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Original Article

Impact of Serum Free Triiodothyronine Level in Predicting the Degree of Myocardial Injury in Patients with Acute ST Segment Elevation Myocardial Infarction

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Abstract:

Background: *Free T3 (FT3), the biologically active thyroid hormone, has various effects on the cardiovascular system, including upregulating effective myocardial contractile function, decreasing systemic vascular resistance, as well as improving endothelial function and promoting angiogenesis. In severe illness of non-thyroidal origin, including acute ST elevation myocardial infarction (STEMI), thyroid hormone system may be rapidly down regulated. So, the decrease in FT3 level may lead to decreased cardiovascular protection in patients with AMI.*

Methods: *Total 110 patients with STEMI were approached for this study according to the inclusion and exclusion criteria. Patient were divided into two groups- low serum FT3 level (<3.5 pmol/L) in group A and normal serum FT3 level (>3.5 pmol/L) in group B. The level of cardiac injury as measured by troponin I and LVEF was measured in two groups and was compared.*

Results: *Among 110 patients in our study 40 (36%) were in the low FT3 group (Group A) and 70 (64%) were in normal FT3 group (Group B). Serum troponin-I values were significantly higher in Group A (13.9±11.0) than in group B (9.7±8.9) (p< 0.05). Wall motion abnormality was present in 39(97.5%) vs. 60(85.7%) patients (p< 0.05). LVEF was significantly lower in group A (41.08±6.55) than group B (44.47±6.99) (p< 0.05).*

Conclusion: *Low FT3 level in acute STEMI was associated with significantly lower left ventricular ejection (LVEF) and higher levels of cardiac biomarker, troponin I. Serum FT3 may be a good predictor for myocardial injury in STEMI.*

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Introduction:

Coronary artery disease is the major cause of mortality globally and this health problem is reaching pandemic proportion in developed as well as in developing countries.[1] In 2008, 17.3 million people died from cardiovascular diseases, among them 7.3 million of deaths were due to ischaemic heart disease.[2] Acute myocardial infarction is usually the result of coronary atherosclerosis.[3] At present, STEMI comprises approximately 25% to 40% of MI presentations. In-hospital (approximately 5% to 6%) and 1 year (approximately 7% to 18%) mortality rate from STEMI also have decreased significantly in association with a substantial increase in the frequency of care that includes guideline-directed medical therapy (GDMT) and interventions.[4] In south-east Asian countries , the prevalence of coronary artery disease is increasing rapidly due to increasing prevalence of atherosclerosis, which

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is the major cause of CAD.[5] It is highly prevalent in Bangladesh but data related to different aspects of coronary artery disease are inadequate altered.[6-7] The prevalence rate of coronary artery disease in Bangladesh is 1.85% to 3.4% in rural population and 19.6% in urban population.[8-10]

In severe illness of non-thyroidal origin, including acute STEMI, thyroid hormone system may be rapidly altered.[11] The most common alteration of thyroid function, known as low triiodothyronine syndrome (LT3 syndrome), is characterized by low levels of FT3 , normal levels of thyroid stimulating hormones (TSH) and thyroxine (T4).[12] In the form of free T3 (FT3) as biologically active thyroid hormone, has various effects on the cardiovascular system, including upregulating effective myocardial contractile function, decreasing systemic vascular resistance , as well as improving endothelial function and promoting angiogenesis. So, the decrease in FT3 level may lead to decreased cardiovascular protection in patients with AMI.[13-16]

A slight change in thyroid status can affect ventricular function, serum cholesterol levels, heart rate and rhythm and increases the risk of coronary artery disease and cardiovascular mortality.[17] Low T3 syndrome can lead to decreased maximal rate of contraction and relaxation of the heart.[18] Myocyte apoptosis is a critical consequence after acute MI. Thyroid hormones limit cardiac myocyte apoptosis after stressful conditions. MI being an inflammatory condition, there is a reduction of thyroid hormone levels and this reduction can worsen the pathological cardiac remodelling, further worsening cardiac status.[19]

Triiodothyronine functions through interactions with isoform type α receptors , α_1 or α_2 and type β receptors, β_1, β_2 or β_3 to influence the contractility and diastolic relaxation.[20-22]

