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Research Article

EVALUATION OF THYROID PROFILE AND ITS PROGNOSTIC VALUE IN PATIENTS OF ACUTE CORONARY SYNDROME

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ABSTRACT

Objective: The objective of the study is to study the association of thyroid dysfunction with acute coronary syndrome (ACS), its complications and duration of hospital stay.

Methods: This prospective comparative study was done on 100 patients divided equally into ACS patients with control (normal thyroid function) and ACS patients with thyroid dysfunction admitted in a tertiary care center, Udaipur, Rajasthan with ACS during the period of February 2021–July 2022. We studied the prevalence, prognostic factor of thyroid hormone in these patients.

Results: The mean ejection fraction of the control group was 51.16±11.72%, of hypothyroid group was 49.00±13.55% and of hyperthyroid group was 51.12±13.78%. 29 cases of cardiac failures, 38 cases of arrhythmias, and 32 cases of major adverse cardiac events were observed. 56% of patients required thrombolysis, out of which 67.86% were from the subclinical hypothyroid group. The mean hospital stay in control group was 4.53±1.55, in hypothyroid group was 5.27±1.84 and in hyperthyroid group was 7.00±1.92.18% mortality.

Conclusion: Patients with acute myocardial infarction, initially develop alteration in thyroid hormone levels, which is possibly a compensatory mechanism to reduce the metabolic demand of the heart, by reducing myocardium contraction and cardiac output but may cause cardiac failure and higher rates of cardiovascular complications like arrhythmias and death in some of the patients. Thyroid dysfunctions in patients with ACS may also need a longer duration of intensive care and close monitoring during follow-up.

Keywords: Coronary artery disease, Acute coronary syndromes, ST-segment elevation myocardial infarction, Non-ST-segment elevation myocardial infarction, Myocardial infarction.

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INTRODUCTION

Coronary artery disease (CAD) is the leading cause of mortality and morbidity globally and acute coronary syndromes (ACSs), which consists of ST-segment elevation myocardial infarction (STEMI), non-ST-segment elevation myocardial infarction (NSTEMI) and unstable angina (UA) and are the commonest causes of mortality in patients with CAD [1]. The mortality related to ACS has significantly reduced in the developed world over the past 20 years due to the introduction of huge resources equipment and drug of invasive and noninvasive therapeutic strategies. However, the mortality remains high among Indians. Acute myocardial ischemia's clinical manifestation is represented by ACS.

Cardiovascular diseases have been associated with serious public health problems. The abnormalities of the thyroid functions both hyperthyroidism and hypothyroidism by way of affecting the cardiovascular system directly or through indirect means can have a major impact on health and disease. Low T_3 circulating levels have been associated with typical pattern of altered thyroid hormone metabolism and have been described in patients with acute myocardial infarction and heart failure in adults [2]. In spite of advances in pharmacotherapy and myocardial reperfusion procedures, short- and long-term prognosis of ACS remains continuously high in terms of mortality and morbidity of patients [3].

The present study is an attempt to observe the prognosis of patients of ACS with a focus on thyroid dysfunction.

To estimate the prevalence of thyroid dysfunction in patients of ACS.

To study the association of thyroid dysfunction with ACS, its complications, and duration of hospital stay.

METHODS

This prospective, observational study was conducted on all patients admitted with ACS at a tertiary care setting, Udaipur, Rajasthan 18 months from February 2021 to July 2022.

All patients with new onset of ACS admitted at tertiary care setting, Udaipur, Rajasthan, willing to give written informed consent.

Patients taking medications affecting thyroid hormone levels previously were excluded from the study.

Method of collection of data

Detailed clinical history and physical examination were done. ACS was diagnosed by ECG, 2D Echocardiography, and cardiac markers such as Troponin-T, CPK-MB, and lactate dehydrogenase. Thyroid dysfunction was assessed in these patients by blood investigations such as free T_3, free T_4, and thyroid-stimulating hormone (TSH) levels. All the samples were collected on admission.

