

**A COMPARATIVE STUDY OF DYSLIPIDAEMIA IN SUBCLINICAL VERSUS OVERT HYPOTHYROIDISM**Anjali Jayakumar<sup>1</sup>, Sharath Kumar D Shah<sup>2</sup>, Suma K. R<sup>3</sup><sup>1</sup>Junior Resident, Department of General Medicine, Sri Siddhartha Medical College, Tumkur, Karnataka.<sup>2</sup>Professor and HOD, Department of General Medicine, Sri Siddhartha Medical College, Tumkur, Karnataka.<sup>3</sup>Professor, Department of General Medicine, Sri Siddhartha Medical College, Tumkur, Karnataka.**ABSTRACT****BACKGROUND**

Hypothyroidism is a metabolic disorder with a cluster of clinical signs and symptoms, especially in middle-aged women. Spectrum of cardiovascular manifestation includes hypertension and dyslipidaemia, which are major causes of atherosclerosis and coronary artery disease. Altered lipid profile is a major expression in overt hypothyroidism according to many previous studies. We have established the relationship in subclinical hypothyroidism.

Aim and Objective-

1. The aim of this study is to improve the ability to diagnose unsuspected dyslipidaemia, especially in subclinical hypothyroidism to reduce further morbidity.
2. The objective of this study is to assess and compare varying degree of dyslipidaemia in subclinical and overt hypothyroidism patients.

**MATERIALS AND METHODS**

This is a descriptive study. The present study was carried out in the Department of General Medicine at Sri Siddhartha Medical College, Tumkur, Karnataka, with 100 patients (50 subclinical hypothyroidism and 50 overt hypothyroidism patients). Thyroid Profile was done with CLIA (chemiluminescence immunoassay) system. Lipid Profile was done with semi-automated analyser.

**RESULTS**

In the present study, the mean total cholesterol values were  $195.2 \pm 42.27$  and  $180.76 \pm 41.32$ ; Triglycerides values were  $155.44 \pm 42.69$ ,  $152.2 \pm 32.82$ ; HDL values were  $45.46 \pm 5.02$ ,  $46.64 \pm 5.32$ ; and LDL values were  $124.43 \pm 42.45$ ,  $119.75 \pm 39.99$  respectively in the subclinical hypothyroidism and overt hypothyroidism.

**CONCLUSION**

In overt hypothyroid group, TSH showed statistically significant positive correlation with total cholesterol ( $r = 0.434$ ,  $p < 0.0164$ ), Triglyceride ( $r = 0.339$ ,  $p < 0.05$ ) and LDL cholesterol ( $r = 0.409$ ,  $p < 0.05$ ). TSH had negative correlation with HDL cholesterol ( $r = -0.394$ ,  $p < 0.05$ ). In Subclinical hypothyroid group, TSH showed statistically significant correlation with total cholesterol ( $r = 0.387$ ,  $p < 0.05$ ), LDL-C ( $r = 0.404$ ,  $p < 0.05$ ). The correlation between TSH was statistically not significant for Triglyceride, VLDL and HDL-C. No direct correlation was found between TSH levels and degree of dyslipidaemia. The study has demonstrated and has further proved that hypothyroidism also causes significant dyslipidaemia in subclinical hypothyroidism.

**KEYWORDS**

Subclinical Hypothyroidism, Overt Hypothyroidism, TSH, Dyslipidaemia, Lipid Profile, Atherogenic Pattern, Cardiovascular Morbidity.

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**BACKGROUND**

Hypothyroidism is a common metabolic disorder in the general population. World Health Organisation (WHO) estimates that about 2 billion people are iodine-deficient based on urinary excretion data.<sup>1</sup> It is estimated that about 200 million people are at the risk of Iodine Deficiency Disease in our country.<sup>2</sup> A cross-sectional, multi-centre, epidemiological study conducted in eight major cities (Bangalore, Chennai, Delhi, Goa, Mumbai, Hyderabad, Ahmedabad and Kolkata) of India concluded that the prevalence of hypothyroidism was high affecting 1 in 10 adults in the

study population, is higher in females.<sup>3</sup> In general overt and subclinical hypothyroidism is associated with hypercholesterolaemia, mainly due to elevation of low density lipoprotein (LDL) cholesterol levels, whereas high density lipoprotein (HDL) cholesterol concentration is usually normal or even elevated.<sup>4-6</sup> Thyroid hormone has a major effect on the lipoprotein metabolism, which stimulates the hepatic de novo cholesterol synthesis by inducing the 3-hydroxy-methyl-glutaryl-coenzyme A (HMG-CoA) reductase that catalyses the conversion of HMG-CoA to mevalonate, the first step in the biosynthesis of cholesterol.<sup>7</sup> It is proved that thyroid substitution is beneficial for patients with overt hypothyroidism, but whether or not to treat subclinical hypothyroidism remains controversial. Subclinical hypothyroidism (SH) refers to biochemical evidence of thyroid hormone deficiency in patients who have few or no apparent clinical features of hypothyroidism. There are no universally accepted recommendations for the management. When TSH levels are below 10 mIU/L, treatment should be considered when patients have suggestive symptoms of hypothyroidism, positive TPO antibodies or any evidence of

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heart disease. It is important to confirm that any elevation of TSH is sustained over a 3-month period before treatment is given.

