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Prevalence of Subclinical Hypothyroidism in Acute Myocardial Infarction Patients from Northern India

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Abstract

Introduction: Subclinical hypothyroidism (SCH) is defined as a serum thyroid-stimulating hormone (TSH) level above the upper limit of normal despite normal levels of serum free thyroxine. There is growing evidence that SCH is associated with increased cardiovascular risk.

Objective: Thyroid hormones have important effects on the cardiovascular system through direct and indirect mechanisms. The present study was done to evaluate the prevalence of SCH in acute myocardial infarction patients.

Methods: This prospective, cross-sectional study was conducted for a period of 12 months from june 2018 to june 2019 in the Medicine department at GMC, Azamgarh (UP) and included 104 patients admitted with the diagnosis of acute myocardial infarction (either STEMI or NSTEMI) with close follow up during the inhospital stay to detect any morbidity or mortality. All subjects underwent complete lipid profile (TC, TG, LDL-C, HDL-C &VLDL-C) and thyroid profile (free T3, free T4 &TSH).

Results: Our study revealed male predominance with MI than female. Patient aged group 50-60 (40.38%) was prone to MI. Patient presenting with sub-clinical hypothyroidism (SCH) were 18 (17.30%) while 86 (82.69%) patients were euthyroid. 12 patients of SCH presented with STEMI while 6 presented with NSTEMI. Association of SCH Patients with STEMI and NSTEMI was more in males (72.22.6%) than females (27.77%).

Conclusion: Prevalence of SCH is 17.30% in Acute MI patients and it has no association with inhospital morbidity and mortality. Large-scale studies are needed to clarify the effects of SCH on myocardial infarction both on etiologic and prognostic grounds.

Keywords: Prevalence, Acute Myocardial Infarction, Mortality, Morbidity, Subclinical hypothyroidism

Introduction

Subclinical hypothyroidism, also referred to as mild thyroid failure, is diagnosed when serum free thyroid hormone levels are within the normal range but thyroid stimulating hormone (TSH) is mildly elevated[1]. It is a common problem, occurring in 3% to 8% in the population without known thyroid disorders and carries a risk of development to overt hypothyroidism of 2-5% per year. [2, 3] There is growing evidence that SCH is associated with lipid abnormalities, increasing cardiovascular risk at advancing age and particularly in older women[4, 5]. Clinical hypothyroidism is associated with premature atherosclerosis and increased prevalence of coronary disease.

After the sixth decade of life, the prevalence in men approaches that of women, with a combined prevalence of 10%. Antithyroid antibodies can be detected in 80% of patients with SCH and 80% of patients with SCH have a

serum TSH of less than 10 mIU/L. Clinical hypothyroidism is associated with premature atherosclerosis and increased prevalence of coronary disease. This is at least partly due to the lipid abnormalities often found in hypothyroidism[6,7]. Possible mechanisms behind the link between hypothyroidism and atherosclerosis other than dyslipidemia include the effects of thyroid hormones on coagulation, vasodilation, parasympathetic function and homocysteine metabolism [5,8].

A study, which examined the relation between cardiovascular disease and TSH levels in euthyroid patients found significantly higher TSH in patients with coronary events compared to controls matched for age, gender, and body mass index[9]. The cross-sectional Rotterdam study showed an association of SCH with myocardial infarction and aortic calcification[10]. Several observational studies comparing the outcome of SCH individuals with euthyroid subjects have shown divergent results and it has been debated for some time whether SCH is independently associated with ischemic heart disease (IHD)[11, 12]. Because of these conflicting reports and the large numbers of populations afflicted by this condition, there is an urgent need for settling the controversy. As findings of several studies support the influence of SCH on ischemic heart disease, we tried to investigate prevalence of SCH in acute myocardial infarction patients.

