Research article

Evaluation of the diagnostic value and differentiation efficacy of high sensitivity cardiac troponin T2 (hscTnT2) for STEMI and NSTEMI Iraqi patients

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ABSTRACT

Introduction and Aim: Two major clinical forms of acute coronary syndrome (ACS) were categorized; acute myocardial infarction (MI) showing ST-segment elevation (STEMI) with ECG, the other non-ST-segment elevation (NSTEMI). This study was designed using a new generation of high sensitivity cardiac troponin T2 (hscTnT2) in patients with acute coronary syndrome to evaluate the diagnostic value and its efficacy in differentiation of STEMI from NSTEMI.

Materials and Methods: one hundred twenty (120) patients diagnosed to have ACS were included in the study. Apparently, sixty-four (64) healthy subjects were considered as control. ECG and body mass index (BMI) were performed. Blood analysis of levels of glucose, lipid profile and glutamic-oxaloacetic transaminase (GOT) were measured as well as estimated the human hscTnT2 concentrations by enzyme linked immunosorbent assay (ELISA).

Results: ACS patients (STEMI & NSTEMI) showed significant high levels (hscTnT2), Cholesterol, TG, HDL, GOT, FBS and VLDL compared to control. Furthermore, (hscTnT2) serum level in STEMI 225.95 ±120.66 ng/L is significantly higher (P value <0.001) than NSEMI 102.32 ± 58.542 ng/L. the discrimination efficacy of hscTnT2 to differentiating STEMI from NSTEMI is high with cut off value 90.3 ng/L with high sensitivity.

Conclusion: The use of new generations of high sensitivity troponin T aided to reduce the time for accurate diagnosis of acute MI to less than 2 hours. The hscTnT serum value was higher in STEMI than NSTEMI patients and shown to be positively correlated with the degree of cardiac damage in ACS patients. The level of hscTnT can be considered as good discriminating diagnostic biomarkers to differentiate STEMI from NSTEMI patients.

Keywords: High sensitivity troponin T2; Acute coronary syndrome; Ischemia; STEMI; NSTEMI.

INTRODUCTION

Ischemic heart disease (IHD) is a pathological condition caused by an inadequate myocardial oxygen supply due to obstruction and narrowing of the coronary arteries and represents the commonest cause of death worldwide (1). Clinically, the major acute clinical manifestation of coronary heart disease is termed Acute Coronary Syndrome (ACS), which includes acute myocardial infarction (MI) with ECG showing ST-segment elevation (STEMI), the other no ST-segment elevation (NSTEMI) and unstable angina (UA) (2). The clinical management of these different subtypes of ACS is variable, for that finding of novel cardiac biomarkers is of great importance. Troponins for a long time were used for diagnosis of ischemic heart disease. Measurements of blood level of cardiac-specific troponin has a vital role in diagnosis of cardiac injury (3). Historically, serum troponin was adopted as a sensitive and reliable biomarker for detection of myocardial injury in the late 1990s (3). The pattern of troponin elevation as documented by many studies is that, troponin rises in serum 4-10 hours after onset of acute myocardial infarction and peaks serum level at 12-48 hours and is still elevated for 4-10 days (4). Cardiac specific troponins (I and T) have been regarded as favorable biomarkers for diagnosis of myocardial infarction since 2000 (5). A new generation of cardiac troponins emerged in 2011, and are referred to as high sensitivity troponins that can detect cardiac injury more efficiently and immediately than conventional cardiac troponin even with a very low serum value detection. These biomarkers were FDA approved in 2017 for high sensitivity cardiac troponin T (hscTnT) and in 2019 for (hs-cTnI) (6).

Measurement of cardiac specific troponins (TnI and TnT) is of invaluable role in early diagnosis of cardiac ischemia. These troponins (TnI and TnT) are highly and specifically expressed in cardiac muscle cells and released to serum in high level in response to myocardial damage associated with (IHD) (7), and improve the diagnostic accuracy of acute chest pain presentation of MI compared with classical cardiac biomarkers (8). According to the American College of Cardiology (ACC), and the American Heart Association (AHA) elevated levels of cardiac specific troponins (TnI and TnT) in chest pain presentation can discriminate STEMI and NSTEMI from stable and unstable angina (9). Discrimination between STEMI and NSTEMI using cardiac biomarkers is complex and difficult to identify. Depending on ECG, ST-elevation MI diagnosis is rapid and simple which could help starting reperfusion therapy. On the other hand, diagnosis of non-ST-elevation MI takes time

and is problematic by ECG as it cannot rule out other causes of chest pain. A study conducted by Di Stefano (10) showed a significantly higher level of troponin I (TnI) in STEMI compared to NSTEMI. Another study conducted in Iraq showed the same pattern (elevated troponin I (TnI)) (11). Regarding cardiac specific troponin T(TnT), studies showed controversy. Haider (12) demonstrated that there were no significant differences in serum level of (TnT) in STEMI compared to NSTEMI. However, Mueller (13) showed a significantly higher level of (TnT) in patients with STEMI compared to NSTEMI. This study was designed using a new generation of high sensitivity cardiac troponin T (T2 isotype) in Iraqi patients with acute coronary syndrome to evaluate the diagnostic value of this biomarker in differentiation of STEMI from NSTEMI.