Inflammation, hypoxia and oxidative stress have been found to be involved in the down regulation of T3 levels by modulating the activity of deiodinase and these conditions are often found in acute heart disease altered.[23-24] Low FT3 level reduces cardiac output, blood volume, chronotropism, ionotropism and increases systemic vascular resistance, diastolic blood pressure, vascular wall thickness and stiffness, and afterload. Changes in arterial wall elasticity are involved in the progression of atherosclerotic processes.[25] Low FT3 is also associated with higher right atrial, pulmonary artery and pulmonary capillary wedge pressure and with lower ejection fraction and cardiac index.[26]

Studies showed a high incidence of low FT3 level (27.5%) among patients with STEMI. This study has also revealed that low FT3 group had more serious myocardial injury, as assessed by peak cardiac TnI levels and more severe cardiac dysfunction, as assessed by LVEF.[27,28]

The present study evaluated whether serum FT3 level could predict the degree of myocardial injury in patients with acute STEMI. The purpose of our study is to investigate whether the lower FT3 level in STEMI is associated with severer myocardial injury, which is evaluated by cardiac troponin I (cTnI) and echocardiography as LVEF.

Methods:

This prospective observational study was carried out in the Department of Cardiology, Dhaka Medical College Hospital, Sir Salimullah Medical College and Mitford Hospital and NICVD, Dhaka from July, 2020 to September, 2021. All the patients of newly diagnosed acute STEMI after exclusion and inclusion criteria were taken as sampling population. Patients with raised FT3, taking corticosteroids, amiodarone, lithium, patients with chronic liver disease, renal disease, malignancy and lung disease (COPD, ILD), H/O PCI or CABG, patients with congenital heart disease, primary myocardial disease (HCM), patients with prior myocardial infarction and chronic inflammatory disease- RA, SLE were excluded from the study. Serum FT3, FT4 and TSH were done for all patients within 24 hours of admission by SIEMENS ADVIA Centaur XPT Chemiluminescence Immunoassay System and radioimmunoassay at the laboratory for Nuclear Medicine and Ultrasound , Bangladesh Atomic Energy Commission, Dhaka Medical college Campus and Mitford Hospital, Dhaka . Echocardiography was done by the machine PHILIPS CLEARVUE 550" for each patient within 24 hours of admission and when needed.

Patients were followed up in CCU for 48-72 hours as per standard protocol.

Patients were divided into two groups- low serum FT3 level (<3.5 pmol/L) in group A and normal serum FT3 level (>3.5 pmol/L) in group B.[29] Then the degree of myocardial injury as assessed by serum cTn I & LVEF and was compared between two groups. Occurrence of in-hospital death and complications like acute LVF, cardiogenic shock, ventricular tachycardia, ventricular fibrillation or AV block (2nd and 3rd degree) were also recorded till discharge or death of the patients. In-hospital adverse outcomes were compared between two groups. All statistical analysis was performed using the statistical package for social science (SPSS) program, version 26 for Windows. Statistical significance was set as 95% confidence interval at 5% acceptable error level. Differences was considered significant at the p< 0.05 level for all these tests.

Results:

This prospective observational study was performed in the Department of Cardiology, Dhaka Medical College Hospital, Sir Salimullah Medical College and Mitford Hospital and NICVD, Dhaka from July 2020 to September 2021. The main objective was to assess whether admission serum FT3 value improves prediction of degree of myocardial injury in acute STEMI patients.

Bar diagram (Fig 1) shows, majority of the patients 40 (36.4%) belonged to 50-59 years age group and 31 (28.2%), 19 (17.3%), 11 (10.0%) patients belonged to 60-69, ≥17.3, 40-49 years age group respectively. The least number of patients (8.2%) belonged to <40 years age group. Mean age was 57.25±12.16 years. Among the patients, 75 (68.2%) were male and 35 (31.8%) were female. Male and female ratio was 2.14: 1 (Fig 2). Out of CAD risk factors, hypertension 21(52.5%) vs. 22(31.4%) and Diabetes mellitus 18 (45.0%) vs. 17(24.3%) were significantly different between two groups (p value <0.05), but smoking, dyslipidemia was not significantly different between two groups (Table-I). Among the presentation characters, DBP, total cholesterol and TG were significantly different between two groups (p value < 0.05) but SBP, HR, S. Creatinine, S. Electrolytes, RBS, SGPT, LDL-C and HDL-C were statistically insignificant between groups (p value > 0.05) (Table-II).