TSH electrochemiluminescence immunoassay is a three-step sandwich immunoassay. In the first step, the sample is combined with a reagent containing a biotinylated TSH antibody and a N-hydroxysuccinimide ester of a modified ruthenium-tris(bipyridyl) (Ru[bpy]32+) TSH-specific antibody in an assay cup. During a 9-min incubation step, antibodies capture the TSH present in the sample. In the second step, streptavidin-coated paramagnetic microbeads are added. During a second 9-min incubation, the biotinylated antibody attaches to the streptavidin-coated surface of the microbeads. After the second incubation, the reaction mixture containing the immune complexes is transported into the measuring cell; the immune complexes are magnetically entrapped

on the working electrode, but unbound reagent and sample are washed away by a system buffer (Procell). In the ECL reaction, the conjugate is a ruthenium-based derivative and tripropylamine; the chemiluminescent reaction is electrically stimulated to produce light at 620 nm. The amount of light produced is directly proportional to the amount of TSH in the sample. Evaluation and calculation of the concentration of TSH are carried out by means of a calibration curve that was established using calibrators of known TSH concentration [4].

Free T_3 (normal range 2.0–4.4 pg/mL), Free T_4 (0.9–1.7 ng/dL) and Thyroid stimulating hormone (0.27–4.2 uL/dL).

Cardiogenic shock is reduced heart ejection fraction and hypotension leading to reduced blood supply. This is caused by severe myocardial infarction or use of drugs such as beta-blockers, calcium channel blockers or myocarditis, sarcoidosis, sino-atrial node dysfunction, atrioventricular dysfunction pulmonary hypertension, and cardiac tamponade. Arrhythmia is an irregular heart rate or rhythm; the heart can be slow (bradycardia to a slow heartbeat – a resting heart rate <60 beats a minute.) or fast (Tachycardia refers to a fast heartbeat a resting heart rate >100 beats a minute). Types of bradycardias are sick sinus syndrome and conduction block. Types of atrial tachycardia are atrial fibrillation, atrial flutter, supraventricular tachycardia. Types of ventricular tachycardia are ventricular tachycardia, ventricular fibrillation. Bleeding clinically overt hyperthyroidism and hypothyroidism modify the coagulation-fibrinolytic balance, indicating that thyroid hormone excess or deficit is the probable cause of bleeding and thrombosis. Death is the end complication.

The cardiac markers included in the study for comparison are CPK-MB, Trop-T, and LDH. In 2D-Echocardiography left ventricular ejection fraction was observed.

Statistical analysis

The data were entered into MS Excel Software version 20 and analyzed using SPSS, IBM Comp, Version 21. Descriptive analysis of the data was performed presenting the results as frequency and percent for qualitative variables and as mean and standard deviation for age. The relation between qualitative variables was evaluated by Chi-square test and Fisher's Exact test if needed. The quantitative data were analyzed using an independent student's t-test. $p<0.05$ was considered statistically significant.

RESULTS

Myocardial infarction is more common in the 5th and 6th decade with more cases in the 5th decade. The youngest patient was 33-years-old and the oldest was 80-years-old. The mean age was higher in females compared to males (Table 1).

There are higher number of patients with hypertension, diabetes mellitus, and smoking in the control group but dyslipidemia is higher in the thyroid dysfunction group. p-value is statistically insignificant >0.05 (Graph 1).

There were a total of 50 patients of ACS in the thyroid dysfunction group, out of which 33 were in the subclinical hypothyroidism group, 12 were in overt hypothyroidism, 2 were overt hyperthyroidism, and 3 were in subclinical hyperthyroidism. p-value is statistically insignificant >0.05 (Table 2).

The total number of cardiac failures that occurred was 29 in control group and thyroid dysfunction group, out of which 23 cardiac failures occurred in the thyroid dysfunction group. p-value is statistically significant <0.01 (Table 3).

The total number of arrhythmias that occurred was 38 in control group and thyroid dysfunction group, out of which 26 arrhythmias occurred in thyroid dysfunction group. p-value is statistically insignificant >0.05.

There was a higher complication in thyroid dysfunction group than control group. p-value is statistically insignificant >0.05.

The lowest ejection fraction was seen in overt hypothyroidism group (EF-10%). p-value is statistically insignificant >0.05, but few patients in thyroid dysfunction group had significant reduced ejection fraction (Table 4).

There is a significant difference in mean hospital stay with hypothyroidism and hyperthyroidism patients than with control group, with the highest number of stay in hospital in the overt hypothyroidism group (11 days). p-value is statistically significant <0.01 (Table 5).