Hypothyroidism is defined as failure of the thyroid gland to produce sufficient thyroid hormone to meet the metabolic demands of the body. Untreated hypothyroidism can contribute to hypertension, dyslipidaemia, infertility, cognitive impairment and neuromuscular dysfunction. The prevalence increases with age and is higher in females than in males. Efsthadiadou et al<sup>8</sup> evaluated the serum lipid parameters of 66 patients with SH and 75 age- and sex-matched euthyroid controls and found SH had significantly higher levels of total cholesterol, LDL cholesterol, apolipoprotein B and Lp (a), whereas levels of triglycerides, HDL cholesterol and apolipoprotein did not differ significantly compared to euthyroid controls.

A recent Indian study by Marwaha RK et al<sup>9</sup> on dyslipidaemia in subclinical hypothyroidism in an Indian population shows that no atherogenic lipid abnormalities were found in adult subjects with subclinical hypothyroidism with TSH < 10.0 mIU/L; however, significant correlation has been found when the TSH is between 10.1 mIU/L and 20 mIU/L in subjects with subclinical hypothyroidism.

### Aim

To improve the ability to diagnose unsuspected dyslipidaemia, especially in subclinical hypothyroidism to reduce further morbidity. The objective is to assess and compare varying degree of dyslipidaemia in subclinical and overt hypothyroidism patients.

### MATERIALS AND METHODS

This is a descriptive study. The present study was carried out in the Department of General Medicine, Sri Siddhartha Medical College, Tumkur, Karnataka, with 100 patients (50 Subclinical hypothyroidism and 50 Overt hypothyroidism patients). Sample size was taken conveniently. The period of the study extended to about two years. All the patients' venous blood sample was withdrawn for investigation of Total triiodothyronine (T3), Total thyroxine (T4) and thyroid stimulating hormone (TSH) and in Lipid Profile- Total cholesterol, LDL, Triglyceride, Cholesterol, HDL and VLDL was done. After explaining the nature, procedure, purpose and other relevant details of the study, verbal informed consent were taken from all the subjects.

Thyroid Profile was done with CLIA (chemiluminescence immunoassay) system. Lipid Profile was done with semi-automated analyser.

### The following guidelines for lab values were followed- LDL Cholesterol

Optimal: Less than 100 mg/dL (2.59 mmol/L); for those with known disease (ASCVD or diabetes), less than 70 mg/dL (1.81 mmol/L) is optimal.

Near/above optimal: 100-129 mg/dL (2.59-3.34 mmol/L)

Borderline high: 130-159 mg/dL (3.37-4.12 mmol/L)

High: 160-189 mg/dL (4.15-4.90 mmol/L)

Very High: Greater than 190 mg/dL (4.90 mmol/L)

### Total Cholesterol

Desirable: Less than 200 mg/dL (5.18 mmol/L)

Borderline High: 200-239 mg/dL (5.18 to 6.18 mmol/L)

High: 240 mg/dL (6.22 mmol/L) or higher.

### HDL Cholesterol

Low level, increased risk: Less than 40 mg/dL (1.0 mmol/L) for men and less than 50 mg/dL (1.3 mmol/L) for women.

Average level, average risk: 40-50 mg/dL (1.0-1.3 mmol/L) for men and between 50-59 mg/dL (1.3-1.5 mmol/L) for women.

High level, less than average risk: 60 mg/dL (1.55 mmol/L) or higher for both men and women.

### Fasting Triglycerides

Desirable: Less than 150 mg/dL (1.70 mmol/L)

Borderline high: 150-199 mg/dL (1.7-2.2 mmol/L)

High: 200-499 mg/dL (2.3-5.6 mmol/L)

Very High: Greater than 500 mg/dL (5.6 mmol/L)

T4 - 70-151 nmol/L

T3 - 1.2-2.1 nmol/L

TSH - 0.34-4.25 mIU/L

### Inclusion Criteria

1. Newly detected hypothyroidism.
2. Old uncontrolled hypothyroidism.

### Exclusion Criteria

1. Subjects with known dyslipidaemia.
2. Patients taking lipid lowering medicine.
3. Patients with congenital heart disease, rheumatic heart disease, diabetes mellitus, smoking, alcohol, COPD and severe anaemia.