Majority of the patients presented with anterior wall MI 60(54.5%) (Anterior, anteroseptal, extensive anterior) followed by inferior wall MI 50(45.5%). There were no significant differences between the two groups of patients regarding ECG pattern (p-value >0.05) (Table-III). Serum FT3 was significantly lower in Group A (2.82±0.399) than Group B (4.95±1.488). The differences were statistically significant between two groups (P-value <0.001) (Table- IV). Assessment of echocardiographic parameters shows that RWMA was present in 39(97.5%) vs. 60 (85.7%) patients with p value 0.047. LVEF was significantly lower in group A (41.08±6.55) than group B (44.47±6.99) with a p value of 0.014 (Table-V). S. Troponin I were significantly higher in group A (13.9±11.0) than Group B (9.7±8.9) with statistical significance (p value- 0.027) (Table-VI). In-hospital complications like acute LVF, cardiogenic shock and in-hospital mortality were significantly higher in Group A than Group B, but ventricular tachycardia, ventricular fibrillation and AV block were not significant statistically.

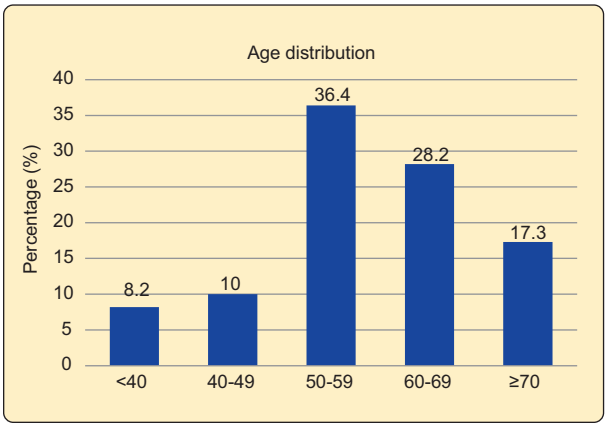

Fig.-1: *Age distribution of patients (N=110).*

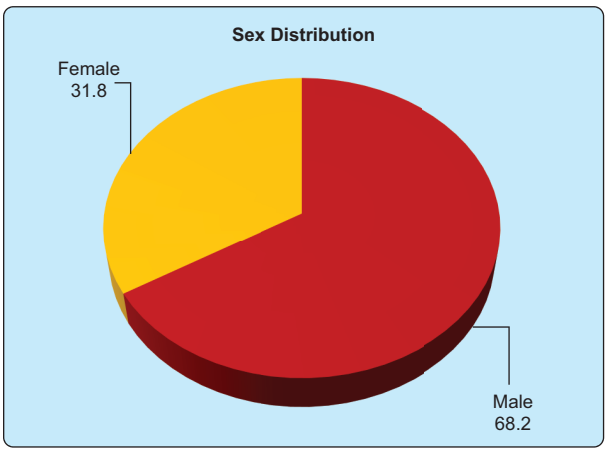

Fig.-2: *Pie chart showing the distribution of patients by sex (N=110).*

Table-I

Comparison of risk factors between two groups (N=110).

Risk factors	Group A (n=40) No. (%)	Group B (n=70) No. (%)	Total (N=110) No. (%)	p-value
Hypertension	21(52.5%)	22(31.4%)	43(39.1%)	0.029[s]
Diabetes mellitus	18(45.0%)	17(24.3%)	35(31.8%)	0.025[s]
Smoking	13(32.5.5%)	21(30.0%)	34(30.9%)	0.352[ns]
Dyslipidemia	12(30.0%)	19(27.2%)	31(28.2%)	0.542[ns]
Family history of CAD	15(37.5%)	29(41.4%)	44(40.0%)	0.686[ns]

Table-II

Distribution of presentation characteristics among all patients (N=110)

