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Correlation of cardiac markers with thyroid stimulating hormone in subclinical hypothyroid elderly

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Article

ABSTRACT

Cardiac markers (CPK-MB and TroponinT (TnT)) are often used to differentiate between cardiac and non-cardiac chest pain. Subclinical hypothyroidism (SCH) has increased incidence of cardiovascular risk factors and disease. Elderly have an increased incidence of SCH. However, no study has specifically examined the association between cardiac markers and SCH in elderly population. This study is meant to determine the association of cardiac markers with thyroid stimulating hormone (TSH) in elderly patients with subclinical hypothyroid and euthyroid. The present study was designed as a retrospective cross-sectional study conducted in Biochemistry department of Adesh institute of medical sciences and research (AIMSR) Bathinda from a period of May 2023 to April 2024.The data was obtained from the lab computers and the subjects were divided into four groups. Group 1 included patients who had MI and SCH. Group 2 consisted of patients who had MI and were euthyroid. Group 3 were those who presented with chest pain only (no MI) and SCH. Group 4 were those who had acute chest pain (no MI) and were found to be euthyroid. Group 1 and 3 showed a highly significant association between the the cardiac markers and TSH. Group 2 and 4 showed a significant correlation. Conclusion: Elevations of TSH levels may cause a significant rise in the cardiac markers in SCH as compared to euthyroid.

Keywords: Clinical studies, Cardiac markers, Thyroid hormone, hypothyroid, euthyroid, heart disease, chest pain.

INTRODUCTION

SCH is biochemically defined as a TSH level above the upper limit of the reference range with normal thyroid hormone levels.[1] SCH is associated with an increased risk of coronary heart disease (CHD) and mortality.[2] Incidence of cardiovascular disease increases with age. At the same time TSH values are found higher with advancing age.[1] Thus Subclinical hypothyroidism (SCH) is a common condition present in the geriatric age group that significantly affects the cardiovascular system.[3] The sensitivity and specificity of ECG are low in diagnosing acute myocardial infarction (AMI), hence the criteria for AMI were decided by the European Society of Cardiology (ESC) and the American College of Cardiology (ACC). Accordingly, a patient has to have at least two of the following: typical symptoms, a characteristic elevation pattern in cardiac markers (eg, CK-MB izoenzymes), preferably serum troponins (cTnI or cTnT), or a typical ECG trace with Q waves that indicate a diagnosis of AMI.[4] The present study tried to find association between TSH and cardiac markers in elderly subclinical hypothyroid patients presenting with chest pain and myocardial infarction. An ideal cardiac marker: 1) must be sensitive enough to detect a small degree of damage to the heart, 2) should be specific to the heart muscle (it must exclude damage to other [skeletal] muscles), 3) should give information regarding the severity of the infarct and the prognosis of the disease, 4) should also show the result of reperfusion therapy in AMI, 5) needs to distinguish between reversible and irreversible damage, 6) ought not to be detected in patients showing no myocardial damage, 7) should help in early and late diagnosis, 8) should be easy to measure, fast, cheap, and quantitative, and finally, 9) should have long-term storage conditions and be stable under them.

Objectives of the study:

To determine the association between cardiac markers (CPK-MB, TroponinT) and TSH in elderly subclinical hypothyroid patients.

MATERIAL AND METHODS

Study design:

The study was designed as hospital-based retrospective cross-sectional study conducted in Central Clinical Laboratory of Adesh Institute of Medical Sciences and Research, Bathinda, a tertiary care teaching hospital in Punjab, India, from a period of May 2023 to April 20234. All participants were in the age group of >60 years. The average age group of the subjects came out to be 70 ± 8 years. Hence serum TSH reference range in relation to age for the present study was 0.48 IU/L to 4.59 IU/L.[5] Subjects were divided into four groups. Group 1 consisted of 100 patients presenting with chest pain and MI and were found to have subclinical hypothyroidism. Group 2 consisted of subjects presenting with chest pain and MI but were euthyroid. Group 3 included patients presenting with chest pain only and were having SCH. GROUP 4 consisted of subjects who presented with

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chest pain only and were found euthyroid. Both emergency and outdoor patients were included in this study.

Sample size: The sample size was calculated based on the average prevalence rate of hypothyroidism (18%)[3] by using Cochran's formula.

$Z^2 PQ/e^2$

Where Z is Z score.

It was increased to 100 to have adequate number and to draw significant conclusion. Hence, we included 100 subjects for each group.

