM PROFILE AND PREVALENCE OF DYSLIPIDEMIA AMONG THE STUDY PARTICIPANTS

Four out of the 71 participants in this study had hypothyroidism for longer than five years, accounting for more than 57.7% of the total; 63.5% of the 71 participants in this trial were taking 100 mcg of Thyroxine, which was followed by Thyroxine 50mcg (22.5%).

In the current study, nearly half of the subjects were not following any specific diet pattern according to their health condition (46.5%). About 23.9% were on thyroid diet, 18.3% on DASH diet and 11.3% on diabetic diet. In this study, hypertension (62.0%) and diabetes (56.3%) were found to be the most common co-morbidities among hypothyroid subjects. The mean plasma levels of Free T3, Free T4 and TSH were 2.21 ± 0.97, 1.34 ± 0.50 and 30.2 ± 22.7 respectively. In the present study, of 71 subjects, 80.3% had overt hypothyroidism and only 19.7% with sub-clinical hypothyroidism. The mean plasma levels of Total Cholesterol, Triglycerides, High-Density Lipoproteins, Low-Density Lipoproteins and Very Low-Density Lipoproteins were 196.1 ± 38.4 mg/dl, 165.5 ± 42.8 mg/dl, 31.5 ± 11.0 mg/dl, 133.8 ± 36.5 mg/dl and 35.9 ± 6.28 mg/dl respectively. The dyslipidemia among hypothyroid subjects was found to be as

hypercholesterolemia (16.9%), hypertriglyceridemia (23.9%), low HDL (100.0%), high LDL (38.0%) and high VLDL (70.4%).(Table 2)

MEAN LIPID PROFILE ACROSS CLINICAL AND BMI SUBGROUPS IN HYPOTHYROID PATIENTS

Except for HDL, all the lipid profile parameters were found to be high in overt hypothyroidism (57) and this association is found to be statistically significant ($p<0.05$). The mean TC, LDL, VLDL, TG were found to be more in CKD patients (220.5 mg/dl), also HDL seen in CKD patients (25.0 mg/dl). However, the TC and VLDL values are almost same for other co-morbidities. Statistically significant association was found with HDL and Overweight, Obese, where high values were found compared to the other group ($p<0.05$). Except for TC, all the lipid profile parameters were found to be high in overweight and obese group, however this association is found to be not statistically significant ($p>0.05$). TSH is found to be high in Overt hypothyroidism group ($p<0.05$), whereas Free T3 and Free T4 was high in sub-clinical hypothyroidism group. All parameters were found to be high in CKD patients, whereas low levels found in all COPD patients. Except for Free T3, all the parameters are high in overweight and obese group and this association is not statistically significant ($p<0.05$). (Table 3,4,5)

DISCUSSION

The study's mean age was 43.0±13.0 years, with the bulk of participants (43.7%) being between the ages of 31 and 40 and those over 50 coming in second (22.5%). According to Anubhuti et al., the mean age of hypothyroid people was 39.1 years, while the total mean age was 44.2 years.(13) Similarly, the majority of patients in Hiregoudar et al., were between the ages of 41 and 60.(14) The gender distribution of the current study revealed that women made up the majority (97.2%), which is in line with Pradhan et al., who found that women made up 84%.(15) Nonetheless, according to Anubhuti et al., there were roughly equal numbers of males (50.75%) and females (49.25%).(13)

Mean BMI of 27.2±4.52 kg/m² was found, with 67.6% of patients classified as obese, 15.5% as overweight, and 15.5% as normal based on the Asian-Pacific BMI classification. A mean BMI of 25.7±2.89 kg/m² was reported by Chen et al., but Anubhuti et al., discovered that 30% of hypothyroid participants were overweight and 50% had normal BMIs.(16, 13) In the current study, the majority of participants lived in metropolitan regions (77.5%) and were unemployed (76.1%). A considerable percentage (57.7%) had hypothyroidism for longer than five years; 22.5% were taking 50 mcg of thyroxine and 63.5% were taking 100 mcg of the medication. A low percentage of people (46.5%) did not follow any particular diet, while 23.9% followed a thyroid diet, 18.3% followed DASH, and 11.3% followed a diabetic diet. Among co-morbidities, diabetes (56.3%) and hypertension (62.0%) were most prevalent.