Risk factors	Group A (n=40) Mean±SD	Group B (n=70) Mean±SD	Total (N=110) Mean±SD	p-value
SBP	103.30±31.67	132.11±139.45	121.64±113.41	0.201[ns]
DBP	65.90±16.34	74.36±14.44	71.28±15.63	0.006[s]
Heart rate	94.68±27.86	84.64±26.95	88.29±27.59	0.066 [ns]
S. Creatinine	1.65±1.19	1.59±1.62	1.61±1.48	0.834 [ns]
S. Electrolyte- K^+	4.05±0.75	5.81±9.22	5.18±7.43	0.237 [ns]
S. Electrolyte- Na^+	136.72±4.71	135.93±4.75	136.21±4.73	0.406 [ns]
RBS	13.65±13.66	12.57±5.31	12.96±9.21	0.557 [ns]
SGPT	42.76±25.27	45.53±41.07	44.52±36.03	0.700[s]
Total Cholesterol	240.18±48.31	214.09±41.85	223.57±45.85	0.004[s]
LDL-C	141.04±25.57	135.59±33.97	137.57±31.17	0.380[ns]
TG	205.48±55.95	184.20±50.28	191.94±53.16	0.043[s]
HDL-C	35.66±7.71	41.04±27.29	39.08±22.35	0.226 [ns]

Table-III

Comparison of ECG pattern between two groups (N=110).

ECG (ST-Elevation)	Group A (n=40) No. (%)	Group B (n=70) No. (%)	Total (N=110) No. (%)	p-value
Antero-septal	7(17.5%)	8(11.4%)	15(13.6%)	0.224**[*ns]**
Anterior	17(42.5%)	22(31.4%)	39(33.5%)	
Extensive Anterior	3(7.5%)	3(4.3%)	6(5.5%)	
Inferior	13(32.5%)	37(52.9%)	50(45.5%)	
Total	40(100%)	70(100%)	110(100%)	

Table-IV

Comparison of serum FT3 level between two groups (N=110)

	Group A (n=40) Mean±SD	Group B (n=70) Mean±SD	Total (N=110) Mean±SD	p-value
FT3(p mol/L)	2.82±0.399	4.95±1.488	4.18±1.586	<0.001[s]

Table-V

Comparison of Echocardiographic parameters between two groups (N=110).

	Group A (n=40) Mean±SD	Group B (n=70) Mean±SD	Total (N=110) Mean±SD	p-value
RWMA	39(97.5%)	60(85.7%)	99(90.0%)	0.047[s]
LVEF	41.08±6.55	44.47±6.99	43.24±7.00	0.014[s]

Table-VI

Comparison of degree of myocardial injury between two groups (N=110).

	Group A (n=40) Mean±SD	Group B (n=70) Mean±SD	Total (N=110) Mean±SD	p-value
S. Troponin	13.9±11.0	9.7±8.9	11.2±9.9	0.027[s]
Ejection fraction	41.08±6.55	44.47±6.99	43.24±7.00	0.014[s]

Discussion

This prospective observational study was carried out in the Department of Cardiology, Dhaka Medical College Hospital, Sir Salimullah Medical College and Mitford Hospital and NICVD, Dhaka, from July, 2020 to September, 2021. The main objective was to assess whether admission serum FT3 value improves prediction of in-hospital adverse outcomes in acute STEMI patients.

For this purpose total 110 patients admitted with acute ST-segment elevation myocardial infarction fulfilling inclusion & exclusion criteria were included in this study. The study population were categorized into two groups: low serum FT3 level (<3.5 pmol/L) in group A and normal serum FT3 level (>3.5 pmol/L) in group B. Among 110 patients in our study 40(36%) were in the low FT3 group and 70 (64%) were in normal FT3 group. Other studies conducted in STEMI, distribution of high and low FT3 was similar.[27,29,30] In our study mean FT3 level was 2.82±0.399 (Group A) vs 4.95±1.488 (Group B). A study by Zhang et al. showed similar results.[29]

In our study, among the 110 patients with acute STEMI, mean age of the total patients was 57.25±12.16 years. Majority of the patients belonged to 50-59 years age group. This age distribution is consistent with other studies conducted with STEMI Bangabandhu Sheikh Mujib Medical University and Department of Cardiology, Dhaka Medical College Hospital, showed similar results.[31,32]

Among the important risk factor of coronary artery disease in our study, hypertension and diabetes mellitus were significantly different between two groups, but dyslipidemia, smoking and family history of coronary artery disease observed between two groups were not significant statistically.

