

Thyroid Hormone Abnormalities and Associated Risk Factors among Acute Coronary Syndrome Patients at a Tertiary Care Hospital

Shreewastav RK,¹ Dhungana SP,² Pokhrel S,² Jayshwal R,² Pandey H²

¹Department of Biochemistry,

²Department of Internal Medicine, Cardiology Unit,

Nobel Medical College Teaching Hospital,

Biratnagar, Nepal.

Corresponding Author

Rupesh Kumar Shreewastav

Department of Biochemistry,

Nobel Medical College Teaching Hospital,

Biratnagar, Nepal.

E-mail: rupeshaiims4@gmail.com

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ABSTRACT

Background

Thyroid dysfunction and associated factors like age, sex, diabetes mellitus, hypertension, smoking, family history of coronary artery disease and dyslipidemia contributes the risk for acute coronary syndrome.

Objective

To find out the prevalence of thyroid dysfunction and associated risk factors among acute coronary syndrome patients at this tertiary care hospital in eastern Nepal.

Method

A descriptive cross-sectional study was carried out prospectively among acute coronary syndrome patients at a tertiary care Hospital. Diagnosis of acute coronary syndrome was made based on the medical history, Electrocardiogram abnormalities, and cardiac markers. Thyroid function test and estimation of other blood parameters were done in the blood of the patients. Other relevant information and medical history of the patients were collected by using proforma.

Result

Out of 186 total acute coronary syndrome patients, 127 (68.28%) were male and mean age of all patients was 60.0 ± 13.7 years. Thyroid dysfunction was observed in 52 (27.95%) patients, out of that subclinical hypothyroidism was mostly seen in 30 (16.12%) patients followed by hypothyroidism in 13 (6.98%). The number of patients with hyperthyroidism and subclinical hyperthyroidism was 6 (3.23%) and 3 (1.62%) respectively. Associated factors like hypertension, diabetes mellitus, smoking, family history of coronary artery disease and dyslipidemia was observed in 80 (43.01%), 42 (22.58%), 83 (44.62%), 11 (5.91%) and 79 (42.47%) patients.

Conclusion

Acute coronary syndrome was predominantly seen in male and subclinical hypothyroidism was a major thyroid dysfunction observed among the patients. Hypertension, dyslipidemia, diabetes mellitus and smoking was found to be associated in a proportion of patients with acute coronary syndrome.

KEY WORDS

Acute coronary syndrome, Diabetes mellitus, Hypertension, Risk factors, Thyroid function test

INTRODUCTION

The clinical spectrum of unstable ischemic heart disease known as acute coronary syndrome (ACS) is characterized by rapid constriction and occlusion of the coronary arteries as a result of atheromatous plaque breakdown and thrombogenesis, which results in myocardial ischemia and necrosis.^{1,2} Globally, the leading cause of death is still cardiovascular disease with ischemic heart disease accounting for approximately half of all fatalities.^{3,4}

A significant impact of thyroid hormone lies on the cardiovascular system like improving the systolic and diastolic function of the heart, regulating heart rate and cardiac contractility, decreasing systemic vascular resistance.⁵⁻⁸ Cardiac cell contraction, demand of oxygen and resistance exerted in blood vessels are all affected by alteration in the level of thyroid hormones in blood, whether they are high or low.⁹ Thyroid dysfunction increases the risk of heart disease and the rate of mortality among the cardiac disease patients. Both hyper and hypothyroidism are associated with increased cardiovascular risk factors and mortality. For example, hyperthyroidism increases risk of atrial fibrillation and heart failure. Similarly hypothyroidism is associated with hypertension and dyslipidemia and also causes cardiovascular disease.^{10,11}

Conventional risk variables such as age, gender, diabetes mellitus (DM), hypertension (HTN), smoking, and family history of cardiovascular disease were closely associated with the diagnosis of ACS.¹²⁻¹⁴ Similarly, dyslipidemia with elevated level of all parameters of lipid profile except HDL also contributes as a risk factor for ACS.¹⁵

Therefore, the purpose of conduction of this study is to find out the prevalence of thyroid dysfunction and also the other associated risk factors like age, sex, diabetes mellitus, hypertension, smoking, family history of coronary artery disease (CAD), smoking and dyslipidemia in acute coronary syndrome patients attending a tertiary care hospital in our setting.

