ORIGINAL ARTICLE

COMPARISON BETWEEN RAPID KIT BASED CONVENTIONAL TROPONIN-T AND HIGH SENSITIVE TROPONIN-I CHEMILUMINESCENCE IMMUNOASSAY TECHNIQUE IN PATIENTS PRESENTING WITH TYPICAL CHEST PAIN

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Objectives: Cardiac troponins are keystone in diagnosing and risk stratification of patients with suspected non-ST elevation myocardial infarction (NSTEMI). We aimed to analyze and compare hs-TropI and c-TropT in patients presenting with typical chest pain to emergency department (ER) in our institute.

Methodology: Consecutive patients between ages of 20 to 80 years of both genders presenting with typical chest pain for more than 30 minutes were included in the study. Patients with ST elevation on ECG, acute left ventricular failure (LVF), sepsis and chronic kidney disease were excluded from the study.

Results: Hundred patients were analyzed presenting with typical chest pain. Mean age of participants was 50+10.75 years. 72 (72%) patients presented with early (<4hrs) chest pain and 28 (28 %) with late ≥4hrs) chest pain. On ECG 57 (57%) patients showed T-wave inversion, 33 (33%) had ST depression and 1 (1%) had left bundle branch block (LBBB). Sensitivity and negative predictive value for hs-TropI was found to be 87% and 94% respectively, while for c-TropT these were 72% and 96%, respectively.

Conclusion: This study demonstrated that positive predictive value of c-TropT (conventional troponin T) in diagnosing NSTEMI is low as compared to hs-Trop I (high sensitive troponin I). Thus, it is recommended that lab-based hs-TropI should be preferred over kit-based c-TropT for screening or diagnostic purposes, even though the latter is cost effective and takes less time.

Keywords: Cardiac troponins, non-ST segment elevated myocardial infarction, typical chest pain, left bundle branch block, ST depression

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INTRODUCTION

Chest pain is one of the most common initial symptoms in many serious conditions including non-ST segment elevated myocardial infarction (NSTEMI), aortic dissection and pulmonary embolism. It may, however, develop due to a variety of other non-cardiovascular and potentially less serious causes such as pneumonia, pleurisy and psychogenic causes.[1] Majority of these patients will not have main adverse cardiac events like myocardial infarction (MI), necessity of prompt revascularization or sudden cardiac death within the subsequent 30 days.[2] It is important to exclude NSTEMI patients in this setting to prevent catastrophic and lethal outcomes to segregate out the patients into those categories which need a prompt therapeutic intervention.

NSTEMI is characterized by a sudden reduced blood flow to heart muscles leading to myocardial ischemia and necrosis. Symptoms of the patients evocative of NSTEMI represent more than 10% of reporting to emergency service for consultations,[3] even though only 10–20% of them eventually are found to be suffering from NSTEMI.

The clinical guidelines have recommended diagnostic workup of patients presenting with low or intermediate risk features suggestive of NSTEMI. Those with typical chest pain but non-specific findings on Electrocardiography (ECG) are more heterogeneous. However, these patients make up the biggest percentage reporting to emergency facilities for assessment of suspected NSTEMI. Initial evaluation is often misleading, so efficient and accurate identification of these patients at the early stage is a challenge. ECG and cardiac troponins estimation are the necessary initial investigations to diagnose the patient in initial clinical evaluation. ECG alone, as single diagnostic modality, is often inadequate to diagnose a case of NSTEMI or acute MI. ST-segment eccentricity can be noticed in some other clinical conditions like left ventricular hypertrophy, acute

pericarditis, left bundle-branch block, Brugada syndrome, and early repolarization patterns in cardiovascular problems.[4] In the past the diagnosis of MI was made on the basis of monitoring trends and determinants in cardiovascular disease (MONICA) criteria, which comprises the existence of chest pain, pathological Q waves in ECG tracing and increased levels of cardiac iso-enzymes where creatinine kinase for cardiac muscle marker (CK-MB) was taken as gold standard while according to fourth universal explanation of MI, standards to diagnose MI is based on raised levels of cardiac troponins in conditions when ischemia is suspected in clinical presentation of the patient, changes in ECG and rise or fall of troponin level above the 99th percentile upper reference limit.[5] Troponins are complex of three protein subunits i.e. I, C and T that help in interaction between actin as well as myosin filament of myocyte.