Data collection: The data was collected from the previous one-year data (May 2023 to April 2024) maintained in the laboratory computer.

Sampling procedure:

Patients presenting with acute chest pain and MI with SCH or euthyroids whose cardiac markers and TSH available in the records were enrolled for study analysis.

Sample estimations: Cardiac markers were analysed by poct technique. The thyroid function tests were estimated by chemiluminescence assay (Maglumi 2000 Fully automated analyzer) and Lipid profile was analyzed by Biosystem BA200 fully automatic analyzer.

Inclusion Criteria: Patients >60 years of age presenting with acute chest pain or MI or both, having SCH OR euthyroid.

Exclusion criteria: Patients with history of myocarditis, cardiomyopathies, arrhythmias, valvular heart disease cardiac contusion, renal failure, sepsis, anemia, hypotension, hypoxia, and noncardiac surgery were excluded.

Statistical analysis: Data was analyzed using SPSS software. Pearson's correlation was calculated. The data was presented as mean ± SD. A p value of < 0.05 was taken as statistically significant.

RESULTS

There was no significant difference between age and gender of the groups. Average age group of the subjects was 70 ±8 years. The present study showed a non-significantly high (r=0.268, p=0.03) levels of TSH in cases (Group 1&3) (90.9 ± 6.6 uIU/ml) as compared to the controls Group 2&4) (1.6 ± 0.8 uIU/ml). The average age for the subjects came out to be 70 ± 8 years. Our study showed significant correlation of TSH with CPK-MB (r=0.69, p=0.001) and Troponin T (r=0.201, p= 0.04) in Group 1 while a non-significant correlation was found in Group 2, CPK-MB (r=0.06, p=0.67) and Troponin T (r= 0.156, p= 0.57). There was a significant correlation of TSH with CPK-MB (r=0.71, p=0.02) and Troponin T (r=0.84, p= 0.001) in Group 3. A non-significant correlation was found in Group 4, between TSH and CPK-MB (r=0.116, p=0.68) and Troponin T (r= 0.001, p= 0.99). (Table 1 and 2)

Table 1: Correlates the levels of CPK-MB, TnT and BNPin Group 1 and 2

Variables		TSH in Group 1	TSH in Group 2
CPK-MB	r	0.69	0.06
	p	0.001	0.67
TnT	r	0.21	0.15
	p	0.04	0.57
BNP	r	0.64	0.01
	p	0.001	0.62

r is the correlation coefficient, p is the values obtained from Spearman correlation analysis, p<0.05 is considered statistically significant.

Table 2: Correlates the levels of CPK-MB, TnT and BNPin Group 3 and 4

Variables		TSH in Group 3	TSH in Group 4
CPK-MB	r	0.71	0.11
	p	0.02	0.68
TnT	r	0.84	0.001
	p	0.001	0.99
BNP	r	0.13	0.08
	p	0.58	0.55

r is the correlation coefficient, p is the values obtained from Spearman correlation analysis, p<0.05 is considered statistically significant.

