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Prevalence of Subclinical Hypothyroidism in Acute Coronary Syndrome in South Indian Population

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ABSTRACT

Among the patients developing coronary heart diseases, the risk factors are identified only when they succumbed to life threatening events like acute coronary syndrome. Prevention of the emergence of risk factors for a disease constitutes the primordial prevention. Similar to pre hypertensive and pre diabetic states, subclinical hypothyroidism also could be a risk factor for coronary artery heart disease as thyroid hormones too have their influence on lipid metabolism. This study was carried out to find out the prevalence of the subclinical hypothyroidism and its role as a risk factor in patients presenting with acute coronary syndrome in south Indian population.100 patients diagnosed as acute coronary syndrome in a tertiary care hospital, Tamil Nadu were divided into STEMI group (ST Elevation Myocardial Infarction) and Non STE-ACS group (Non-ST Elevation Myocardial infarction and Unstable Angina). Blood levels of thyroid hormones and fasting lipid profile were estimated in all patients. The prevalence of SCH and the association of thyroid hormones on lipid profile were studied. The prevalence of subclinical hypothyroidism in patients presenting with acute coronary syndrome was 7%. Among SCH patients, 71.4% were found in STEMI group and 28.6% in non-ST-elevation ACS group. In 71.4% of SCH cases altered lipid profile was observed predominantly in triglycerides and HDL-Cholesterol levels.

Keywords: ACS -Acute Coronary Syndrome, SCH – Sub Clinical Hypothyroidism, TSH – Thyroid Stimulating Hormone, fT3- free Triiodothyronine, fT4-free Thyroxine

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INTRODUCTION

Coronary artery heart disease is a global health problem and also an important cause of death in all age groups.[1] Studies are being done in both developed and developing countries to find its risk factors. The results of various studies have revealed atherosclerosis of the coronary vessels due to altered lipid profile as the commonest mechanism in most of the patients. Smoking, hypertension, diabetes mellitus, high fat intake and sedentary life style are well recognised risk factors for acute coronary syndrome. Thyroid dysfunction can also cause altered lipid profile, like other risk factors. Subclinical hypothyroidism is defined as a serum Thyroid Stimulating Hormone (TSH) above the defined upper limit of the reference range, with a serum free thyroxin (fT4) and free triiodothyronine (fT3) within the reference range.

It is a common problem and occurs in 3% to 8% of the population and 2-5% of SCH carries a risk of progression to overt hypothyroidism in every year.[2, 3] The results of many prospective studies have revealed variable association of SCH with lipid profile. There is a significant association between subclinical hypothyroidism and increased risk of coronary artery heart disease, cardiac failure and death with higher TSH levels, particularly those patients with TSH levels ≥ 10.0 μ IU/ml.[4]

Aim Of The Study

The primary objective was to define the prevalence of sub clinical hypothyroidism in patients of acute coronary syndrome which includes, ST Segment Elevation Myocardial Infarction (STEMI), Non ST-segment Elevation Myocardial Infarction (NSTEMI), and unstable angina. The secondary objective was to determine the association of thyroid hormones levels with components of lipid profile.

MATERIAL AND METHODS

This cross-sectional study was done on 100 patients who were admitted as cases of acute coronary syndrome at a tertiary care hospital, Tamil Nadu.

Inclusion Criteria

100 cases of ACS irrespective of age, sex, race and clinical severity were included for this study.

Exclusion Criteria

- The patients who refused to give consent.
- Those having thyroid disorders
- Patients known to have neoplasia anywhere in the body, chronic kidney disease, obstructive air way disease, chronic liver disease or active infection.
- Patients taking steroids, amiodarone or lithium and
- Patients for whom iodinated contrast medium was given in the recent past. (2 weeks)

Patients were included into STEMI group (ST Elevation Myocardial Infarction) and Non-STE ACS group (cases of Non-ST Elevation Myocardial infarction and Unstable Angina) for prevalence study.

To study the lipid profile changes, patients were included into Euthyroid-ACS and SCH-ACS groups.

Thyroid hormones assays were done in ELISA method. Fasting lipid profiles were done in fully automated clinical chemistry analyser. Reference ranges for the biochemical parameters estimated in this study is given table 1:

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Table 1: Reference ranges for thyroid and lipid profile

Biochemical Test	Reference Range
Total Cholesterol	Less than 200mg/dl
Triglycerides	Less than 150mg/dl
HDL-C males	30-60mg/dl
HDL-C females	35-75mg/dl
Free T3	1.16 - 4.34 pg/dl
Free T4	0.58-2 ng/ml
TSH	0.4 - 5 µIU/ml
Calculated LDL-Cholesterol [5]	Less than 130mg/dl

Analysis

Graph pad prism version 7 was used for statistical analysis. Paired *t* test and Pearson's correlation analysis were done between data of TSH and lipid profile of euthyroid and subclinical hypothyroid patients. P value less than 0.05 was considered as statistically significant.

