

Lipid Patterns in Sub Clinical Hypothyroidism of Non-Obese Group in Rural Tertiary Care Centre

Krishna Murthy V¹, Venkata Madhav M², Anjaneya Prasad V³, Pradeep Babu K⁴

¹Associate Professor, Department of Biochemistry, Dr. PSIMS, Chinoutpally, Gannavaram Mandal, Krishna District, Andhra Pradesh, India. 521286

²Associate Professor, Department of Internal Medicine, Dr. PSIMS, Chinoutpally, Gannavaram Mandal, Krishna District, Andhra Pradesh, India, 521286

³Associate Professor, Department of Internal Medicine, Dr. PSIMS, Chinoutpally, Gannavaram Mandal, Krishna District, Andhra Pradesh, India, 521286

⁴Resident, Department of Internal Medicine, Dr. PSIMS, Chinoutpally, Gannavaram Mandal, Krishna District, Andhra Pradesh, India, 521286

Abstract: *Dyslipidemia is an abnormal lipid metabolism leads to elevation in serum lipids results in hyperlipidemias, particularly hypercholesterolemia and hypertriglyceridemia or combined, which intern predisposes atherosclerosis and then triggers micro or macro vascular complications like cardiovascular and cerebro vascular system. The purpose of this case - control study was to correlate atherogenic lipid abnormalities in sub clinical hypothyroidism to non sub clinical hypothyroid patients. This study was done at the Department of Biochemistry, DR. PSIMS & RF foundation Chinaoutpally, A.P. India between Jan 2012 to Dec 2012. 100 patients (50 Sub Clinical Hypothyroidism, 50 age and sex matched controls) above 18 years of age were included in the study. The mean TSH was Sub Clinical Hypothyroidism was 9.96 ± 3.57 and in controls was 2.26 ± 1.45 ($p = 0.05$). The mean Cholesterol levels were 218.1 ± 35.75 and 158.95 ± 26.45 in Sub Clinical Hypothyroidism and control groups respectively. The mean Triglyceride levels were 172.85 ± 81.25 and 131.05 ± 60.65 in Sub Clinical Hypothyroidism and control groups respectively Mean HDL - Cholesterol levels of males was lower than females in Sub Clinical Hypothyroid groups (p - Value < 0.05). The study concludes that Dyslipidemia is more common in sub clinical hypothyroidism and it enhances the risk of premature atherosclerosis causing cardiovascular and cerebro vascular complications.*

Keywords: Hypothyroidism, serum cholesterol, lipids, thyrotropin

1. Introduction

Sub Clinical Hypothyroidism is a mild thyroid gland dysfunction, with or without symptoms of hypothyroidism¹⁻³. Based on decreased thyroid function, pituitary is stimulated and releases TSH on the basis of positive feedback mechanism. Subclinical hypothyroidism is diagnosed biochemically by elevated serum thyrotropin (TSH) level, with normal serum tri iodo thyronine (FT₃) and free thyroxine (FT₄) levels. Sub clinical hypothyroidism is a risk factor for increased incidence of coronary events, increased rates of congestive heart failure⁴ and lipid abnormalities⁵. Dyslipidemia is one of many modifiable and non modifiable cardiovascular risk factors like diastolic hypertension, impaired endothelial function, increased arterial stiffness, and coagulation parameters and elevated C-reactive protein levels are associated with subclinical hypothyroidism⁶. Sub clinical hypothyroidism was associated with elevated serum total cholesterol and LDL-cholesterol, decreased LDL-cholesterol/LDL-triglycerides due to decreased hepatic lipase activity⁷. The influence of Sub clinical hypothyroidism on lipid metabolism was directly proportional to the degree of thyrotropin (TSH) elevation and indirect proportion of hepatic lipase activity⁷. Patients with thyroid dysfunction particularly in sub clinical hypothyroidism, significant lipid alterations like serum total cholesterol, triglyceride, and high - density lipoprotein and low - density lipoprotein cholesterol were associated with the changes in the activities of hepatic lipase and lipoprotein lipase⁸. The Pathophysiology lies behind the lipid alterations of overt and subclinical hypothyroidism includes elevations in serum total cholesterol and LDL- cholesterol due to

changes in the synthesis, metabolism, and mobilization of lipids in liver and adipose tissue. Thyroid hormone particularly thyrotropin (TSH) level induces the hepatic expression of hydroxymethylglutaryl coenzyme A reductase, which results in increased cholesterol synthesis⁹.