Aims and Objectives

The aim of the study is to detect prevalence of sub clinical hypothyroidism in acute myocardial infarction, to correlate sub clinical hypothyroidism in STEMI and in NSTEMI patients

Material and Methods

Study Design

This prospective, cross-sectional study which showed an association of SCH with myocardial infarction was conducted for a period of 12 months from june 2018 to june 2019 in the Medicine department at GMC, Azamgarh (UP). This study involved 104 patients admitted with the diagnosis of ST-segment elevation Myocardial infarction (STEMI)/Non ST-segment elevation Myocardial infarction (NSTEMI) irrespective of age, gender, race, clinical severity and patients were followed up during the in hospital stay.

The study was carried out in accordance with the ethical standards on human experimentation after getting ethical clearance. A written informed consent in English and Hindi was taken from all the participants in the study after properly describing about the purpose of the study prior to their enrolment.

104 patients with Acute Myocardial Infarction (AMI) of Adult (age > 18 years) males and females were selected from the patients attending Medicine OPD or admitted in Medicine department as a case of AMI. Age and sex matched healthy volunteers were included in our study.

Inclusion Criteria

All Acute Myocardial Infarction Patients wether Euthyroid or SCH based on TSH level between 6-10µIU/ml and normal T4 value 4.9-12.5 µg/dl. Age and sex matched euthyroid subjects having normal TSH and T4 values were included in our study.

Exclusion Criteria

All subjects with TSH values > 20mU/L or < 4.5mU/L and Known cases of Thyroid diseases with hyperthyroid disease like Graves disease, Toxic multi-nodular goiter or with hypothyroid disease like Pituitary Adenoma or hypothyroidism induced with drugs like Lithium, Phenytoin, & Rifampin and Chronic autoimmune thyroiditis were excluded in our study.

The clinical examination consisted of medical history, physical examination and anthropometric measurements. Laboratory data included electrocardiogram, lipid profile and thyroid function tests. All laboratory investigations were collected at the time of admission to the hospital.

Study Procedure

- Free T3, free T4, and TSH levels of 104 patients (age >18years) who were admitted to the Medicine department with the diagnosis of ST elevation (STEMI) or non-ST elevation acute myocardial infarction (NSTEMI) were obtained by different tests & Patients were classified into 2 groups based on their thyroid function tests.

➢ Group-I TSH Level >4.5 to 9.9mU/L

➢ Group-II TSH Level >10 to 20mU/L

Laboratory Procedures

After overnight fasting blood samples were collected from all participants for measuring biochemical parameters. Serum T3, T4 and TSH levels were measured by the enzyme-linked immunosorbent assay (ELISA) method using commercial kits. Measured hormones and their respective reference values were: free T3 (1.3-5 pg/ml), free T4 (0.8-2 ng/dl) and TSH (0.4-4 mIU/l).

Similarly serum levels of TC, TG, LDL-C and HDL-C were measured using a spectrophotometric assay with commercial kits. We defined high serum levels as TC ≥ 200 mg/dl, LDL-C ≥130 mg/dl, VLDL-C ≥ 40 mg/dl and TG ≥ 150 mg/dl; a low serum level of HDL-C was defined as ≤ 40 mg/dl. All the patients were followed up during the inhospital stay for any morbidity and mortality.

The data was compiled and analysis were performed using SPSS program; version 17. The numerical data were statistically presented in terms of mean and standard deviation. Categorical data were summarized as percentages. Comparisons between numerical variables were done by unpaired Student's t-test. Comparing categorical variables were done by Chi-square test for small sample size. A probability value $p<0.05$ was considered statistically significant, a P value <0.001 was considered highly significant and P value >0.05 was considered non-significant.

Results

During the study period out of 104 patients, 63(60.57%) were males and 41(39.42%) were females. Males were found more susceptible to myocardial infarction than female as shown in Fig no 1.