Categorical data (different age groups, gender, clinical severity types) were analyzed with Chi square or fisher's exact test

RESULTS

The data regarding age, gender, severity of ACS and risk factors in the study population are given in table 2. Among the risk factors for ACS, smoking is the leading one.

Table 2: Categorical data (Age, Gender and Severity of ACS) and risk factors

Variables			Total patients - 100	
			No of patients	Percentage
Age	Mean ± SD 57.05 ± 11.15 Range 34- 95 years	60 yrs. and above	44	44
		Less than 60 yrs.	56	56
Gender	Male		72	72
	Female		28	28
ACS type	STEMI		61	61
	Non ST Elevation ACS		39	39
	Smoking		42	42
	Diabetes mellitus		36	36
	Hypertension		24	24
	Family history of premature CAHD		12	12

The results of thyroid profile of the study population has shown euthyroid state in majority of patients (69%). The prevalence of subclinical hypothyroidism was found to be 7%. The results of thyroid profile of all ACS patients are shown in table 3.

Table 3: Distribution of Thyroid profile in ACS patients

Thyroid profile	No of patients
Euthyroidism	69
Subclinical hypothyroidism	7
Isolated low TSH	4
Low fT3 with or without low fT4	16
Isolated low fT4	3
Overt hypothyroidism	1

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The comparision study of the prevalence of SCH in accordance with gender, age and clinical severity was done**.** The prevalence of sub clinical hyothyroidism in patients aged 60 yrs and above was 4.54% and 8.93% in patients aged below 60 years.There was no statistical difference in prevalence of subclinical hypothyroidism between these groups.

Regarding the gender, prevalence of SCH in males was 5.56% and 10.71% in females.

There was no statistical difference in males and females.

The prevalence of SCH in STEMI patients was 8.2%. It was 5.13% in Non STE-ACS.

There was no statistical difference in these clinical severity groups.

The prevalence of SCH according to age, gender and clinical severity is shown in table 4.

Table 4. The prevalence of SCH in different age, gender and clinical severity groups.

Variable	Age	Total No.	No of SCH	Percentage	P value
Age	60 and above	44	2	4.54%	0.461 (ns)*
	Less than 60	56	5	8.93%	
Gender	Males	72	4	5.56%	0.3963 (ns)*
	Females	28	3	10.71%	
ACS Type	STEMI	61	5	8.2%	0.7021 (ns)*
	Non ST Elevation ACS	39	2	5.13%	

*ns- not significant

Altered lipid profile of Euthyroid patients and SCH patients

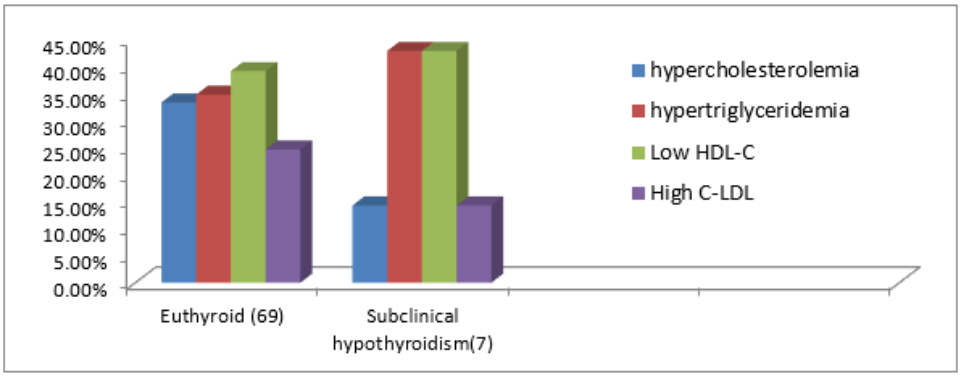
Patients with euthyroid profile had hypercholesterolemia in 33.3%, hypertriglyceridemia in 34.8%, high calculated LDL-C level in 24.6% and low HDL in 39.1%.