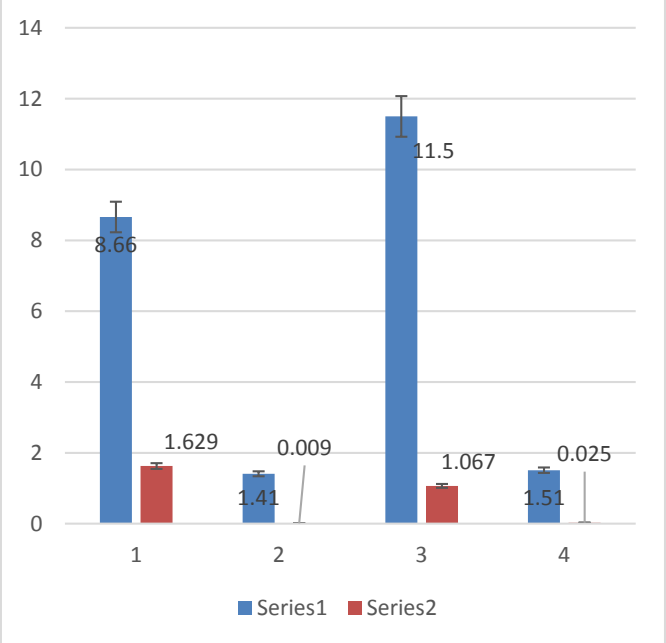

Figure 1. Correlation of CPK-MB and TnT with TSH in Group 1, 2, 3 and 4

Discussion

There was no significant difference in age and gender ratio in cases and controls. The present study showed a non-significant (r=0.04, p=0.65) elevation in the levels of TSH in subclinical hypothyroid patients (7.9 ± 1.9 uIU/ml) as compared to euthyroid subjects (2.0 ± 1.0 uIU/ml). Similar results were found by C. Baumgartner et. Al (6). Reference range for TSH is 0.48 IU/L to 4.59 IU/L. (5). Our study showed significant correlation of TSH with CPK-MB (r=0.69, p=0.001) Troponin T (r=0.201, p= 0.04) and BNP (r= 0.64, p=0.001) in Group 1 while a non-significant correlation was found in Group 2, CPK-MB (r=0.06, p=0.67) Troponin T (r= 0.156, p= 0.57) and BNP (r= 0.07, p=0.62). This shows that slight elevations of TSH levels causes a significant rise in the cardiac markers in SCH as compared to euthyroid.

Though a large amount of data is available which gives an explanation on the association of the cardiac functions and subclinical hypothyroidism.[1,5,7,8] Another view point of our study can be, despite the non-significant difference in the levels of TSH in pairs of group 1 & group 2 and group 3 & 4, there exists a significant rise in the levels of the cardiac markers. These results may point towards a need for revised reference ranges for the cardiac markers with respect to age in cases of acute chest pain or MI in order to reduce the over diagnosis of MI patients based on cardiac markers.

CK is an enzyme that catalyzes the reversible transformation of creatine and ATP to creatine phosphate and ADP. The dimeric enzyme, consisting of two subunits, M and B, has three isoenzymes: CK-BB (CK1), CK-MB (CK2), and CK-MM (CK3). CK-MB can be found in the heart, skeletal muscle, small intestine, diaphragm, uterus, tongue, and prostate. About 20% of total CK in the myocardium is in the MB form, giving sensitivity and specificity in the diagnosis of AMI. Therefore, its increasing level during trauma and inflammation reduces its specificity. Another limitation of CK-MB is that it cannot detect minor myocardial damage, due to its high molecular weight. CK-MB reaches its highest point within 24 hours, starting to increase 4–9 hours after myocardial injury and decreasing to the normal range after 48–72 hours.[4]

One of the conditions in which CK-MB is false positive in diagnosis of AMI is hypothyroidism. It can cause false-positive results in CK-MB measurements. Therefore, this condition should be considered when using CK-MB as a biomarker in the diagnosis of AMI.[9]

The amount of TnC present in the cytosolic pool is similar to the amount of CK-MB,40 but there is also a significant amount of cTn in the contractile apparatus. Therefore, the amount of TnC per gram of myocardium is 13–15 times greater than the amount of CK-MB. This can thus explain the higher sensitivity of cTn compared with CK-MB in the early period and the elevated level of cTn in peripheral blood despite the normal level of CK-MB after myocardial tissue damage. Therefore, elevation of troponins should not always be interpreted in favor of coronary ischemia. Unlike the CK-MB level, the reason for the long-lasting elevation is the continuation of the release of cTn from the contractile apparatus in the late period.[10]

There are many proteins released into the circulation by the cardiac system, such as myoglobin, BNP, TnI (blocking actin–myosin interaction), and TnT (bound to tropomyosin). Cardiac troponin (cTn) acts on myocardial contraction by regulating the calcium-dependent interaction of actin and myosin. cTn has many isoforms specific to tissue.[4]

Cardiac troponin assays were developed for the purpose of diagnosing acute MI, and they have since become the preferred diagnostic biomarkers supported by the Universal Definition of MI.[11] Elevated cardiac troponin (representing true myocardial injury) is present in several cardiac and noncardiac conditions in the absence of acute MI. This scenario has been encountered many times. Heterophile antibodies are widely accepted to be risk factors for true false positive troponin results in the absolute absence of myocardial injury. In addition to interfering with troponin assays, heterophile antibodies can also interfere with thyroid function tests, hormones, and tumor markers.[12,13]

Limitations of the study: Our study is just a proposed conclusion on the findings obtained, more large-scale detailed studies may be required to prove the facts.

Conclusion

Our study is a significant reminder of the importance behind consideration of impact of high TSH levels in elderly SCH on cardiac markers.

Conflict of Interest Statement

Authors do not have conflict of interest.

Ethical Statement

The study was performed as per Ethical clearance from the institute. The clinical study norms have been adopted throughout the analysis from study.

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