METHODS

A descriptive cross-sectional study was adopted and conducted prospectively at a tertiary care Hospital, Nobel Medical College Teaching Hospital (NMCTH) on the patients having been diagnosed with acute coronary syndrome (ACS) in the cardiology unit of internal medicine department for a period of 25th May 2022 to 24th May 2023 after getting the ethical approval for the study by institutional review committee, NMCTH. All the cases of ACS were enrolled for the study. The patients under the age of 20 year and having no willingness for the study were excluded. After obtaining the approval from either patient or attendant, the study was carried out. A convenient sampling strategy was employed. The formula, $n = Z^2 pq / d^2$ [where, n=minimum necessary sample size, Z= 1.96 at 95% Confidence Interval

(CI), p= prevalence taken as 23.5%, q= 1-p, error, d= 7%] was used to determine the sample size and was obtained as 139; however a total of 186 sample in the study period was considered for the present study.¹⁶

Personal information like age, sex, height, and weight were compiled using a proforma. Height was measured by stadiometer and weight was measured on weight balance. Body mass index (BMI) is calculated as follows: $BMI = \text{Weight in Kg} / (\text{Height in meter})^2$. All patients underwent an electrocardiogram (ECG) at the time of presentation, and the cases were classified as unstable angina (USA), non-ST elevation myocardial infarction (NSTEMI), and ST-elevation myocardial infarction (STEMI) based on the medical history, ECG abnormalities, and cardiac markers.¹⁷ History of prior associated disease (diabetes mellitus, hypertension, others), smoking, dyslipidemia and family history of coronary artery disease were documented in a predesigned proforma. Thyroid function test was performed in the blood sample of the patients. Free triiodothyronine (T3), free thyroxine (T4) and thyroid stimulating hormone (TSH) levels were calculated in a fully automatic analyzer (Maglumi 800) by chemiluminescence immunoassay at the department of Biochemistry laboratory, NMCTH by a standard protocol.¹⁸ The estimation of other biochemical parameters for lipid profile (total cholesterol, triglyceride, HDL and LDL), sugar, renal profile were performed by the sera of the patients using the reagents provided by the manufacturer in fully automated analyzer (LabSystems Diagnostics, Nano Lab 200) in the laboratory, NMCTH. The whole blood sample of patients was used to compute HbA1c in a fully automated analyzer that used the high performance liquid chromatography (HPLC) method.

Any of the fasting lipid profile levels found within 24 hours of the event was considered to be dyslipidemia in accordance with the guidelines for the diagnosis of dyslipidemia: Total Cholesterol > 200 mg/dl, Triglyceride > 150 mg/dl, LDL > 130 mg/dl, and HDL < 40 mg/dl, or already taking medicine for dyslipidemia by the patients.¹⁹ Analysis of dyslipidemia in relation to sex, age, and other risk variables was done.

The gathered information was imported into Microsoft Excel 2010 and examined using SPSS 20.0. For numerical variables, mean and SD were used to generate descriptive statistics, and for categorical variables, percentages were employed. The significance of variance between the mean values with standard deviation among different groups was calculated by one-way ANOVA test whereas one sample t test was used to compute the statistical significance between mean values of other biochemical parameters of patients with healthy people. At 95% confidence interval (CI), if value of p was < 0.05, the data were deemed significant.

RESULTS

The total number of study participants with acute coronary syndrome enrolled for the present study was 186. Among them, 127 (68.28%) were male and 59 (31.72%) were female. The mean age was 60.0 ± 13.7 years. ACS was more seen in age group 51-75, in which 139 (74.73%) patients were reported. The mean value of body mass index (BMI) among them was 21.9±4.01 kg/m². Out of 186 ACS patients, thyroid dysfunction was observed among 52 (27.95%) patients. Hypertension and diabetes mellitus were observed to be associated in 80 (43.01) and 42 (22.58) ACS patients respectively. Among ACS patients, 117(62.9%) were diagnosed with STEMI, 46 (24.74) with NSTEMI and 23 (12.36) with unstable angina. Past history of smoking was noted in 83 (44.62%) patients and dyslipidemia was found to be noted in 79 (42.47%). Patients reported of having family history of CAD was 11 (5.91%) as shown in table 1.