In subclinical hypothyroid patients hypercholesterolemia was seen in 14.3% and hypertriglyceridemia in 42.9%. High level of calculated LDL-C level was seen in 14.3% and HDL-C level was decreased in 42.9 %of SCH patients. The results are shown in table 5.and figure 1.

Table 5. Shows Lipid profile abnormalities in Euthyroid and SCH patients.

Thyroid state	ACS Type & No	High TC		High TGL		High LDL -C		Low HDL - C	
Euthyroidism Total- 69	STEMI (38)	20	23	15	24	11	17	10	27
	Non STE-ACS (31)	3		9		6		17	
SCH Total - 7	STEMI- (5)		1	2	3	1	1	2	3
	Non STE- ACS - (2)	-		1		-		1	

Figure 1: lipid profile changes in Euthyroid and SCH patients.



Paired t test between the data of TSH and lipid profile in SCH and Euthyroid patients revealed significant statistical difference in both groups. Results are shown in table 6.

Pearson's correlation study between the data of TSH and lipid profile of Euthyroid and SCH patients revealed no statistical difference in both groups. The results are shown in table 6.

Table 6: Comparison of TSH level with lipid profile of Euthyroid and SCH patients

Lipid profile	Paired T test (Significance α < 0.05)					
	Subclinical hypothyroidism (7); df = 6 Mean TSH ± SD=9.61±5.4			Euthyroidism (69) ;df= 68 Mean TSH ± SD=1.91 ±1.03		
	Mean ± SD	t value	P value	Mean ± SD	t value	P value
TC	153.88± 37.98	9.793	< 0.0001	168.36± 43.45	31.73	< 0.001
TGL	142.6 ± 48.66	6.835	< 0.0005	142.4 ± 76.14	15.43	< 0.001
HDL-C	34.9 ± 12.71	6.532	< 0.0006	35.48 ± 12.01	22.7	< 0.001
c-LDL-C	89.99 ±33.74	6.01	< 0.0010	105.02 ± 34.06	25.1	< 0.001

Pearson's correlation study on TSH level with lipid profile of SCH and Euthyroid patients was done. There was no significant statistical difference in both groups. (P value > 0.05 for all lipid fractions).The results are shown in table 7 and 8

Table 7: Pearson's correlation of TSH with lipid profile of SCH patients.

Analyte	Lipid profile	Pearson's Correlation ratio	P value	Lower 95% Cl	Upper 95% Cl
TSH	TC	-0.095	0.839	-0.792	0.709
	TGL	-0.437	0.327	-0.895	0.471
	HDL-C	0.611	0.145	-0.263	0.934
	LDL-C	-0.203	0.663	-0.829	0.650

Table 8: Pearson's correlation of TSH with lipid profile of Euthyroid patients.

Analyte	Lipid profile	Pearson's correlation ratio	P value	Lower 95% Cl	Upper 95% Cl
TSH	TC	0.118	0.334	-0.345	0.122
	TGL	-0.140	0.251	-0.365	0.100
	HDL-C	-0.107	0.383	-0.350	0.133
	LDL-C	-0.063	0.608	-0.295	0.196

XY plot for correlation study (TSH level and lipid profile of 7 SCH patients) is shown in the figure 2. The observed mean blood TSH level was 9.61 mIU/ml.

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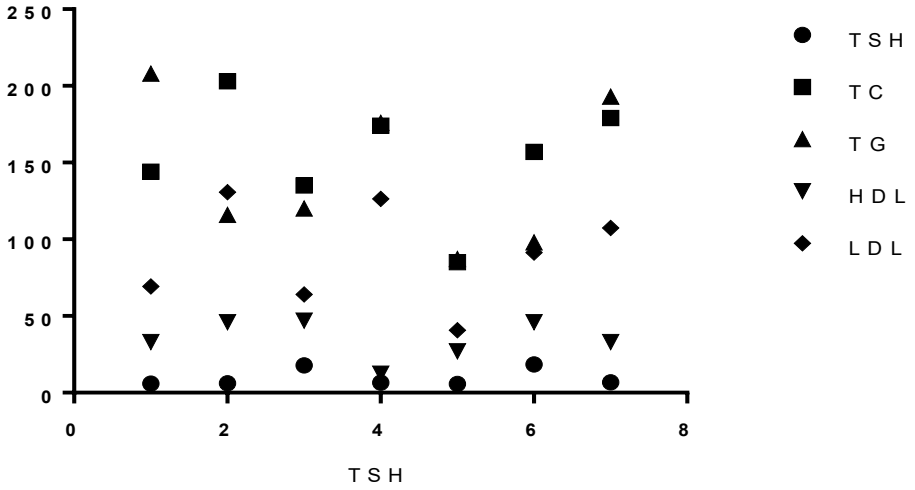
Figure 2: XY plot of TSH and lipid profile in SCH patients.