Cardiac troponins are the fundamental investigations in diagnosing and risk stratification of NSTEMI among the patients presenting with assumed NSTEMI.[6,7] Amino acid sequence in structural composition of troponins differentiates them from the sequence of that skeletal muscles are made up of. This difference in amino acid composition detection is basis for the creation of monoclonal-antibody based assay of troponin T (Trop T) and troponin I (Trop I). This is the key to success of these biomarkers utility in clinical practice in decision making about the diagnosis and treatment of the patient. Thrombolysis in myocardial infarction (TIMI) risk score combines seven risk factors in patients with NSTEMI/ non-ST segment elevated myocardial infarction (NSTEMI) that estimates their mortality.[8] Raised cardiac biomarker is one of them. Troponins mainly bound to myo-filaments while the rest remain present in the cytoplasm. Creatinine kinase also play a role in detection of myocardial infarction, but troponins are more effective as they are not cleared as early from the cytoplasm as compared to creatinine kinase.[9] Troponins also have low rate of cross reactivity with skeletal muscles due to which troponins have now replaced creatinine kinase. The early release of Trop T and Trop I help detection within 3 to 4 hours of the commencement of symptoms of MI and remain elevated for next 7 to 14 days. Trop T and Trop I can detect myocardial injury of 40ng of myocardial necrosis measuring 0.015% of total heart which is the 99th percentile of other group taken as control at accuracy of 10% cardiovascular (CV) and it is the recommended value of troponins. By detecting early NSTEMI, length of hospital stay and admission can be mitigated.[10]

Objective of this research study was to analyze and make a comparison between the diagnostic accuracy of hs-TropI and c-TropT.

METHODOLOGY

Descriptive cross-sectional study was conducted at Emergency department, Armed Forces Institute of Cardiology and National Institute of Heart Diseases (AFIC & NIHD). Review board of our institute (AFIC/NIHD) approved this prospective study and written informed consent was taken from every participant according to the Declaration of Helsinki. From May 2021 to July 2021, we enrolled 100 patients presenting in ER with chest pain at onset of at least 03 hours duration. Patients with acute or chronic renal failure (CKD) requiring hemodialysis, sepsis, and left ventricular failure (LVF) are excluded from the study. All patients presenting in ER with typical chest pain and no ST elevation on ECG, either gender (male / female) and age between 20 -80 years were included in this study.

All the selected patients underwent both tests i.e. lab-based, chemi-luminescence immune-assay hs-TropI, and kit-based c-TropT from same blood sample. For qualitative measurement, heparinized blood samples for troponin measurement were obtained and few drops placed in the STAT immune chromatographic kit for troponins assay as per manufacturer's guidelines. For quantitative measurement, chemiluminescent micro particle immunoassay is designed to measure cardiac troponins in serum and plasma using the Architect STAT troponin assay (Abbott diagnostics) which uses three monoclonal antibodies against individual troponins. Two antibodies are coated with paramagnetic micro particles which act as capture antibodies and the third is labeled with acridinium which measure troponins up to 50.00ng/L as per guidelines. Trop T is labelled as positive when double line appears on the kit after reaching the threshold of 100ng/L and Trop I is considered positive if the result is higher than 40ng/L.

All the data was recorded and analyzed by SPSS-23. Continuous variables are stated as mean $\pm$ SD and categorical variables as frequencies and percentages. Chi square test was applied in which p-value $\leq$0.05 was considered as significant value.