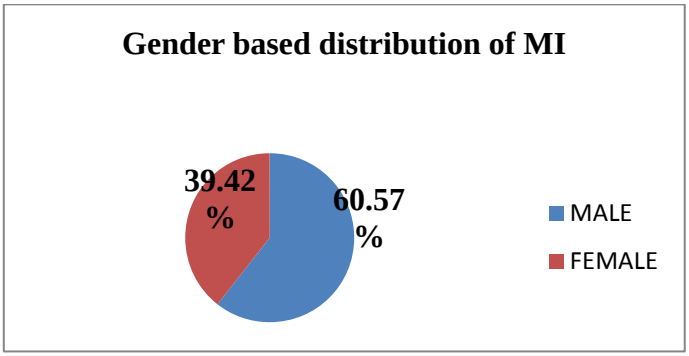

Fig 1: Distribution of Acute MI Patients according to Sex

Age group distribution of Patients

Out of 104 patients, Patients belonging to age group 50-60(40.38%) were maximum followed by 61-70(29.80%), 40-50(24.03%) and >=70(5.76%) respectively which clearly shows that advancing age of patients are more susceptible for myocardial infarction as shown in Fig no 2.

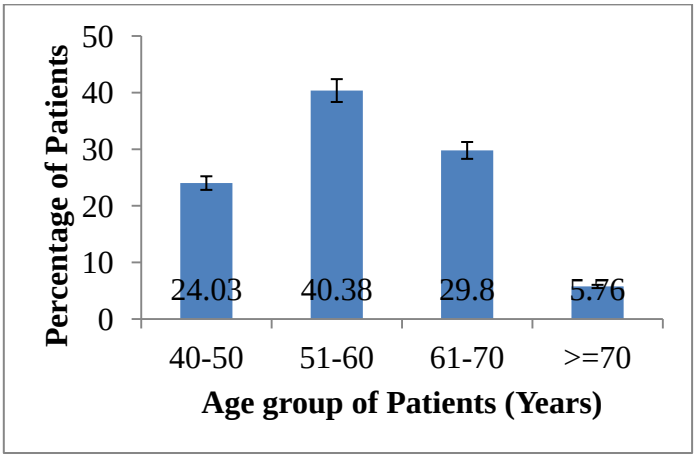

Fig 2: Age group of patients in years

Prevalence of Subclinical Hypothyroidism(SCH) and Euthyroid in patients of Myocardial infarction

Out of 104 Patients 18(17.30%) were of SCH and 86(82.69%) were Euthyroid Patients which clearly shows that the prevalence of SCH low.

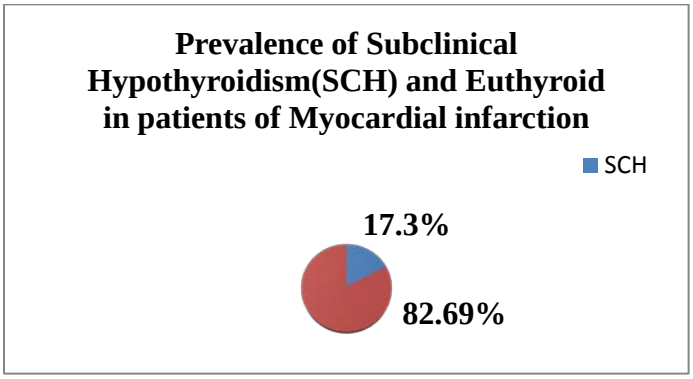

Fig. 3: Prevalence of SCH and Euthyroid in Acute MI Patients

Association of age and gender with MI

Out of 104 patients, Patient with age group of 61-70(23.07%) were more prone to Myocardial Infarction in both male and female while least being in patient with age group of >=70(2.88%) in both male and female. Myocardial infarction was found significantly associated (p=0.036) with the gender of the patients as shown in table no 1.

Table no 1: Association of age and gender with MI

			Gender		Total	P Value
			Male	Female		
Age	40-50	Count	19	06	25	.036
		% Of Total	18.26%	5.76%	24.03%	
	51-60	Count	24	18	42	
		% Of Total	23.07%	17.30%	40.38%	
	61-70	Count	17	14	31	
		% Of Total	16.34%	13.46%	29.80%	
	>=70	Count	03	03	06	
		% Of Total	2.88%	2.88%	5.76%	
Total		Count	63	41	200	
		% Of Total	60.57%	39.42%	100.0%	

Subclinical Hypothyroidism with STEMI and NSTEMI

Out of 104 patients, Patient presenting with STEMI was 12(66.66%) while Patient Presenting with NSTEMI was 06(33.33%) as shown in fig no 4.