MATERIALS AND METHODS

The patients included in the study were from a coronary care unit (CCU) inpatient admitted and diagnosed as ACS by specialist cardiologists at Al-Yarmouk Teaching Hospital for the period between November 2017 and April 2018. The total number of patients was 120 (43 female and 77 male), the patients' age range were (30-72) years. The diagnostic criteria to confirm presence of ACS was based on the existence of two out of three of the following findings: the presentation of the patient, ECG changes and presence of troponin positive test. Based on the same adopted criteria, ACS patients were classified into (NSTEMI) and (STEMI) via presence or absence of ST- segment elevation. The subjects' controls of this study were collected from staff and patients' relatives of Al-Yarmouk Teaching Hospital; those who were apparently healthy with no history of previous illnesses underwent a thorough physical examination with age and sex matching. Body mass index (BMI) were accounted for and calculated with the following formula: BMI= Weight in kilograms over an individual's height in square meters.

Blood analysis

The fasting blood samples from both patients and controls were collected, immediately, serum was separated, and aliquots of serum were used for the measurement of parameters of the study. By using either enzymatic spectrophotometric methods for (glucose, lipid profile and GOT), or by enzyme linked immunosorbent assay (ELISA) using ELISA kits from my BioSource, USA, human hscTnT2 concentrations which were assayed according to manufacturer's instructions.

Statistical analysis

Data were analyzed using the statistical package of SPSS-24. After assuring that the data was normally distributed, the data presentation was as simple measures, like mean, standard deviation of the mean, frequency, and percentage. ANOVA method was used to test the presence of difference in means among groups, while unpaired Student's-t-test was used for difference between two means. Correlation study of hscTnT2 with the other parameters was performed using Pearson's correlation. The P value of < 0.05 was considered statistically significant. ROC curve analysis and measurement of the area under the curve (AUC) was analyzed for the hscTnT2 results for all the study population according to the method of Hanley and McNeil, but only the results of (NSTEMI) and (STEMI) were presented to evaluate the use of hscTnT2 as a differentiation marker between these two groups. The optimum cutoff was used for calculating the diagnostic sensitivity and the specificity.

RESULTS

Comparison of study biomarkers between patients (STEMI vs NSTEMI) with controls

On comparison of ACS patients (STEMI vs NSTEMI) with controls are shown hscTnT2 had a highly significant increase. In addition, the cholesterol, TG, GOT, FBS and VLDL showed a highly significant increase in patients with ACS compared to controls (P value <0.001). The results of HDL were significantly lower in patients (STEMI & NSTEMI) compared with controls (P value <0.01). These results were presented in (Table 1).

Correlation analysis of biomarkers of STEMI (ACS) patients

In Table 2, hscTnT2 showed significant positive correlations with BMI (r= 0.416*, P value= 0.013) and GOT (r= 0.503**, P value = 0.000) in STEMI (ACS) patients. A significant negative correlation was observed between hscTnT2 and HDL (r= -0.467*, P value = 0.049).

Correlation analysis of biomarkers of NSTEMI patients

As shown in Table 3, hscTnT2 showed significant positive correlations with both GOT (r=0.628**, P value = 0.0001) and BMI (r= 0.321*, P value = 0.043) in NSTEMI (ACS) patients.