Table 1. Baseline Characteristics of Study Participants with Acute Coronary Syndrome (n=186)

Characteristics	Number	Percentage
Age in year (Mean±SD)	60.0±13.7	(Min-21, Max-89)
Male	127	68.28
Female	59	31.72
ACS in diverse age group		
< 25	4	2.15
25-50	25	13.44
51-75	139	74.73
> 75	18	9.68
BMI in Kg/meter² (Mean ± SD)	21.9±4.01	
< 18.5	22	11.83
18.5-24.9	146	78.49
25-30	11	5.92
> 30	7	3.76
Thyroid dysfunction	52	27.95
Associated disease		
HTN	80	43.01
DM	42	22.58
Others	25	13.44
Cardiac disease		
STEMI	117	62.9
NSTEMI	46	24.74
USA	23	12.36
History of smoking		
Yes	83	44.62
No	103	55.38
Dyslipidemia		
Yes	79	42.47
No	107	57.53
Family history of CAD		
Yes	11	5.91
No	175	92.3

Thyroid dysfunction was seen in 52 (27.95%) ACS patients. Out of 52 patients, subclinical hypothyroidism was the most common and seen in 30 (16.12%) patients followed by hypothyroidism in 13 (6.98%). Subclinical hyperthyroidism and hyperthyroidism were observed among 3 (1.62%) and 6 (3.23%) patients respectively. Euthyroidism was noted among remaining 134 (72.05%) patients as shown in figure 1.

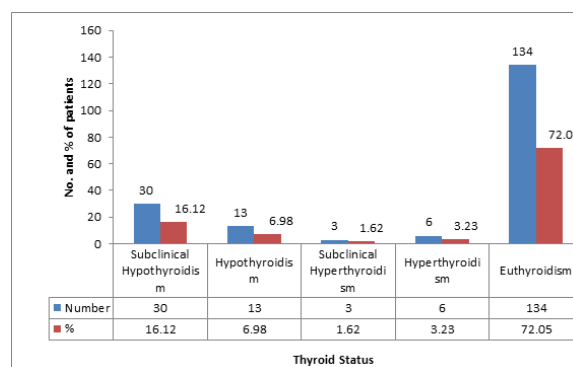


Figure 1. Analysis of ACS patients with different thyroid status (n=186)

The mean value of T3 (pg/ml) among the patients with subclinical hypothyroidism, hypothyroidism, subclinical hyperthyroidism, hyperthyroidism and euthyroidism was 3.28±0.46, 1.73±0.41, 3.62±0.51, 7.95±2.03 and 3.18±0.39 respectively, which was found to be significantly (p=0.001) altered among them. The mean value of T4 (ng/dl) among the patients with subclinical hypothyroidism, hypothyroidism, subclinical hyperthyroidism, hyperthyroidism and euthyroidism was 1.13±0.34, 0.71±0.46, 1.39±0.29, 4.39±1.47 and 1.1±0.28 respectively, which was found to be significantly (p=0.001) deviated. The mean TSH (uIU/ml) value was significantly (p=0.001) varied among individuals with subclinical hypothyroidism, hypothyroidism, subclinical hyperthyroidism, hyperthyroidism, and euthyroidism, respectively and the values in uIU/ml were 10.57±18.33, 28.67±37.49, 0.17±0.06, 0.09±0.05 and 3.05±1.27 respectively as shown in table 2.

Table 2. Mean value of thyroid hormones among the ACS patients with different thyroid status

Thyroid Status	T3 (pg/ml)	T4 (ng/dl)	TSH (uIU/ml)
Subclinical Hypothyroidism	3.28±0.46	1.13±0.34	10.57±18.33
Hypothyroidism	1.73±0.41	0.71±0.46	28.67±37.49
Subclinical Hyperthyroidism	3.62±0.51	1.39±0.29	0.17±0.06
Hyperthyroidism	7.95±2.03	4.39±1.47	0.09±0.05
Euthyroidism	3.18±0.39	1.1±0.28	3.05±1.27
P-Value	0.001	0.002	<0.001
Reference Range	2.5-4.16	0.89-1.76	0.34-5.12

We had also estimated the blood level of other biochemical parameters among all the ACS patients. Among all the biochemical parameters, it was noted that the mean value of serum triglyceride (144.16 mg/dl), sugar (128.66 mg/dl), urea (36.83 mg/dl) and creatinine (1.16 mg/dl)

was significantly ($p=0.046$, 0.01 , 0.01 , 0.006 respectively) elevated in ACS patient than that of healthy people whereas mean value of HDL (42.63 mg/dl) was significantly ($p=0.01$) decreased. No significant change was observed between the mean values of other parameters as shown in table 3.