The mechanism of Lipoprotein lipase lowers serum triglyceride levels through hydrolysis of triglyceride-enriched lipoproteins and augments transfer of cholesterol from these lipoproteins to HDL-C. Lipoprotein lipase activity is increased by serum tri iodo thyronine (FT₃) and free thyroxine (FT₄) levels. Higher serum triglycerides are associated with lower lipoprotein lipase activity¹⁰.

The diagnosis is based upon biochemical testing which is done by chemiluminiscence technique. The normal TSH range is 0.4 – 4.5 μ L TSH. Wide variations in serum thyrotropin (TSH) level were seen in individuals with different ethnic origin, age, health status and body mass index (BMI). On this background, our study aims at comparing the occurrence of atherogenic lipid abnormalities in sub clinical hypothyroidism to non sub clinical hypothyroid patients.

2. Materials and Methods

This case – control study was done in the department of Biochemistry in Dr. PSIMS & RF, Chinaoutpally, Gannavaram, Krishna (Dist), Andhra Pradesh. 100 patients (50 Sub Clinical Hypothyroidism, 50 age and sex matched

controls) above 18 years of age were included. All patients survive till the end of study period of one year duration i.e. Jan-2012 to Dec – 2012.

Diagnosis of sub clinical hypothyroidism were done as per the biochemical parameters such as thyroid function tests were carried out by chemiluminiscence (CLIA) method and the reference values in our laboratory were TSH : 0.4 – 4.5 μ IU/L, T₃ – 0.8-2.0 μ g/ml T₄ – 5.13 – 14.06 μ g/dl. Lipid profile (Cholesterol, triglyceride. HDL- Cholesterol and LDL - cholesterol was estimated in both cases and controls. The study was approved by the Ethics committee of our college. After fulfilling the inclusion and exclusion criteria, prior consent was obtained from the subjects.

2.1 Inclusion criteria

Patients with TSH: >4.5 μ IU/L in Sub Clinical Hypothyroid patients and TSH: 0.4 – 4.5 μ IU/L in controls Normal serum tri iodo thyronine (FT₃) and free thyrosine (FT₄) levels Age 18 or older.

2.2 Exclusion criteria

Patients with heart failure, acute febrile illness, renal, hepatic, malignant disorders, chronic illnesses, asymptomatic infections and smokers.

2.3 Sample collection and analysis

Both heparinised and plain blood samples were collected from each case and control. For analysis of FBS, lipid profile - serum was used and for HBAlc - whole blood was used. Serum glucose estimation was done by Trindlers GOD - POD method (commercial kit ERBA - MANNHEIM), cholesterol estimation was done by CHOD – POD method⁹ (Commercial kit - ERBA - MANNHEIM), Triglycerides estimation was done by GPO¹⁰ method (commercial kit - ERBA - MANNHEIM), HDL cholesterol estimation was done by APO protein precipitation or PTA¹¹ method (ERBA - MANNHEIM), and HBAlc estimation was done by Ion exchange resin method (commercial kit - Randox Rx series). All these estimations were performed by Randox Daytona Auto analyzer. VLDL-c or LDL-c levels of all cases and controls were calculated by using Friedwald's formula.

3. Results

The mean age was 53.47 \pm 8.64 in Sub Clinical Hypothyroidism and control groups. Among males mean ages were 56.64 \pm 9.07 ,among females mean ages were 50.3 \pm 8.21 which showed mean age of sub clinical hypothyroid females was less than sub clinical hypothyroid males.(p-value <0.05).The mean BMI was 23.8 \pm 1.1 , 23.4 \pm 0.9 in Sub Clinical Hypothyroidism and control groups respectively. Among males mean BMI were 23.7 \pm 1.01 and among females mean BMI was 23.9 \pm 1.1 groups respectively, which showed mean BMI of females was more than males in sub clinical hypothyroid group. The mean T₃ among Sub Clinical Hypothyroidism was 1.08 \pm 0.24and in controls was 1.23 \pm 0.38 (p 0.0203) mean T₄ among Sub Clinical Hypothyroidism was 6.86 \pm 1.28 and in controls was 9.56 \pm 0.94 (p = 0.05) The mean TSH was Sub Clinical Hypothyroidism was 9.96 \pm 3.57 and in controls was 2.26 \pm 1.45 (p = 0.05)

The mean Cholesterol levels were 218.1 \pm 35.75 and 158.95 \pm 26.45 in Sub Clinical Hypothyroidism and control groups respectively. Among males mean Cholesterol levels were 224.8+ 38.9 and 166.1 \pm 28.5, in Sub Clinical Hypothyroidism and control groups respectively. Among females mean Cholesterol levels were 211.4 \pm 32.6 and 151.8 \pm 24.4 in Sub Clinical Hypothyroidism and control groups respectively, which showed mean Cholesterol levels of males was more than females in Sub Clinical Hypothyroid groups. (p – value <0.05).