Free T3, Free T4, and TSH had mean plasma levels of 2.21±0.97, 1.34±0.50, and 30.2±22.7, respectively. According to Chen et al., TSH was 3.58 mIU/L, FT3 was 2.57 pmol/L, and FT4 was 7.25 pmol/L.(16) TSH was measured at 11.8±2.65 µIU/L, T4 at 6.35±1.61 µg/dl, and T3 at 1.94±0.18 ng/ml by Dheyaa et al.(17)

Regarding thyroid dysfunction, 19.7% of participants had subclinical hypothyroidism and 80.3% had overt hypothyroidism. Khatri et al. reported 81.7% overt and 18.3% subclinical hypothyroidism, which is comparable to this range.(18) On the other hand, subclinical hypothyroidism was the most common (11.4%), according to Pradhan et al.(15)

Examination of the lipid profile showed mean values of 133.8±36.5 mg/dl (LDL), 35.9±6.28 mg/dl (VLDL), 31.5±11.0 mg/dl (HDL), 196.1±38.4 mg/dl (TC), and 165.5±42.8 mg/dl (TG). Higher levels of HDL (42.2±2.80), LDL (124.4±34.83), VLDL (34.45±16.55), TC (254.2±42.41), and TG (172.3±82.77) were reported by Muthireddy et al., TC was 210.6±9.90, HDL was 28.8±3.70, LDL was 144.9±12.0, TG was 193.5±14.0, and VLDL was 38.7±2.79.(19) These values were reported by Dheyaa et al., in contrast to other thyroid conditions, hypothyroid individuals also had higher lipid levels, according to Anubhuti et al.(17, 13) High LDL of 38.0%, high VLDL 70.4%, hypercholesterolemia 16.9%, hypertriglyceridemia 23.9% and low HDL 100% were among the dyslipidemia prevalence in the current study. Omar et al., found that the following rates were higher: 41.8% low HDL-C, 42.5% hypercholesterolemia, 48.2% high LDL-C, and 34.1% hypertriglyceridemia. Overall, 69.0% of people had dyslipidemia, according to Khatri et al.(20,18)

Among subjects with CKD, lipid levels were notably elevated with TC, LDL, VLDL, and TG averaging 220.5 mg/dl, and HDL at 25.0 mg/dl. TC and VLDL levels were similar across other co-morbidities. Muthireddy et al., also highlighted elevated serum TG and VLDL levels were also found to be significantly raised in both CKD and hypothyroid individuals.(19)

When compared to people with normal thyroid function, cardiac patients in the study by Alsalmi et al. showed lower levels of high-density lipoproteins (HDL) and higher levels of total cholesterol (TC), low-density lipoproteins (LDL), very low-density lipoproteins (VLDL), and triglycerides (TG).(21) These results are supported by the current investigation, which found that overt hypothyroidism was associated with considerably higher levels of all lipid markers except HDL ($p<0.05$). In a similar vein, Abdel-Gayoum 2014, found that overt hypothyroid individuals had lower HDL and higher LDL and VLDL than other groups.(9)

Khatri et al., confirmed the substantial correlation between thyroid dysfunction and lipid abnormalities by finding dyslipidemia in 75.9% of overt hypothyroid cases and 38.5% of subclinical hypothyroid cases.(18) Additionally, Hiregoudar et al., found statistically significant variations in TC, TG, and LDL values among the various forms of hypothyroidism ($p<0.05$).(14)

A significant association was noted between HDL levels and BMI categories, with higher HDL values in overweight and obese individuals ($p<0.05$). Although other lipid parameters were elevated in these groups, the association was not statistically significant ($p>0.05$). Humerah et al., found a significant correlation between BMI and altered lipid profiles among hypothyroid subjects ($p<0.01$), supporting the link between obesity and dyslipidemia.(22)

Thyroid function analysis revealed significantly elevated TSH levels in overt hypothyroidism ($p<0.05$), while Free T3 and Free T4 were higher in subclinical hypothyroidism. Hiregoudar et al., also demonstrated statistically significant differences in thyroid hormone levels across hypothyroidism types ($p<0.001$).(14) In the current study, all thyroid parameters were elevated in chronic kidney disease (CKD) patients, whereas lower levels were observed in chronic obstructive pulmonary disease (COPD) patients. Among overweight and obese individuals, all thyroid parameters except Free T3 were elevated, though these associations were not statistically significant ($p<0.05$).