Table 3. Mean value of biochemical parameters in ACS patients

Blood Parameters	ACS Patients (Mean±SD)	Healthy People (Mean±SD)	p-value
Total Cholesterol (mg/dl)	155.37±45.74	149.6±25.28	0.448
Triglyceride (mg/dl)	144.16±78.01	112.9±21.56	0.046
HDL (mg/dl)	42.63±9.74	57.1±6.40	0.011
LDL (mg/dl)	91.95±38.23	94.9±9.16	0.58
Sugar (mg/dl)	128.66±57.1	103±10.40	0.01
Urea (mg/dl)	36.83±26.87	22.3±5.31	0.011
Creatinine (mg/dl)	1.16±0.77	0.76±0.16	0.006
Sodium (mmol/l)	134.77±23.92	139.2±2.70	0.185
Potassium (mmol/l)	4.24±0.52	4.11±0.26	0.107
Uric acid (mg/dl)	5.73±1.6	5.07±0.73	0.931
HbA1c (%)	8.8±2.36	6.24±0.37	0.15

DISCUSSION

The total number of patients, having been diagnosed with ACS, considered for this study was 186. Out of that, 52 (27.95%) were found to have thyroid dysfunction. Among thyroid disorder patients, subclinical hypothyroidism was most commonly observed in 30 (16.12%), whereas hypothyroidism was seen 13 (6.98%). Three (1.62%) and six (3.23%) ACS patients were found to have subclinical and hyperthyroidism, respectively. One hundred thirty four (72.05%) patients were not found to have thyroid disorder. Similar finding was observed in a study conducted in Pokhara, Nepal which revealed that among ACS patients, 23.5% had abnormal TFTs overall, of whom 59.5% had Euthyroid Sick Syndrome, 25.5% had subclinical hypothyroidism, 10.6% had subclinical hyperthyroidism and 4.25% had low ft_4 with normal ft_3 and normal TSH.¹⁶ Another study from Saudi-Arabia reported that 23% of patients with coronary heart disease reported having thyroid abnormalities. In their study, subclinical hyperthyroidism occurred in 2.7% of participants whereas overall hypothyroidism prevalence was 7.8%. There were reports of 0.5% and 2.0% preclinical and overt hyperthyroidism, respectively. Of the critically ill patients, 41 (10.2%) had the euthyroid unwell state.²⁰ A report from eastern India revealed the prevalence of subclinical hypothyroidism among ACS patients was 15.27%.²¹ A study carried out among AMI patients in UK showed that there were 79.9% euthyroid individuals, 17.3% subclinically hypothyroid individuals, 1.2% subclinically hyperthyroid individuals and 1.3% individuals with low T3 syndrome.²²

Among them, 68.28 % were male and the mean age of the study participants was 60.0 ± 13.7 year. The maximum

cases (74.73%) of ACS were observed in the age group 51-75 in the present study. Majority (78.49%) of patients had their BMI in the normal range ($18.5-24.9$ kg/m²). A study on ACS patients here in NMCTH only in 2018 concluded that among the participants, 77.1% were male proportion, the mean age of all patients was 59.19 ± 19 year and 59.3% had normal BMI.²³ Similar findings were observed in the study conducted at Shahid Gangalal National Heart Centre, Kathmandu, Nepal among ACS patients, in which 70% were male with mean age of 60.8 ± 13.4 years in the range of 20-98 years and the maximum cases (27.3%) were in the age group 65-74 year.²⁴ A study carried out among ACS patients in India showed the prevalence of 76.4% male and mean age of patients was 57.5 year. The maximum cases (56.7%) were seen in the age group of 51-70 years. Similar to the present study, the majority (52.9%) of ACS patients had normal BMI ($20-24.9$ kg/m²).²⁵

In the present study, among ACS patients, the maximum cases were STEMI (62.9%) followed by NSTEMI (24.74%) and USA (12.36%). A study carried out at Shahid Gangalal National Heart Centre, Kathmandu, Nepal, reported that amongst ACS patients, 44.74% cases were of STEMI whereas NSTEMI and USA were observed in 31.59% and 23.68% respectively.²⁶ According to results of another study conducted in Palpa, Nepal, 50% of ACS patients experienced STEMI, followed by NSTEMI and USA in 35% and 15% of cases, respectively.²⁷ The cases of STEMI and NSTEMI were 60.6% and 39.4% respectively among ACS patients in the study conducted in different cities of India.²⁵