Ethical approval was granted by SSAHE University, Tumkur, Karnataka.

### Methodology Data Analysis

The analysis was done using standard Statistical Package for Social Sciences (SPSS) software version 24. The collected data were entered into an excel sheet. The data were expressed in means, medians and proportions and presented in the form of tables and graphs wherever necessary. Simple descriptive measures like mean, standard deviation and variables of lipid profile in hypothyroidism analysed using Chi-square test, student's 't' test. The continuous variables were expressed in means or medians and categorical variables were expressed in proportions. Correlation between variables were done using Pearson correlation test. The comparison of means of various parameters with normal subjects, subclinical and overt hypothyroid patients was done using independent t-test. The association of categorical variables were analysed using Chi-square test. P-value of < 0.05 was taken as statistically significant.

### RESULTS

The study was conducted in Sri Siddhartha Medical College Hospital, Tumkur, Karnataka over a period of two years, a total of 100 patients were enrolled in this study.

	<20 years	20-30 years	31-40 years	41-50 years	51-60 years	>60 years	Total
Overt	3 (6%)	15 (30%)	12 (24%)	11 (22%)	6 (12%)	3 (6%)	50
Subclinical	2 (4%)	16 (32%)	13 (26%)	11 (22%)	7 (14%)	1 (2%)	50

**Table 1. Distribution of Overt and Subclinical Hypothyroidism by Age**

Overt		Subclinical	
Male	Female	Male	Female
10 (20.0%)	40 (80%)	0	50 (100%)

**Table 2. Distribution of Overt and Subclinical Hypothyroidism by Gender**

Overt	Gender	<20 years	20-30 years	31-40 years	41-50 years	51-60 years	>60 years	Total
Male	Count	0(0%)	3(30%)	3(30%)	2(20%)	2(20%)	0(0%)	10(100%)
Female	Count	3(8%)	12(30%)	9(23%)	9(23%)	4(10%)	3(8%)	40(100%)
Chi Square=2.377, P=.795								
Subclinical	Female	2(4%)	16(32%)	13(26%)	11(22%)	7(14%)	1(2%)	50(100%)

**Table 3. Age Wise Distribution among Males and Females of Subclinical and Overt Hypothyroidism**

	N	Minimum	Maximum	Mean	Std. Error	Std. Deviation
Overt	50	18	70	38.56	1.889	13.360
Subclinical	50	17	61	37.72	1.703	12.044

**Table 4. Mean of Age in Different Groups**

	Overt	Subclinical	Comparison between Overt and Subclinical		Comparison between Normal and Overt		Comparison between Normal and Subclinical	
			t	P	t	P	t	P
Total cholesterol	195.2 ± 42.27	180.76 ± 41.32	1.728	.087	-31.79	0.000	-30.05	0.000
Triglycerides	155.44 ± 42.69	152.2 ± 32.82	.425	.672	-25.47	0.000	-32.43	0.000
LDL	124.43 ± 42.45	119.75 ± 39.99	.567	.572	-20.30	0.000	-20.72	0.000

HDL	Overt		Subclinical	Comparison between Overt and Subclinical		Comparison between Normal and Overt				Comparison between Normal and Subclinical	
	Male	Female	Female	t	P	t		P		t	P
	F	F	F	F	F	M	F	M	F	F	F
	43.87 ± 6.0	45.85 ± 4.75	46.64 ± 5.32	-7.29	.468	50.16	65.96	0.000	0.000	-59.99	0.000

**Table 5. Mean Value and the Significant Difference between the Factors among Overt and Subclinical**

TSH Level (mIU/L)	Overt		Subclinical	
	No. of Cases	%	No. of Cases	%
< 5.5	0	0	4	8.0
5.6-10.9	0	0	45	90.0
11-30	3	6.0	0	0.0
31-60	15	30.0	0	0.0
61 and above	32	64.0	1	2.0

**Table 6. Distribution of Cases according to TSH Level Range**

	Overt		Subclinical	
	No. of Cases	%	No. of Cases	%
<5.5	38	76.0	40	80.0
5.6-10.9	2	4.0	0	0
11-30	2	4.0	1	2.0
31-60	1	2.0	1	2.0
61 and above	7	14.0	8	16.0
<b>Total</b>	<b>50</b>	<b>100.0</b>	<b>50</b>	<b>100.0</b>