The mean Triglyceride levels were 172.85 \pm 81.25 and 131.05 \pm 60.65 in Sub Clinical Hypothyroidism and control groups respectively. Among males mean Triglyceride levels were 186.8+ 85.6 and 142.9 \pm 74.9, in Sub Clinical Hypothyroidism and control groups respectively. Among females mean Triglyceride levels were 158.9 \pm 76.9 and 119.2 \pm 46.4 in Sub Clinical Hypothyroidism and control groups respectively, which showed mean Triglyceride levels of males was more than females in Sub Clinical Hypothyroid group. (p – Value <0.05).

The mean HDL - Cholesterol levels were 45.22 \pm 7.32 and 49.75 +9.005 in Sub Clinical Hypothyroidism and control groups respectively. Among males mean HDL - Cholesterol levels were 42.2+ 6.53 and 48.9.9 \pm 10.6, in Sub Clinical Hypothyroidism and control groups respectively. Among females mean HDL - Cholesterol levels were 48.24 \pm 8.12 and 50.61 \pm 7.41 in Sub Clinical Hypothyroidism and control groups respectively, which showed mean HDL - Cholesterol levels of males was lower than females in Sub Clinical Hypothyroid groups. (p – Value <0.05). The mean LDL - Cholesterol levels were 130.3 \pm 43.15and 111.25 \pm 17.15in Sub Clinical Hypothyroidism and control groups respectively. Among males mean LDL - Cholesterol levels were 144.9+ 43.7 and 116.9 \pm 22.8, in Sub Clinical Hypothyroidism and control groups respectively. Among females mean LDL - Cholesterol levels were 115.7 \pm 42.6 and 105.5 \pm 11.5 in Sub Clinical Hypothyroidism and control groups respectively, which showed mean LDL - Cholesterol levels of males was more than females in Sub Clinical Hypothyroid groups. (p – Value <0.05).

Table 1: Mean age and BMI in cases and controls

Variable	Cases n 50	Controls n 50	P value
Mean age	53.47 \pm 8.64	53.47 \pm 8.64	
Males	56.64 \pm 9.07	56.64 \pm 9.07	
Females	50.3 \pm 8.21	50.3 \pm 8.21	
BMI	23.8 \pm 1.1	23.4 \pm 0.9	0.0494
Males	23.7 \pm 1.01	23.1 \pm 0.7	0.0008
Females	23.9 \pm 1.1	23.7 \pm 1.1	0.3655

Table 2: Mean thyroid levels in cases and controls

Variable	Cases	Controls	t value	P value
TSH	9.96 \pm 3.57	2.26 \pm 1.45	14.1303	<0.05
T4	6.86 \pm	9.56 \pm	12.0220	<0.05

	1.28	0.94		
T3	1.08 ± 0.24	1.23 ± 0.38	2.3599	0.0203

Table 3: Mean lipid levels in cases and controls

Variable	Cases	Controls	t value	P value
Cholesterol	218.1±35.75	158.95±26.45	9.4051	0.0001
Triglyceride	172.85±81.25	131.05±60.65	2.9152	0.0044
LDL	130.3 ± 43.15	111.25 ± 17.15	2.9010	0.0046
HDL	45.22 ± 7.32	49.75 ± 9.005	2.7602	0.0069

Table 4: Mean Cholesterol levels in males and females of cases and controls

	Males	Females
Cases	224.8 ± 38.9	211.4 ± 32.6
Controls	166.1 ± 28.5	151.8 ± 24.4
P value	<0.0001	<0.0001

Table 5: Mean Triglyceride levels in males and females of cases and controls

	Males	Females
Cases	186.8 ± 85.6	158.9 ± 76.9
Controls	142.9 ± 74.9	119.2 ± 46.4
P value	> 0.0774	<0.0231