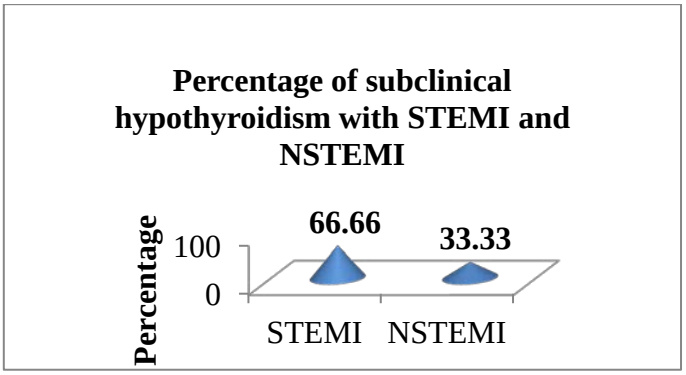

Fig. 4: SCH with STEMI and NSTEMI in MI Patients

Euthyroid patients with STEMI and NSTEMI

Out of 104 patients, Patient presenting with STEMI was 68(79.06%) while Patient Presenting with NSTEMI was 18(20.93%) as shown in fig no 5.

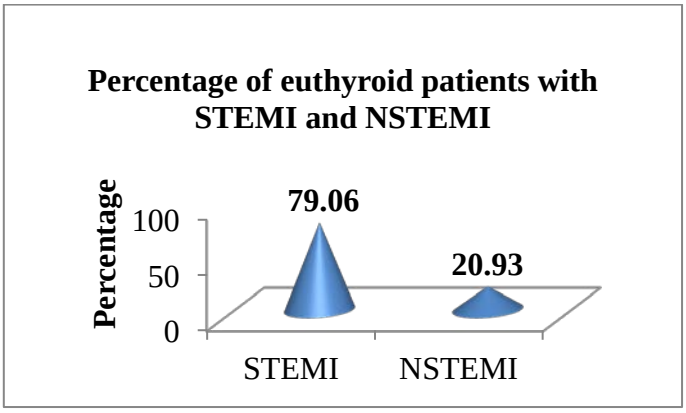

Fig. 5: Euthyroid patients with STEMI and NSTEMI in MI Patients

Association between gender of SCH Patients with STEMI and NSTEMI

Out of 104 patients, Male patient with STEMI were 09(50.0%) and female Patient with STEMI were 03(16.66%) while Male patient with NSTEMI were 04(22.22%) and female Patient with NSTEMI were 02(11.11%). No association between gender with SCH and the MI with STEMI and NSTEMI was observed as shown in Fig no 2.

Table 2: Association between gender of SCH Patients with STEMI and NSTEMI

	Sch		Total	. X^2 (P)
	Male	Female		
Stemi	09 50.0%	03 16.66%	12 66.66%	.430[ns]
Nstemi	04 22.22%	02 11.11%	06 33.33%	
	13 72.22.6%	05 27.77%	18 100.0%	

Association between SCH and Euthyroid in Myocardial infarction Patients

Out of 104 Patients, SCH Patients presenting with STEMI Myocardial infarction were 12(11.53%) while with NSTEMI Myocardial infarction were 06(5.76%) while Euthyroid Patients presenting with STEMI Myocardial infarction were 68(65.38%) and Euthyroid Patients presenting with NSTEMI Myocardial infarction were 18(17.30%) as shown in table no 3.

Table 3: Association between SCH and Euthyroid in Myocardial infarction Patients

			Myocardial infarction		Total	. χ^2 (p)
			STEMI	NSTEMI		
Thyroid status	SCH	Count	12	06	18	.056[ns]
		% of Total	11.53%	5.76%	17.32%	
	Euthyroid	Count	68	18	86	
		% of Total	65.38%	17.30%	82.68%	
Total		Count	80	24	104	
		% of Total	76.92%	23.07%	100.0%	

Mean LDL level of SCH and euthyroid group

Out of 104 Patients, SCH Patients presenting with Myocardial infarction were 18 whose mean LDL was found to be 114.2461and Euthyroid Patients presenting with Myocardial infarction were 86 whose mean LDL was found to be 96.2121. The significant difference (p=.012) was found in the LDL level of SCH and euthyroid group. The LDL level was found higher in SCH group as compared to Euthyroid as shown in table no 4.