**Table 7. Distribution of Cases according to T3 (Triiodothyronine) Level Range**

	Overt		Subclinical	
	No. of Cases	%	No. of Cases	%
<5.5	45	90.0	30	60.0
5.6-10.9	4	8.0	17	34.0
11-30	1	2.0	2	4.0
61 and above	0	0.0	1	2.0

**Table 8. Distribution of Cases according to T4 (Tetraiodothyronine) Level Range**

		<20 years	20-30 years	31-40 years	41-50 years	51-60 years	>60 years
		Total cholesterol	Overt	217.67 ± 60.12	185.33 ± 38.03	200.67 ± 38.95	196.91 ± 50.28
	Subclinical	203.5 ± 86.97	155.31 ± 25.06	195.46 ± 49.17	188.45 ± 43.97	189.43 ± 19.55	206 ± 0
Triglycerides	Overt	141.33 ± 4.16	143.33 ± 21.39	151.83 ± 59.8	163.09 ± 46.54	187 ± 47.38	153.33 ± 23.09
	Subclinical	140.5 ± 34.65	143.01 ± 42.75	161.92 ± 31.85	153.09 ± 22.72	152.29 ± 21.7	186 ± 0
HDL	Overt	50 ± 3.46	45.82 ± 5.64	46.01 ± 3.33	43.29 ± 5.17	44.2 ± 5	47.33 ± 7.57
	Subclinical	49 ± 7.07	46.82 ± 5.74	44.17 ± 4.69	46.64 ± 6.02	49.94 ± 2.83	48 ± 0
LDL	Overt	113 ± 16.46	133.81 ± 58.27	116.37 ± 14.85	126.73 ± 54.49	120.33 ± 29.23	121 ± 23.81
	Subclinical	149 ± 80.61	99.56 ± 17.9	139.38 ± 53.61	125.51 ± 38.92	110.57 ± 22.82	130 ± 0

**Table 9. Parameters Observed in Overt and Subclinical Hypothyroidism in Different Age Group**

		Overt		Subclinical	
		Correlation coefficient	P value	Correlation coefficient	P value
HDL vs. TSH		-0.084	0.561	-0.092	0.525
Total cholesterol vs. TSH		0.144	0.317	0.01	0.943
Triglycerides vs. TSH		0.196	0.173	0.072	0.622
LDL vs. TSH		0.124	0.391	-0.007	0.96

**Table 10. Correlation between of TSH and Thyroid Profile**

None of the values are significant.

## DISCUSSION

At least one in every 10 persons in India is suffering from hypothyroidism<sup>3</sup>; hence, the predisposition towards morbidity, especially cardiovascular is high, out of which a number of cases go undiagnosed. It is estimated that 2% - 5% of SCH has a propensity to progress to overt hypothyroidism in 2 - 3 years. Our study included 100 cases of subclinical and overt hypothyroidism, who underwent lipid profile estimation. 50 cases belonged to subclinical and 50 cases belonged to overt hypothyroidism. Out of 50 subclinical cases, all were females (100%). Similarly, out of 159 cases of overt hypothyroidism, majority (80%) were females. This shows female preponderance of this clinical condition. Mean age of subclinical and overt hypothyroidism cases were 37.72 and 38.56 respectively. This range of presentation implies a preponderance to early presentation in females. Mean total cholesterol in between SCH and overt hypothyroidism patients was found to be non-significant. Sharma et al<sup>10</sup> showed a statistically significant positive correlation with total cholesterol ( $r=0.434$ ,  $p < 0.0164$ ). The Rotterdam study reported that total cholesterol was not elevated in SCH.<sup>9</sup> We found statistically no significant difference in total TG levels between subclinical and overt hypothyroidism patients. Sharma et al<sup>10</sup> concluded that the correlation between TSH was statistically not significant for Triglyceride. This result was similar to our study result. A recent study in SCH showed that transfer of triglycerides to HDL and phospholipids was lower than that in controls, while transfer of free and esterified cholesterol to HDL, HDL particle size and paraoxonase 1 activity did not exhibit any difference.<sup>10</sup>

In our study, the mean LDL levels between SCH and overt hypothyroidism patients were found to be statistically non-significant. In SCH, thyroid hormone deficiency leads to a

decreased number of LDL receptors on the liver cell surface resulting in decreased uptake and degradation of LDL-C.

The key findings to our study was the positive correlation of Total cholesterol, Triglycerides, HDL and LDL in SCH patients when compared with normal range values. This is an indication that SCH has an atherogenic serum lipid profile pattern.