DISCUSSION

Subclinical hypothyroidism is a common form of thyroid disorder and usually asymptomatic. Most of the cases of SCH are diagnosed by screening with the support of laboratory methods. It is identified by abnormally elevated serum TSH levels with FT_4 and FT_3 concentrations within the reference range. Studies are being done to find the association of SCH with increased risks of altered cardio vascular haemodynamics, adverse cardiac events and lipid profile.

Prevalence of SCH in ACS

Our study has shown that the prevalence rate of SCH was 7% among the 100 patients presenting with ACS with varied clinical severity. These results are in support with the study of Cooper and Biondi which reported 4% to 20% as the prevalence of SCH in adult population. This vast range could be due to differences in age, gender, race, nutritional status of the study populations, availability of Iodine in food and dietary intake of Iodine as well as methods used to do assay of serum TSH [6].

Regarding age and prevalence of SCH, it was 4.54% in patients who are sixty years and above; 8.93% in patients who are below the age of sixty years.

Our results were not in concordance with results of NHANES III cohort study in which the prevalence increases with increasing age and also with the results of Whickham Survey [6] in which higher prevalence of SCH was observed in elderly population. But, there was no statistically significant difference in the prevalence of SCH between patients who are sixty years and above in comparison with patients who are less than sixty years.

Our results showing the prevalence 5.56% in males and 10.71% in females are also concordant with the that of the Colorado study in which the prevalence of SCH in males was 3-16% and 4- 21% in females[7]. But there is no statistically significant difference in the prevalence of SCH between males and females.

Thyroid profile of Subclinical hypothyroidism was observed in 3 females. All of them were post-menopausal women. They had the TSH level of less than 10μIU/ ml. TSH levels of two SCH patients were above10μIU/ ml. Both of them were males.

Altered lipid and Thyroid Profile in ACS patients.

On comparing thyroid status and lipid profile, our study has shown that ACS patients with euthyroid profile had hypercholesterolemia in 33.3%, hypertriglyceridemia in 34.8%, increased LDL-C level in 24.6% and lowered HDL-C in 39.1%. Normal lipid profile at the time of presentation was observed in 30.4% of euthyroid ACS patients.

In the subclinical hypothyroid status, hypercholesterolemia occurred in 14.3% and hypertriglyceridemia in 42.9%. LDL-C level was increased in 14.3% and HDL-C level was decreased in 42.9% of SCH patients. Normal lipid profile was observed in 28.6% of SCH patients.

The results of our study revealed that patients with sub clinical hypothyroidism have changes in their lipid profile predominantly in HDL-C and Triglycerides fractions rather than Total cholesterol and LDL-C.

The results of our study are discordant with the observations of Duntas and Wartofsky study in which patients with the thyroid profile of Subclinical hypothyroidism had serum lipid profile abnormalities more in Total cholesterol and LDL-Cholesterol fractions and also with the results of Colorado study in which subclinical hypothyroid patients had more elevated serum total cholesterol concentrations than euthyroid individuals [7]. However, our results were partially concordant with NHANES III cohort study in which higher total cholesterol and triglycerides concentrations were observed in subclinical hypothyroid patients. Our study showed higher serum triglycerides concentration along with reduced HDL-C in subclinical hypothyroidism. Discrepancy between these studies may be due to the differences of the study populations, selection criteria, age, gender, race, smoking and dietary habits. Determination of normal upper limit of serum TSH concentrations to define SCH is also an important factor for these variations.

CONCLUSION

This cross sectional study reveals that prevalence of subclinical hypothyroidism in patients presenting as Acute Coronary Syndrome is 7% with mean blood TSH level of 9.61 mIU/ml.
The prevalence of SCH is more in STEMI (71.43%). Among the SCH patients presenting as STEMI, 80% have altered lipid profile.

The prevalence of SCH in non ST-elevation ACS patients is 28.57%. Among the SCH patients with Non ST Elevation ACS, 50 % have altered lipid profile.

The changes in lipid profile have been predominantly on blood levels of HDL-Cholesterol and triglycerides. The number of patients identified as subclinical hypothyroidism in this study is 7. The role of SCH as a risk factor for coronary heart disease may be revealed with significant results if large study population is selected.

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