Diabetes mellitus and hypertension were associated in 22.58% and 43.01% among the study participants in the present study. History of smoking, family history of coronary artery disease and dyslipidemia was noted in 44.62%, 5.91% and 42.47% of ACS patients respectively in the current study. The prevalence of diabetes mellitus and hypertension among ACS patients was reported to be 25.3% and 36.6% and history of smoking and dyslipidemia in 54% and 7.8% respectively in a study done at Shahid Gangalal National Heart Centre, Kathmandu, Nepal.²⁴ Earlier report from this institute reported the prevalence of diabetes mellitus, hypertension, dyslipidemia, smoking and family history of coronary artery disease was 31.4%, 33.3%, 48.6%, 10.5% and 5.7% respectively among ACS patients.²³ The study conducted in Kerala, India reported that diabetes mellitus, hypertension and smoking were seen 37.6%, 48.4% and 34.4% cases respectively among ACS patients.²⁸ A study on ACS patients in the Gulf States found that there were 30.6% cases of diabetic mellitus, 20.3% cases of hypertension, 10.3% cases of dyslipidemia, and 50.4% cases of smoking.²⁹ A research report from Argentina revealed that smoking was associated with 66.3% cases, dyslipidemia in 51.7%, diabetes mellitus in 22.1%, hypertension in 63.8% among ACS patients.³⁰

The blood level of thyroid hormones and TSH in ACS patients with different status of thyroid disorder was evaluated in

the present study. The mean value of T3 and T4 in ACS patients with hypothyroidism (1.73 ± 0.41 pg/ml, 0.71 ± 0.46 ng/dl) and hyperthyroidism (7.95 ± 2.03 pg/ml, 4.39 ± 1.47 ng/dl) was significantly ($p=0.001$ for T3, $p=0.002$ for T4) altered than the normal value. Similarly, the mean value of TSH among the patients with subclinical hypothyroidism (10.57 ± 18.33 uIU/ml), hypothyroidism (28.67 ± 37.49 uIU/ml), subclinical hyperthyroidism (0.17 ± 0.06 uIU/ml) and hyperthyroidism (0.09 ± 0.05 uIU/ml) was significantly changed ($p < 0.001$) than the normal reference range. The mean value of TSH and fT4 were reported as 7.72 uIU/ml and 0.83 ng/dl respectively in a study conducted in Kolkata, India among ACS patients suffering subclinical hypothyroidism.²¹ Similarly, the mean value of fT3, fT4 and TSH were found to be 4.2 ± 1.3 pmol/L, 14.6 ± 3.7 pmol/L and 4.4 ± 1.7 uIU/ml respectively in a study on patients with ischemic changes in Saudi Arabia.³¹

In the present study, other biochemical parameters like lipid profile, blood sugar, renal function test were also analyzed. Out of all these parameters, the mean value of total cholesterol, triglyceride, HDL, LDL and sugar was 155.37 ± 45.74 mg/dl, 144.16 ± 78.01 mg/dl, 42.63 ± 9.74 mg/dl, 91.95 ± 38.23 mg/dl, 128.66 ± 57.1 mg/dl respectively. The mean value of triglyceride, HDL and sugar were significantly altered ($p=0.04$, 0.01 , 0.01 respectively). In an study among patients with ischemic changes, the mean value of total cholesterol (174.4 ± 48.3 mg/dl) and triglyceride (158.2 ± 100.0 mg/dl) were significantly elevated ($p= <0.001$, $p=0.007$ respectively) than the non-ischemic patients, whereas the mean value of HDL (38.4 ± 14.7 mg/dl) was non-significantly ($p=0.73$) reduced and the mean value of LDL (109.3 ± 43.8 mg/dl) was significantly ($p=0.001$) elevated.³¹ The mean value of total cholesterol, triglyceride,

HDL, LDL in mg/dl was reported as 183.43 ± 35.91 , 140.59 ± 46.82 , 109.90 ± 26.37 and 41.17 ± 4.77 respectively among ACS patients in a study conducted previously in this institute.²³ The mean value of lipid profile parameters in mg/dl (Total cholesterol, Triglyceride, HDL and LDL) among the ACS (STEMI) patients in a study in Pakistan were reported as 207.5 ± 30.5 , 153.8 ± 10.2 , 46.6 ± 9.9 , 149.0 ± 41.2 .³² Similarly, the study carried out among ACS (STEMI) patients in Kathmandu, Nepal reported the mean value of Total cholesterol, Triglyceride, HDL, LDL and sugar in mmol/L as 4.0 ± 1.2 , 1.6 ± 0.9 , 1.0 ± 0.1 , 2.1 ± 0.8 and 7.2 ± 5.4 respectively.²⁴

The limitation of the study is the data is collected from only one center at a particular point of time and the patients are not followed up after the treatment.

CONCLUSION

The occurrence of acute coronary syndrome was observed more in male and in advance age of patients. Subclinical hypothyroidism was the most common thyroid disorder and diabetes mellitus, hypertension, smoking, dyslipidemia were observed as associated factors among a fraction of ACS patients. ST-elevation myocardial infarction was predominantly seen among acute coronary syndrome patients at this center. Mean value of many biochemical parameters were found to be significantly altered.

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