Table 4: LDL level of SCH and euthyroid group

	Thyroid Status	n=104	Mean	Std. Deviation	t-test(p)
LDL	SCH	18	114.2461	38.11051	
	Euthyroid	86	96.2121	24.46355	.012[sig]

Mean HDL level of SCH and euthyroid group

Out of 104 Patients, SCH Patients presenting with Myocardial infarction were 18 whose mean HDL was found to be 32.8348 and Euthyroid Patients presenting with Myocardial infarction were 86 whose mean HDL was found to be 41.3382. The significant difference (p=.014) was found in the HDL level of SCH and euthyroid group. The HDL level was found higher in Euthyroid group as compared to SCH as shown in table no 5.

Table 5: HDL level of SCH and euthyroid group

	Thyroid Status	N	Mean	Std. Deviation	t-test(p)
HDL	SCH	18	32.8348	9.31258	.014[sig]
	Euthyroid	86	41.3382	5.03552	

Mean Serum cholesterol (SC) level of SCH and euthyroid group

Out of 104 Patients, SCH Patients presenting with Myocardial infarction were 18 whose mean SC was found to be 196.12 and Euthyroid Patients presenting with Myocardial infarction were 86 whose mean SC was found to be 156.86. The significant difference (p=.023) was found in the SC level of SCH and euthyroid group. The SC level was found higher in SCH group as compared to Euthyroid as shown in table no 6.

Table 6: SC level of SCH and euthyroid group

	Thyroid Status	N	Mean	Std. Deviation	t-test(p)
HDL	SCH	18	196.12	47.23439	.023[sig]
	Euthyroid	86	156.86	33.09876	

Discussion

Subclinical hypothyroidism is a common clinical problem diagnosed mainly by laboratory methods. Screening is needed to detect SCH in most cases since most patients with this disorder are asymptomatic. It is recognized by abnormally high serum TSH value with normal FT4 and FT3 concentrations. Although it was recently reported that SCH is associated with elevated risks of cardiovascular events, cardiac dysfunction, lipid metabolism abnormalities and neuropsychiatric disorders it is still debated whether long term subclinical hypothyroidism is associated with systemic complications.

In our study we observed that male were more prone for Myocardial infarction than female which is in accordance with a study done by national health and nutrition examination survey and Okuyan Ertugrul et al.[13,14] An increase in stress and Cigarette smoking or use of other tobacco products may be responsible for their higher prevalence in male. Our study report was contradictory to the findings of Lerner DJ and Kannel WB[15] who showed that women had higher rates of atypical presentations such paroxysmal dyspnea, or congestive heart failure (CHF).

Our study reports that Patients belonging to age group 50-60(40.38%) were more prone to MI . This was in accordance to a study done by Ng M et al who reported men aged 40–49 years. The attributed reason behind these remarkable findings could be due to an imbalance in changing risk factors for MI like obesity and diabetes which is increasing day by day in our society.[16]

This study showed that the prevalence of SCH was in 17.30% MI patients (STEMI, and NSTEMI) and it is supported by findings of Cooper and Biondi study which showed that the prevalence of SCH in adults has been reported to range from 4% to 20%[17] and contradictory to the findings of Whickham Survey[17] and NHANES III[18.] The wide variations may be due to differences in age, gender, race, body mass index, and dietary iodine intake in the studied populations as well as differences in serum TSH evaluation methods. Our study showed that prevalence of Euthyroid patients was 82.69% among MI patients (STEMI, and NSTEMI) which was almost similar to the finding of Mohammed Mansour Helmy et al. who prevalence of Euthyroid Patients (81%) in comparison with SCH Patients in a study on 300 Patients.[19]