The total number of deaths was 17 in control group and hypothyroid group, out of which 13 deaths were in hypothyroid group. p-value is statistically significant <0.01.

The total number of deaths was 5 in control group and hyperthyroid group, out of which 4 deaths were in hypothyroid group. p-value is statistically insignificant >0.05, it may be due to our low study sample size (Table 6).

DISCUSSION

ACS has become one of leading cause of mortality and morbidity globally. About half of ACS-related death occur before patient can reach hospital. Thyroid hormone function has significant effects on cardiovascular physiology which includes heart rate, blood pressure, cardiac output, myocardial contractility, and systemic vascular resistance.

This study was undertaken to evaluate the thyroid profile in patients with ACS in a tertiary care center, Udaipur, Rajasthan. In this study we observed 100 patients of ACS which were divided into control group and thyroid dysfunction group, all the subjects were fulfilling inclusion and exclusion criteria.

In our study, the mean age was higher in females 60.8 compared to males. Most patients were from 51 to 60 years of age group, which corresponds to 57% of the study population, from 41 to 50 years of age group, which corresponds to 21% of the study population, from >60 years of age group, which corresponds to 19% of the study population and from 31 to 40 years of age group, which corresponds to 3% of the study population. In other studies, conducted by Lavanya, Lymvaios *et al*., Khalil *et al*., Paudel *et al*. and Mukherjee *et al*., the mean age group of patients having ACS was higher after 51–60 years of age group [5-9]. This was in accordance with our study and indicates that age is a non-modifiable risk factor for ACS.

In our study, out of 100 cases of ACS, there were 53 patients with STEMI, 32 patients with NSTEMI and 15 patients with UA. In 53 STEMI patients, there were 26 patients in control groups (49.05%), there were 24 patients in hypothyroid group (45.28%), and 3 patients in UA (5.66%). In 32 NSTEMI patients, there were 16 patients in control groups (50%), there were 14 patients in hypothyroid group (43.75%) and 2 patients in UA (6.25%). In 15 UA patients were 8 patients in control groups (53.34%), there were 7 patients in hypothyroid group (46.67%). In another study conducted by Khalil *et al*., they had divided their study group of 196 in 98 patients with STEMI and other 98 patients NSTEMI and UA, out of which 151 patients were control group and 45 had thyroid dysfunction [7]. There were 72.45% of patients in STEMI were from the control group and 81.63% in NSTEMI and UA were control group. There were 27.55% of patients in STEMI with thyroid dysfunction function and 18.37% in NSTEMI and unstable group with thyroid dysfunction function. This does not simulate with our study as they had different grouping for study population and a higher number of study population. In another study conducted by Paudel *et al*., they had 200 patients study population of ACS patients out of which 58% were STEMI and 42% were NSTEMI and UA [8]. They had 47 patients with thyroid dysfunction in which 59.5% were sick euthyroid syndrome, 25.5% with subclinical hypothyroidism, 10.6% with subclinical hyperthyroidism and 4.25% with normal TSH and deranged free T_4. This is in accordance with our study and indicates that there is not much difference in the prevalence of ACS in control thyroid function and thyroid dysfunction group.

Table 1 : Age distribution of the study population

Age interval	Number of control (n=50)	Hyperthyroid (n=5)		Hypothyroidism (n=45)		Total
		Overt	Subclinical	Overt	Subclinical	
31–40	1	0	0	0	2	3
41–50	11	0	0	1	9	21
51–60	29	2	1	9	16	57
>60	9	0	2	2	6	19
Total	50	2	3	12	33	100

Table 2: Comparison between subclinical versus overt thyroid dysfunction regarding STEMI, NSTEMI and unstable angina

Parameters	NSTEMI	STEMI	Unstable angina	p	Total
Hypothyroidism					
Overt	5	5	2	>0.05	12
Subclinical	9	19	5		33
Hyperthyroidism					
Overt	0	2	0		2
Subclinical	2	1	0		3
Total	16	27	7		50

STEMI: ST-segment elevation myocardial infarction, NSTEMI: Non-ST-segment elevation myocardial infarction

Table 3: Comparison between control, subclinical and overt thyroid dysfunction regarding major adverse cardiac event, cardiac failure and arrhythmia