Table 1: Clinical measures and baseline laboratory tests of ACS patients and controls

Parameters	STEMI n=60 MEAN ±SD	NSTEMI n=60 MEAN ± SD	CONTROLS n=64 MEAN ± SD	P value STEMI vs. NSTEMI	P value ANOVA
Age	56.6 ± 11.43	58.38±9.55	56.05±12.31	0.056	0.067
BMI	33.44±3.82	27.71±3.22	28.45±3.77	**0.043**	0.052
Gender Male/Female	40 / 21 65.57 / 34.42 %	36 / 25 59.01 / 40.98 %	41 / 24 67.21 / 39.50	-	-
hscTnT2	225.95 ±120.66	102.32 ± 58.542	44.3273 ± 17.954	**0.000**	**0.001**
FBS	180.94 ± 92.190	201.13 ± 89.292	92.7441 ± 18.801	0.222	**0.002**
TG	206.21 ± 59.659	195.61 ± 72.592	126.534± 42.40	0.380	**0.001**
Cholesterol	186.98 ± 55.954	158.38 ±36.984	179.38± 37.217	**0.001**	**0.001**
HDL	25.64 ± 6.307	32.66 ±13.921	34.90± 12.65	**0.000**	**0.001**
LDL	101.68 ± 51.613	86.60 ±36.299	80.30± 34.98	0.064	**0.001**
VLDL	40.43 ± 13.386	39.12 ±14.518	25.309± 8.481	0.607	**0.001**
GOT	141.80 ±122.41	25.64 ±23.674	14.425 ± 4.48	**0.00**	**0.001**

BMI; Body Mass Index, FBS; fasting blood sugar, TG; triglycerides, HDL; High density lipoprotein, LDL; Low density lipoprotein, VLDL; very low-density lipoprotein, GOT; glutamic-oxaloacetic transaminase.

Table 2: Correlation analysis results between study parameters and hscTnT2 among STEMI patients

		FBS	TG	CHOL	HDL	LDL	VLDL	GOT	BMI	Age
hscTnT2	r	0.116	-0.074	-0.042	**-0.467**	0.016	0.005	**0.503****	**0.416***	0.132
	p	0.413	0.571	0.749	**0.049**	0.902	0.968	**0.000**	**0.013**	0.075

*. Correlation is significant at the 0.05 level (2-tailed).
**. Correlation is significant at the 0.01 level (2-tailed).

Table 3: Correlation analysis results between study parameters and hscTnT2 among NSTEMI patients

		FBS	TG	CHOL	HDL	LDL	VLDL	GOT	BMI	Age
hscTnT2	r	-0.009	0.245	0.103	-0.146	-0.011	0.245	**0.628****	**0.321**	0.117
	P	0.943	0.057	0.430	0.066	0.934	0.057	**0.000**	**0.043**	0.912

**. Correlation is significant at the 0.01 level (2-tailed).
*. Correlation is significant at the 0.05 level (2-tailed).

ROC analysis

Fig.1 represents a graph representative of ROC–analysis and in Table 4; the results of Area Under Curve (AUC) were presented for the best discriminative cut-off values of hscTnT2 that best predicted STEMI versus NSTEMI subgroups of ACS patients. The results of hscTnT2 showed that the AUC was 0.87333 with cut of value 90.3 ng/L and 93.75% was the sensitivity of the test while the specificity was 74%.

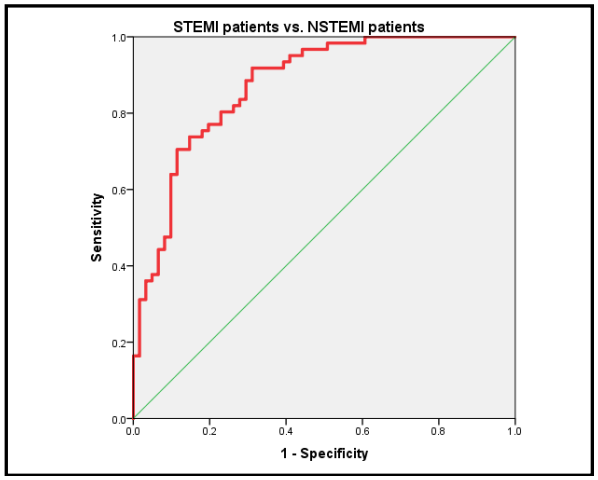

Fig. 1: Graph representative of Receiver Operator Characteristic (ROC) Curves analysis of hscTnT2 for STEMI and NSTEMI subgroups of patients with ACS.

Table 4: Analysis of Area Under Curve (AUC) for diagnosis efficacy and Prediction capability of STEMI and NSTEMI subgroups of ACS patients

	AUC	Cut of value	Sensitivity	Specificity
hscTnT2	0.87333	90.3	93.75	74

DISCUSSION

To our best knowledge, this is the first study conducted in Iraq using high sensitivity cardiac troponin T2 (hscTnT2) in patients with acute coronary syndrome. The main findings of this study were that hscTnT2 is elevated significantly in patients with ACS compared to control. Furthermore, STEMI patients' serum value of this biomarker was significantly higher than NSEMI candidates. In addition, the diagnostic ability of hscTnT2 was very high in discrimination STEMI from NSEMI cases.