Table 6: Mean HDL levels in males and females of cases and controls

	Males	Females
Cases	42.2 ± 6.53	48.24 ± 8.12
Controls	48.9 ± 10.6	50.61 ± 7.41
P value	<0.0155	>0.259

Table 7: Mean LDL levels in males and females of cases and controls

	Males	Females
Cases	144.9±43.7	115.7±42.6
Controls	116.9 ± 22.8	105.5 ± 11.5
P value	<0.0109	>0.2266

Table 8: Comparison of elevated lipid fractions between cases and controls

Variable	Cases n 50	Controls n 50
Cholesterol	8 (16%) M: 3 F: 5	1 (2%) M: 2 F: 0

Triglyceride	7 (14%) M:3 F:4	2 (6%) M:1 F:1
HDL	5 (10%) M:4 F:1	0 (0%) M: 0 F: 0
LDL	6 (12%) M:5 F:1	1 (2%) M:1 F: 0

Table 9: Combined elevated lipid fractions between cases and controls

Variable	Cases	Controls	P value
Females (n 28)	5 (17.8%)	0	<0.05
Males (n 22)	8 (36.3%)	0	<0.05

4. Discussion

In this case control study, the association between lipid levels of subclinical hypothyroid group and non subclinical hypothyroid patients, we observed an association between elevated levels of lipid levels in subclinical hypothyroid patients. The mean age in sub clinical hypothyroid and control group was 53.47 ± 8.64, and 67% of these groups were noticed more between the age group of 41 – 60 years. This study shows the mean TSH levels of sub clinical hypothyroid group 9.96 ± 3.57 was more than normal subjects. 2.26 ± 1.45, when compared with Zoe Efstathiadou et. al study,¹¹ the results were similar that is more in sub clinical hypothyroid group. According to Zoe Efstathiadou et. al study,¹¹ patients with subclinical hypothyroid group had significantly higher levels of Mean Cholesterol levels and Mean LDL levels compared with controls, Whereas levels of Mean Triglyceride levels and Mean HDL levels were contrast to our results.

According to B. U. ALTHAUS et. al study,¹² the lipid profiles (total cholesterol, triglycerides, low-density lipoprotein-cholesterol, high-density lipoprotein-cholesterol, and the electrophoretic low-density lipoproteins and high-density lipoproteins) in patients with subclinical (n= 52) and overt hypothyroidism (n= 18) in comparison to normal controls (28 and 18, respectively), matched for age, sex and body mass index comparison to our study elevated LDL concentration (P <0.01), a diminished HDL fraction (P <0.05) and a borderline elevated LDL-C (not reaching the limit of significance, P=0.07) are similar to our study where as total cholesterol and triglyceride concentrations remained unaltered are contradictory to our study. According to Ph. CARON et. al study,¹³ total cholesterol and triglycerides of women with subclinical hypothyroidism were not different from controls is contradictory to our study group, but HDL cholesterol was significantly decreased in subclinical hypothyroidism compared to the controls (P<0.01), whereas total cholesterol (<0.0001) and triglycerides (<0.0231) of women with subclinical hypothyroidism were significant elevation in our study group. Total cholesterol/HDL cholesterol ratio was increased in subclinical hypothyroidism (P<0.01) of Ph. CARON et. al study,¹³ was matched with our study group.

5. Conclusions

Lipid levels were found to be significantly higher in individuals with subclinical hypothyroidism by 52%. 67% of subclinical hypothyroid patients belong to 41 – 60 years age group. Female to male ratio were found to be 1.27: 1. In subclinical hypothyroid patients with elevated lipid levels in males by 68.1% and females by 39.1%. Females with high cholesterol and triglyceride in subclinical hypothyroidism patients than control group, whereas in males high LDL and low HDL cholesterol levels than controls. Larger studies are required to clarify the significance of development of hyperlipidemias before the development of overt hypothyroidism and to consider the lipid levels and serum TSH as regular and routine screening markers to identify subclinical target organ damage in subclinical hypothyroidism patients.

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Author Profile



Dr. Krishna Murthy Vudaga received the M.B.B.S. and M.D. degrees from Guntur Medical College in 1985 and 1995, respectively. During 2004-2013, he is working as associate professor in the department of Biochemistry in Dr. Pinnamaneni Siddartha Institute of Medical Sciences and Research foundation, Chinavutapalli, Gannavarammandal, Krishna district, Andhra Pradesh, India.