Parameters	Major adverse cardiac events	CF	Arrhythmia	p
Control group	9	6	12	>0.05
Hypothyroidism				
Overt	7	13	7	
Subclinical	16	8	17	
Hyperthyroidism				
Overt	1	1	1	
Subclinical	1	1	1	

Table 4: EF with control and thyroid dysfunction group

Groups	Mean EF (%)	p
Control group	51.16±11.72	>0.05
Hypothyroid	49.00±13.55	
Hyperthyroid	51.12±13.78	
Total	51.05±11.76	

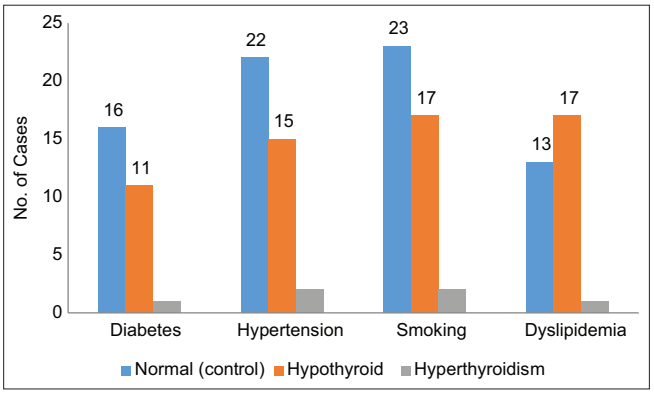
EF: Ejection fraction

Table 5: Duration of hospital stay in control and thyroid dysfunction

Groups	Hospital stay (days)	p
Control group	4.53±1.55	<0.01
Hypothyroid	5.27±1.84	
Hyperthyroid	7.00±1.92	
Total	5.6±1.77	

Table 6: Comparison of mortality rates between hypothyroid group and control group

Outcome	Death	Discharge	Total
Control group	4	46	50
Hypothyroid	13	32	45
Hyperthyroid	1	4	5



Graph 1: Distribution of patients with a history of diabetes mellitus, hypertension, smoking, and dyslipidemia

Major adverse cardiac events (MACE) are referred as the composite of total death, MI, stroke, hospitalization because of heart failure and revascularization including percutaneous coronary intervention and coronary artery bypass graft. In our study, MACE was seen in total 32 number of patients, out of which were from the control group (28.12%) and 23 were in thyroid dysfunction group (71.87%). This was associated with increase in the duration of hospital stay and in-hospital mortality. In other study, conducted by Ozcan *et al*., in their study found that MACE was significantly higher in thyroid dysfunction group (15.2%) compared to the control group (7.8%), with increase in-hospital mortality in thyroid dysfunction group [10]. In other study, conducted by Lavanya, they found that the total number of patients with MACE was 17 (22.66%), from them 70.59% of patients were from thyroid dysfunction group and 29.41% from control group [5]. In other study, conducted by Khalil *et al*., they found that there was 19.2% MACE in control group and 53.34% in thyroid dysfunction group, there was also increase in relative risk of MACE in thyroid dysfunction group consisting of shock (6.04 folds), arrhythmias (2.05 folds) and reinfarction (1.67 folds) [7]. A multifactorial mechanism plays a role, including myocardial ischemia, the presence of atherosclerotic plaque instability, and impaired cardiac contractility of non-infarct zones in the presence of multiple obstructive stenosis in patients with thyroid dysfunction with ACS. This is in accordance with our study and indicates that the incidence of MACE was found to be statistically significant in thyroid dysfunction group (p<0.01)

In our study, there were a total of 29 patients who developed cardiac failure, out of which 6 belonged to the control (20.68%) and 22 patients belonged to the thyroid dysfunction group (79.32%). The maximum number of patients who developed cardiac failure was seen in subclinical hypothyroidism group (44.82%). In another study conducted by Lavanya, they found that 15 patients of total study population group developed cardiac failure, from which 20% were from the control group and 80% were from thyroid dysfunction group [5]. In another study conducted by Paudel *et al*., found that cardiac failure was highly significant in patients with thyroid dysfunction group compared to control group [8]. In hyperthyroidism, cardiac output is increased when compared to that in normal conditions. This enhancement of cardiac output is based on synergistic effects of a raised heart rate,

increased cardiac contractility, and dilation of peripheral blood vessels, which leads increased myocardial demand causing ischemic injury and acute coronary events. In hypothyroidism, cardiac output is reduced when compared to that in a normal state, which leads to cardiac failure. This is in accordance with our study and indicates that the incidence of cardiac failure in the thyroid dysfunction group is statistically significant.