RESULTS

Demographics and clinical details of patients is shown in Table-I. Mean age of patients was found to be 50 ± 10.75 years, out of these 85 (85%) were males while 15 (15%) were females. Among 100 patients 43 (43%) had hypertension while 20 (20%) had diabetes mellitus, 23 (23%) patients were the smokers and 2

(2%) had history of ischemic heart disease. 72 (72%) patients present in ER with early (<4hrs) chest pain and 28 (28 %) with late (>4hrs) chest pain. On ECG 57 (57%) patients showed T-wave inversion, 33 (33%) had ST depression and 1 (1%) had left bundle branch block (LBBB).

Table 1: Demographic characteristics

Characteristics	Summary
Age (mean ± SD)	50 ± 10.75
Hypertension	43 (43%)
Diabetes Mellitus	20 (20%)
Smoker	23 (23%)
History of ischemic heart disease	2 (2%)
Duration of chest pain	
Early (< 4hrs)	72 (72 %)
Late ≥ 4hrs)	28 (28 %)
T wave inversion	57 (57%)
ST depression	33 (33%)
Left bundle branch block	1 (1%)
Trop I (positive)	27 (27%)
Trop T (positive)	8 (8%)

Among patients diagnosed with NSTEMI, 18 (41.9%) were hypertensive with positive hs-TropI while 5(11.6%) patients had positive c-TropT. Fifteen (75%) diabetics had raised hs-TropI levels and 5 (25%) with detectable c-TropT levels. Trop I detected NSTEMI in 33.3% patients while only 8.3% patients have tropT positive within 4 hours. Patients with ST depression had raised trop I level in 26 (78.8%) patients and trop T in 8 (24.2%) patients. Sixteen (28%) had positive trop I and 4 (7%) had positive trop T with T-wave inversions. Four (50%) patients had multiple risk factors with positive trop T and fifteen (55%) with positive trop I. Association of risk factors with hs-TropI and c-TropT is written in Table 2.

Table 2: Association of risk factors with hs-TropI and c-TropT

Variables	hs-TropI	P-value	c-TropT	P-value
Hypertension	18 (41.9%)	0.014	5 (11.6%)	0.24
Diabetes mellitus	15 (75%)	0.001	5 (25%)	0.002
Smoker	9 (39.1%)	0.2	3 (13%)	0.31
Duration				
< 4 hrs.	24 (33.3%)	0.12	6 (8.3%)	0.84
≥ 4 hrs.	5 (17.9%)	0.12	2 (7.1%)	0.84
ST depression	26 (78.8%)	0.001	8 (24.2%)	0.001
T-wave inversion	16 (28%)	0.81	4 (7%)	0.67

Accuracy of troponin levels in diagnosis of NSTEMI is presented in table 3. Sensitivity, specificity, positive predictive value and negative predictive value of hs-TropI and c-TropT was 87%,92% ,81% 94% and 72%, 95%, 66% 96% respectively. To compare NSTEMI at hs-TropI and c-TropT, a paired sample T-test was performed. There was a significant difference in NSTEMI calculated by hs-TropI (M=1.73, SD=0.446) and c-TropT (M=1.92, SD= 0.273) t (99) = -4.53, p=0.001 at 95% CI.

Table 3: Accuracy of troponin levels in diagnosis of NTESMI

	hs-TropI	c-TropT
Sensitivity	87%	72%
Specificity	92%	95%
Positive predictive value	81%	66%
Negative predictive value	94%	96%

DISCUSSION

Early detection of NSTEMI is important in prompt initiation of treatment. Among such patients, strong association between rise and fall of troponins level, myocardial necrosis and 30 days' mortality is observed.[11] Many clinical situations demand serial sampling, which is the time-consuming process to establish diagnosis of NSTEMI, efficiency of troponin assays has been questioned. Introduction of new high sensitivity troponin assays for the purpose of solving that problem, by lowering the limit of detection and thus, helping in more rapid exclusion of MI than old conventional troponin assays.[12] Conventional troponins have revolutionized the management of suspected NSTEMI, including risk stratification. A cutoff value for troponins at the 99th percentile has been recommended, as value beyond it is associated with adverse outcome and need of early invasive strategy. Newer assays have been developed like higher sensitive troponins assay to improve sensitivity and specificity of conventional methods. The mortality rate of acute myocardial infarction can be reduced by early detection of myocardial necrosis with determining cardiac troponins.