The diagnosis of acute MI has changed dramatically using high-sensitivity cardiac troponins. Previously, relying on conventional troponins it was accepted waiting 6 to 9 hours from presentation until detectable serum value could be measured. By using high-sensitivity cardiac troponins the critical time zone is reduced to less than 2 hours with a great degree of sensitivity and specificity to confirm or to rule-out acute MI (14). In this study, a new generation of high

sensitivity cardiac troponin T (T2 isotype) (hscTnT2) was used and the results showed a high significant increase in mean (P value <0.001) for STEMI and NSEMI compared to control. These results come in accordance with other study results confirming the efficacy of hscTnT in diagnosis of acute coronary syndrome (15, 16).

Regardless of the cardiac injury severity, elevated serum level of cardiac specific troponin usually is associated with poor prognosis (17). Different mechanisms have been postulated for elevated serum troponins after myocardial injury. Hammarsten (18) summarized the possible mechanisms as, myocardial necrosis, programmed cell death, myocardial cell membrane wounds and decreased clearance. In all these assumed mechanisms, the troponin amount released depends on severity of cardiac muscle damage. The size of the infarcted area could be one of the differentiation criteria between STEMI and NSTEMI and the use of cardiac specific troponin T was useful to estimate infarction area and severity (19). In concordance with these results, the release of (hscTnT2) in STEMI is significantly higher (P value <0.001) than NSEMI. Moreover, the level of GOT release in STEMI is significantly higher than NSEMI. Furthermore, a significant association has been observed between the level of GOT enzyme and elevated hscTnT in both STEMI and NSTEMI.

Previous study conducted by Bergovec (20) also showed that GOT release in STEMI is higher than that observed in NSTEMI. An acceptable explanation is that the released amount of serum GOT is proportional to the extent of muscle damage in STEMI compared to moderate raise of GOT enzyme in NSEMI when only micro-infarcts occur.

Both male and female subjects are subjected to coronary heart disease, but significant gender differences were recorded. Men were more prone to have STEMI than women and this is attributed to the fact that women are less affected by atherosclerosis than men due to sex hormones (21). Consistent with the literature, this research found that STEMI male patients had about double the number of women and M/F ratio was 40/21 while in the NSTEMI group the ratio was 36/25.

Obesity represents a modifiable risk factor of coronary heart disease and shown to be linked to myocardial injury that is characterized by elevated hscTnT (22). In this study, STEMI patients had significantly higher BMI than NSTEMI. However, correlation analysis revealed that BMI was significantly associated with elevated hscTnT in both STEMI and NSTEMI. This observation can be attributed to obesity rather than increased risk of severe coronary heart disease but it is also an independent risk factor for increased cardiac troponin (23).

Dyslipidemia represents a strong predictor of severity of acute coronary syndrome. A study conducted by González-Pacheco (24) stated that untreated lipid profile abnormality is one of the strongest prognosticators of early death in STEMI patients and progressiveness to more severe myocardial damage in NSTEMI patients. In addition, degree of dyslipidemia was reported to be higher in STEMI compared to NSTEMI patients (25). In line with these findings, different lipid profile abnormalities were found in the current study. No significant differences had been observed regarding triglycerides levels between STEMI and NSTEMI patients. Total cholesterol and LDL level were higher in STEMI compared to NSTEMI patients. In addition, a significantly lower value of HDL was observed in STEMI compared to NSTEMI patients. Moreover, a strong negative association was found between the levels of HDL cholesterol with elevated hscTnT.

To evaluate the diagnostic value of hscTnT in discrimination between STEMI and NSTEMI individuals, (ROC) curve analysis was performed. Both conditions were analyzed using serum hscTnT2 levels. The hscTnT had AUC of 0.873**,** a sensitivity of 93.75 %, specificity 74%, and a diagnostic CUT OF VALUE 90.3 ng/L. These results represent a valuable and promising measures of a single serum parameter could be used to differentiating STEMI from NSTEMI or in other words, every patient with acute coronary syndrome with a value of hscTnT > 90.3 ng/L even without ECG changes are most likely to have severe myocardial injury.

CONCLUSION

Troponins used as biomarkers for diagnosis of ischemic heart disease. The hscTnT serum value was higher in STEMI than NSTEMI patients. The hscTnT is shown to be positively correlated with obesity and degree of cardiac damage in both STEMI and NSTEMI patients. The hscTnT can be considered as good discriminating diagnostic biomarkers to differentiate STEMI from NSTEMI patients.

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CONFLICTS OF INTEREST

We have no potential conflicts of interest relevant to this article.

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