In our study, the mean ejection fraction of control group was 51.16±11.72%, mean ejection fraction of hypothyroid group was 49.00±13.55%, and mean ejection fraction of hyperthyroid group was 51.12±13.78%. The mean ejection fraction was low in the thyroid dysfunction group compared to the control group. The lowest ejection fraction was seen in overt hypothyroidism group (EF-10%). In another study conducted by Mukherjee *et al*., in their study found no significant difference in terms of left ventricular ejection fraction, angiographic pattern, and outcomes when compared with thyroid dysfunction group and control thyroid function group [9]. This is in accordance to our study. In another study conducted by Lymvaios *et al*., they found that nearly half of their patients showed <5% difference in the recovery of left ventricular ejection fraction [6]. However, over time course analysis of thyroid hormone changes in plasma revealed poor recovery of T3 levels in this group of patients, indicating a potential association of T_3 to cardiac function late after ACS. In fact, further analysis revealed that T_3 levels at 6-month interval were an independent predictor of decreased left ventricular ejection fraction and there was a strong correlation between them. Thyroid hormone directly affects the myocardium by altering its contractility, inotropy, and heart rate. It also affects the peripheral vascular system, by dilating peripheral arteries to increase cardiac output. In hyperthyroidism, myocardial contractility and cardiac output are enhanced, and systemic vascular resistance is decreased which in ACS leads to ischemic injury.

In our study, the mean duration of hospital stay in control group was 4.53±1.55, in hypothyroid group was 5.27±1.84, and in hyperthyroid group was 7.00±1.92. There is a significant difference in mean duration of hospital with hypothyroidism and hyperthyroidism patients than with control group, with the highest number of durations in hospital in overt hypothyroidism group 11 days and the lowest number of durations in hospital in control group 1 day. The duration of hospital stay among thyroid dysfunction group is statistically significant. In another study conducted by Paudel *et al*., the mean hospital stay was significantly higher in thyroid dysfunction group (mean difference −3.56–2.45) than control group [8]. This may be due to increased comorbidities and cardiovascular complications in thyroid dysfunction group. This is in accordance with our study and indicates that thyroid dysfunction in patients ACS is associated with a longer duration of hospital stay ($p<0.01$).

In our study, out of 100 ACS patients, there were a total of 18 deaths. The control group had 4 deaths from 50 ACS patients (22.23%). The thyroid dysfunction group had 14 deaths from 50 ACS patients (77.78%), out of which hypothyroid group had 13 deaths (72.23%) and hyperthyroid group had 1 death (5.56%). In another study conducted by Lavanya, found that out of 8 patients who died, 75% of patients were from thyroid dysfunction group [5]. Paudel *et al*. found in their study that thyroid dysfunction increases the relative risk for mortality by 5.49 folds when compared to patients with normal thyroid function [8].

We had few limitations in our study as the study group was small in number. A thyroid profile was done only once, at the time of admission, a repeat thyroid profile may have shown some difference of the thyroid hormone levels. Follow-up of the patients was done only till discharge. Long-term follow-up could have shown further prognostic effects of thyroid hormone dysfunction.

CONCLUSION

In the light of above obtained results, the following conclusion can be drawn: age, male gender, and post-menopausal females are the non-modifiable risk factors. There is also increased risk of dyslipidemia in patients with thyroid dysfunction, which also increases morbidity and mortality.

Patients presenting with an acute myocardial infarction initially develop alteration in thyroid hormone levels, which is possibly a compensatory mechanism to reduce the metabolic demand of the heart, by reducing myocardium contraction and cardiac output but may cause cardiac failure and higher rates of cardiovascular complications such as arrhythmias and death in some of patients (statistically significant). Thyroid dysfunctions in patients with ACS may also need a longer duration of intensive care and close monitoring during follow-up. They are associated with short-term and long-term poor outcomes.

CONFLICTS OF INTERESTS

No.

AUTHORS CONTRIBUTIONS

All authors contributed equally in data collection, analysis and in script writing.

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