The present study revealed predominance of male belonging to age group of 51-60(23.07%) to MI followed age group of 61-70(16.34%). Similarly female belonging to age group of 51-60(17.30%) were more prone to MI followed age group of 61-70(13.46%). These were similar to the findings of Altaf Hussain Banday et al[20] while it was contradictory to the findings of Vijay K S et al[21] and reported patients belonging to >60 age group were more prone to cardiovascular problems. The reason behind it may be attributed to co-morbid conditions like DM, Smoking, Coronary atherosclerosis in males and Menopause and hyperlipidemia in females. This study showed that age is an important factor of sex-based differences in MI presentation, which is relevant because women are older than men when they present with an acute coronary syndrome.

The study results revealed that SCH Patients presenting with STEMI was 12(66.66%) while Patient Presenting with NSTEMI was 06(33.33%). This is in support of the findings done by Vijay kumar Sah et al and Tuzun D et al.[21, 22]

During the study period we observed that out of 104 Patients, Euthyroid Patients presenting with STEMI was 68(79.06%) while Patient Presenting with NSTEMI was 18(20.93%) which almost matches the findings of vijay kumar Sah et al who reported 10 (66.67%) patients belonged to STEMI group while 5(33.33%) belonged to NSTEMI.[21] which a study done by Tuzun D et al. did not

find any significant difference in prevalence of Euthyroid between STEMI and NSTEMI groups.[22] However Mathur P et al. reported higher prevalence 12 out of 18(66.66%) in NSTEMI group and it was 6 out of 18 (33.34%) in STEMI group which was contradictory to from our study [93].

In our study we found that out of 18 SCH Patients, Male patient with STEMI were 09(50.0%) and female Patient with STEMI were 03(16.33%) while Male patient with NSTEMI were 4(22.22%) and female Patient with NSTEMI were 2(11.11%). Not much of studies have been found for comparing this parameter. So further studies are required to substantiate these findings. Our study showed that SCH Patients presenting with STEMI Myocardial infarction were 12(11.53%) and SCH Patients presenting with NSTEMI Myocardial infarction were 06(5.76%) while Euthyroid Patients presenting with STEMI Myocardial infarction were 68(65.38%) and Euthyroid Patients presenting with NSTEMI Myocardial infarction were 18(17.30%). Similar findings were reported by Vijay kumar Sah et al, Tuzun D et al.[21, 22]

Mean LDL of 18 SCH Patients was found to be 114.2461 while of 86 Euthyroid Patients was found to be 96.2121 showing significant difference (p=.012) in SCH and euthyroid group. Our study report regarding LDL of SCH and Euthyroid patients is supported by the findings of Zha et al.[24] Mean HDL of 18 SCH Patients was found to be 32.8348 while of 86 Euthyroid Patients was found to be 41.3382 showing significant difference (p=.014) in SCH and euthyroid group. Similarly serum cholesterol of 18 SCH Patients was found to be 196.12 while of 86 Euthyroid Patients was found to be 156.86 showing significant difference (p=.023) in SCH and euthyroid group. These findings were in concordance with a study done by Ramulu. et al.[25]

Conclusion

This study depicts subclinical hypothyroidism were observed in 17.30% of MI patients and Euthyroid was observed in 82.69% Patients. A higher prevalence of MI was seen in age group 51-60 years in both male (23.07%) and female (17.30%). A statistically higher prevalence of STEMI was seen in SCH and Euthyroid Patients as compared to NSTEMI in SCH and Euthyroid Patients. These findings suggest that there is greater risk of thrombosis, and hence of myocardial infarction, in moderate hypothyroidism, and greater risk of hemorrhage in severe hypothyroidism. The features of this study conclude that hypothyroidism may be associated with MI. So, thyroid hormone levels should be observed in all middle aged population for early diagnosis of cardiac involvement. This may be helpful for better management of the MI patients. Longitudinal prospective study of larger groups of subclinical hypothyroid patients are needed to be done to substantiate these findings.

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