Among the presentation characters, DBP, total cholesterol and TG were significantly different between two groups but SBP, HR, S. Creatinine, S. Electrolytes, RBS, SGPT, LDL-C and HDL-C were statistically insignificant between groups. Yuanbin Song, et al.[27] and Zhang et al.[29] also showed in their study that patients with lower baseline serum FT3 levels had lower blood pressure and higher heart rate. In our study, majority of the patient presented with anterior wall (anterior, antero-septal & extensive anterior) myocardial infarction (54.5%) followed by inferior wall infarction (45.5%) which were insignificantly distributed between two groups. This distribution of wall involvement in STEMI was similar to other studies conducted in Bangladesh.[31]

Assessment of echocardiographic parameters shows that RWMA was present in 39(97.5%) Vs 60(85.7%) patients (p value 0.047). LVEF was significantly lower in group A (41.08±6.55) than group B (44.47±6.99). A study done by Kamal, et

al. [28] represented that 70% of the study population had EF <55% with mean EF of 49.5%. Ceremuzynski L et al[33] also suggested that FT3 was correlated with cardiac injury assessed by echocardiography. Yuanbin Song et al.,(2018)[27] found significantly lower LVEF in low FT3 group than in in the normal FT3 group of Chinese patients with STEMI. But no significant differences were present in the LVEF between two groups of STEMI patients by studies of Zhang, et al.[29] and Wen su, et al.[30]

In our study, we used cardiac biomarkers (troponin I) as a marker for severity of myocardial injury and that was concordant with Setiadi et al.[34] and Kavsak et al.[35] Serum troponin-I values were significantly higher in Group A than in group B. This is similar to the studies conducted by Zhang et al.[29] and WANG Wen-yao et al.[36]

Acute LVF, cardiogenic shock and in-hospital mortality were significantly more in Group A than Group B; ventricular fibrillation, AV block were not statistically significant. These findings are congruent with the study done by Kamal, et al. [28], Yuanbin Song et al.[27] and Zhang, et al.[29] Thyroid hormones exert direct effects on hemodynamics, including increasing cardiac contractility, decreasing vascular resistance and so on. A low FT3 state after acute myocardial infarction worsens hemodynamics and promotes adverse cardiac events. A low FT3 state after acute myocardial infarction changes the transcription of many cardiac structural and functional genes, leading to decreased contractility of myocardium, inhibited Ca2+ transport , a worsened diastolic function, calcium overload, myocardial stunning and reperfusion injury.[29]

The mechanism which may account for the association between serum FT3 level and myocardial injury in acute STEMI was unknown. However, it is accepted that decreased conversion from T4 to T3 in peripheral tissues due to inflammatory factors, hypoxia and so on result in low FT3 levels. Inflammatory cytokines might also contribute to the incidence of low FT3 levels after acute MI. IL6 reduces type 1 iodothyronine deiodinase (D1) and D2 activity by inducing oxidative stress in peripheral tissues.[37] Increased hypoxia induced factor 1 activates D3 in the heart and other tissues, which might contribute to lowering the FT3 levels.[38] The decrease in FT3 was considered to be adaptive response to acute disease by decreasing catabolism and conserving energy expenditure.[39] As the principal bioactive hormone, triiodothyronine (T3) exerts many effects on myocardial contractility, the resistance of arterioles in the peripheral circulation and cardiovascular hemodynamics through the modulation of the transcription of target genes in the cardiovascular system such as myosin heavy chain, phospholamban, sarcoplasmic reticulum Ca2+-ATPase, Na+/ Ca2+ exchanger and so on.[21] Thyroid hormone changes are always combined with changes in markers of cardiovascular hemodynamic phospholamban, instability, such as low fT3 levels, that are often observed in patients with cardiovascular diseases such as coronary artery disease (CAD) and heart failure. Inflammation, hypoxia and hemodynamic instability are considered to be the most important mechanisms underlying a low fT3 state.[14] Thus, the results from these above cited studies are consistent with those of our study where low FT3 patients own worse vascular condition than those with normal FT3 level, and might have more severe coronary disease and worse prognosis.

Conclusion:

This study demonstrated that low serum free triiodothyronine level was an independent predictor of myocardial injury in STEMI patients. Low FT3 level in acute MI was associated with low LVEF, higher levels of troponin, longer hospital stay and poor in-hospital outcomes. Therefore, inclusion of serum FT3 value into routine investigations could predict the degree of myocardial injury and in-hospital adverse outcome more accurately. However, further larger study with appropriate design will be able to shed more light in this matter.

Conflict of Interest - None.

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