Many studies have been published studying rise or fall of troponins at 0,2,4 and 6 hours but in our study, interpretation was concluded from sample taken at time of presentation, we investigated the diagnostic accuracy, sensitivity and negative predictive value of hs-Trop I and c-Trop T test for the diagnosis of NSTEMI. Studies proved that the sensitivity and specificity of both the hs-TropI and hs-Trop T are almost equal but hs-Trop I is more sensitive than conventional kit-based c-TropT.[13]

Findings of our study are consistent with previous studies done, which shows higher sensitivity of hs-Trop I than c-Trop T as shown in Table 3. Results of our study have shown that time period from the start of symptoms may have bearing on the relevant diagnostic superiority of either test over the other. But in early presenters, it is clearly demonstrated that Hs-

trop I should be the preferred option to rule out acute ischemic event. Patients with typical chest pain and ST segment depression presents a high-risk population for acute cardiac event. Hs-Trop I is superior and more accurate with higher sensitivity of up to 87% with negative predictive value of 94% as compared to c-TropT which has a sensitivity of 72% with a negative predictive value of 96%. These results are comparable to other studies which showed similar results with slightly improved sensitivities.[14] Small difference in results can be explained by different inclusion and exclusion criteria and timing of sample collection. Those studies had used 2 hours cut off since chest pain before sample but in our study, it was at time of presentation to ER.

In general, kit based Trop T can be used as an exclusion criterion of STEMI and NSTEMI due to its easy availability, cost effectiveness, time keeping and good negative predictive value.[15] In addition, diagnostic superiority of hs-Trop I in patients reporting early to health care facility is strengthened by an analogous fresh observation with hs-Trop I in critical subgroups such as aged patients and with those who already have some coronary artery disease and therefore pretty factual.[16] Even minor variances in diagnostic accuracy of acute MI can cause enough impact on medical outcome of patients. It can have worst prognostic effects on mortality and morbidity of patients.

As our research was an observational prospective study, we are unable to comment with surety about the benefit to the patient in management with use of either hs-Trop I and c-Trop T. Patients with acute LVF, CKD and sepsis were excluded, we are unable to mention the diagnostic and prognostic preference of c-Trop T and hs-Trop I in those patients but there is clear diagnostic and therapeutic importance of using troponins assays in suspected cases.[17] Study is a single centered and short time duration study with a relatively small sample size which may have affected our statistical powers. It includes patients entertained at AFIC, that may not reflect the general population as majority of them are uniform persons, having a healthy lifestyle in accordance to others. To determine effects and significant association between different risk factors like DM, hypertension, smoking, past ischemic heart disease history, age and sex, need a large-scale study.

CONCLUSION

This study demonstrated that positive predictive value of c-Trop T in diagnosing NSTEMI is low as compared to hs-Trop I. Thus, it is recommended that lab-based hs-Trop I should be preferred over kit-based c-Trop T for screening or diagnostic purposes, even though the later is cost effective and takes less time. Therefore, in suspected NSTEMI, hs-TropI should be used for diagnosis and further management. Scope of our study was very limited and short time based so, a large-scale study is required to draw results for implementation in health care system.

AUTHORS' CONTRIBUTION:

AN, MZK, and NS: Concept and design, data acquisition, interpretation, drafting, final approval, and agree to be accountable for all aspects of the work. MF and WR: Data acquisition, interpretation, drafting, final approval and agree to be accountable for all aspects of the work.

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