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TABLES

Table No. 1: Baseline Demographic Profile and BMI

Age group (in years)	**Frequency**	**Percentage**
≤30	10	14.1
31-40	31	43.7
41-50	14	19.7
>50	16	22.5
Total	71	100.0
Sex	**Frequency**	**Percentage**
Female	69	97.2
Male	2	2.80
Total	71	100.0
Occupation	**Frequency**	**Percentage**
Employed	17	23.9
Unemployed	54	76.1
Total	71	100.0
Residence	**Frequency**	**Percentage**
Urban	55	77.5
Rural	16	22.5
Total	71	100.0
BMI categories	**Frequency**	**Percentage**
Underweight	1	1.40
Normal	11	15.5
Overweight	11	15.5
Obese	48	67.6
Total	71	100.0

Table No. 2: Hypothyroidism Profile and Prevalence of Dyslipidemia among the study participants

Duration of hypothyroidism (in years)		**Frequency**	**Percentage**
≤5		30	42.3
>5		41	57.7
Total		71	100.0
Treatment of hypothyroidism (Dosage of Thyroxine in mcg)		**Frequency**	**Percentage**
25		6	8.45
50		16	22.5
75		2	2.82
100		45	63.5
125		2	2.82
Total		71	100.0
Type of diet		**Frequency**	**Percentage**
Thyroid diet		17	23.9
DASH diet*		13	18.3
Diabetic diet		8	11.3
Not following any diet pattern		33	46.5
Total		71	100.0
Co-morbidities		**Frequency**	**Percentage**
Diabetes		40	56.3
Hypertension		44	62.0
Coronary Artery Disease (CAD)		13	18.3
Chronic Kidney Disease (CKD)		02	2.80
Chronic Obstructive Pulmonary Disease (COPD)		01	1.4
Type of hypothyroidism		**Frequency**	**Percentage**
Sub-clinical hypothyroidism		14	19.7
Overt hypothyroidism		57	80.3
Total		71	100
Prevalence of Dyslipidemia among hypothyroid patients			
Lipid profile	**Grading**	**Frequency**	**Percentage**
TC	Desirable/Borderline	59	83.1
	High	12	**16.9**
TG	Desirable/Borderline	54	76.1
	High	17	**23.9**

HDL	Desirable/Borderline	71	**100.0**
	High	0	0.0
LDL	Desirable/Borderline	44	62.0
	High	27	**38.0**
VLDL	Desirable/Borderline	21	29.6
	High	50	**70.4**
Total		71	100.0

Table No. 3: Mean lipid profile values in hypothyroid patients

Lipid profile	Type of hypothyroidism		Statistical significance
	Sub-clinical 14	Overt 57	
TC	172.8 ± 51.0	201.8 ± 32.7	t=2.65, p=0.01, S
LDL	115.6 ± 42.3	138.3 ± 33.8	t=2.15, p=0.04, S
VLDL	30.4 ± 7.13	37.3 ± 5.28	t=4.08, p<0.00001, S
TG	125.1 ± 25.8	175.4 ± 40.3	t=4.43, p<0.00001, S
HDL	34.1 ± 11.1	30.8 ± 10.9	t=1.02, p=0.31, NS

Table No. 4: Mean lipid profile values in hypothyroid patients with co-morbidities

	Mean Lipid profile values (mg/dl)				
	TC	LDL	VLDL	TG	HDL
DM	193.6 ± 44.1	128.3 ± 37.0	34.8 ± 7.59	162.1 ± 46.1	31.9 ± 11.2
HTN	193.9 ± 42.0	127.1 ± 36.5	34.6 ± 7.36	168.4 ± 48.6	31.7 ± 11.1
CAD	194.9 ± 44.1	116.6 ± 37.2	33.5 ± 7.94	176.8 ± 54.7	27.9 ± 10.1
CKD	220.5 ± 27.6	145.0 ± 49.5	41.0 ± 5.66	180.5 ± 29.0	25.0 ± 5.66
COPD*	160.0	110.0	35.0	110.0	27.0

Table No. 5: Mean lipid profile values in hypothyroid patients by BMI categories

Lipid profile	BMI categories		Statistical significance
	Underweight & Normal	Overweight & Obese	
TC	205.8 ± 45.2	194.2 ± 37.0	t=0.95, p=0.34, NS
LDL	124.6 ± 25.6	135.7 ± 38.2	t=0.96, p=0.34, NS
VLDL	34.8 ± 5.04	36.1 ± 6.52	t=0.64, p=0.52, NS
TG	157.3 ± 31.0	167.1 ± 44.8	t=0.72, p=0.47, NS
HDL	24.3 ± 7.35	32.9 ± 11.1	t=2.60, p=0.01, S