Asranna A et al<sup>11</sup> reported a positive correlation between total cholesterol and mean LDL levels in SH compared to controls, but there was no statistically significant difference in the mean HDL, VLDL and triglyceride levels. Dr. Shivaleela M Biradar,<sup>12</sup> in a study of 60 subjects found a significant reduction in TC and LDL-C levels following levothyroxine therapy in SCH. The Colorado study, which screened 25,862 subjects found that mean TC and LDL-C progressively increased with increasing serum TSH levels. In the NHANES III, mean cholesterol levels were higher in people with subclinical hypothyroidism than in euthyroid controls. There were no differences in LDL-C or HDL-C levels.<sup>13</sup> In the Rotterdam Study, TC was lower in women with subclinical hypothyroidism than in euthyroid women.<sup>14</sup> Milonis et al<sup>15</sup> 2005 and Toruner et al<sup>16</sup> 2008, have delineated an increased triglyceride and decreased HDL levels in SCH.

## CONCLUSION

Hypothyroidism is a female predominant metabolic disorder. No direct correlation was found between TSH levels and degree of dyslipidaemia. There was no significant difference seen in lipid parameters of subclinical and overt hypothyroidism subgroups. Importantly, the SCH patients' lipid profile was notable for an atherogenic pattern, which suggests a need to detect such cases where they are more prone for cardiovascular morbidity.

## REFERENCES

- [1] Fauci AS, Kasper DL, Longo DL, et al. Harrison's principles of internal medicine. Chapter: Disorders of thyroid gland. 19<sup>th</sup> edn. McGraw Hill 2008:2292-3.
- [2] Shah SN, Joshi SR. Think thyroid: special issue on Indian thyroid guidelines. *Journal of Associations of Physicians of India* 2011;59:6.
- [3] Unnikrishnan AG, Kalra S, Sahay RK, et al. Prevalence of hypothyroidism in adults: an epidemiological study in eight cities of India. *Indian J Endocrinol Metab* 2013;17(4):647-52.
- [4] Canaris GJ, Manowitz NR, Mayor G, et al. The colorado thyroid disease prevalence study. *Arch Intern Med* 2000;160(4):526-34.
- [5] O'Brien T, Dinneen SF, O'Brien PC, et al. Hyperlipidemia in patients with primary and secondary hypothyroidism. *Mayo Clin Proc* 1993;68(9):860-6.
- [6] Muls E, Rosseneu M, Bleton V, et al. Serum lipids and apolipoproteins A-I, A-II and B in primary hypothyroidism before and during treatment. *Eur J Clin Invest* 1984;14(1):12-5.
- [7] Khanna VN. Comparison of dyslipidemia between overt and subclinical hypothyroidism. *International Journal of Scientific Research* 2016;5(8).
- [8] Efstathiadou Z, Bitsis S, Milionis HJ, et al. Lipid profile in subclinical hypothyroidism: is L-thyroxine substitution beneficial? *Eur J Endocrinol* 2001;145(6):705-10.
- [9] Marwaha RK, Tandon N, Garg MK, et al. Dyslipidemia in subclinical hypothyroidism in an Indian population. *Clin Biochem* 2011;44(14-15):1214-7.
- [10] Sharma P, Patgiri D, Goyal S, et al. Hypothyroidism causing dyslipidemia in both subclinical & overt hypothyroidism. *Indian J Basic Appl Med Res* 2013;7(2):779-88.
- [11] Asranna A, Taneja RS, Kulshreshta B, et al. Dyslipidemia in subclinical hypothyroidism and the effect of thyroxine on lipid profile. *Indian J Endocrinol Metab* 2012;16(Suppl 2):S347-9.
- [12] Biradar SM, Patil SR. Study of lipid profile in subclinical hypothyroidism. *Int J Pharm Bio Sci* 2015;6(3):(B)1-6.
- [13] Hollowell JG, Staehling NW, Flanders WD, et al. Serum TSH, T(4), and thyroid antibodies in the United States population (1988 to 1994): national health and nutrition examination survey (NHANES III). *J Clin Endocrinol Metab* 2002;87(2):489-99.
- [14] Hofman A, Brusselle GG, Murad SD, et al. The rotterdam study: 2016 objectives and design update. *Eur J Epidemiol* 2015;30(8):661-708.
- [15] Milionis HJ, Tambaki AP, Kanioglou CN, et al. Thyroid substitution therapy induces high-density lipoprotein-associated platelet-activating factor-acetylhydrolase in patients with subclinical hypothyroidism: a potential antiatherogenic effect. *Thyroid* 2005;15(5):455-60.
- [16] Toruner F, Altinova AE, Karakoc A, et al. Risk factors for cardiovascular disease in patients with subclinical hypothyroidism. *Adv Ther* 2008;25(5):430-7.