RESEARCH ARTICLE

Cardiac Biomarkers and their Importance in the Diagnosis of Myocardial Ischemia and Acute Myocardial Infarction

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ABSTRACT

Introduction: Myocardial ischemia and acute myocardial infarction are important episodes of cardiac ailments. Cardiac biomarkers are a growing area of interest, constantly evolving and presenting potential promises diagnostically to supplement the instrumental techniques. They play a vital role in every stage of sequel of cardiac ailment by contributing to the diagnosis and differentiating the conditions.

Aim: To evaluate the diagnostic significance of emerging cardiac biomarkers during myocardial ischemia and infarction (AMI) and to construct a definitive pattern shift of markers in ischemia versus infarction in uncomplicated cases, hence the predictive element.

Materials and methods: In this comparative cross-sectional study, three groups i.e. control (n = 33), ischemia (n = 38), and infarction (42) of either sex with an age group of 70 were included. The cardiac parameters, ischemia-modified albumin (IMA), creatine kinase-MB (CK-MB), creatine kinase (CK), high sensitive cardiac troponin I (hscTnI), N-terminal pro brain natriuretic peptide (NTpro-BNP), myoglobin, and heart type fatty acid binding protein (H-FABP) analyses were carried out for their sensitivity and specificity.

Results: All the parameters in infarction were significantly raised when compared with the control group. In ischemia, the markers NTproBNP, hscTnI, and IMA and in infarction, the NTproBNP, hscTnI, and H-FABP showed more area under the curve.

Conclusion: The markers exhibited different pattern shift in ischemia and infarction. The combination of hscTnI, NTproBNP, and IMA would increase the sensitivity in the detection of ischemia. In case of AMI, the H-FABP in the early stages, and NTproBNP, hscTnI, IMA, and CKMB in the later stages of ACS contribute immensely for the diagnosis.

Keywords: Diagnosis, Infarction, Ischemia, Multi markers, Sensitivity, Specificity.

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INTRODUCTION

Coronary artery disease (CAD) is the leading killer disease worldwide. There are various biophysical techniques including invasive and non-invasive methods that are available to diagnose the disease. The serum cardiac biomarkers play a crucial role in diagnosing the condition and have been constantly assessed clinically at every stage of the sequel of CAD.[1] The evaluative importance of each marker is unique, as each one has got different time elevations based on release kinetics, sensitivity, specificity, and half life. Circulating concentrations of B-type natriuretic peptide (BNP) and the N-terminal fragment of its pro hormone (NT-proBNP), IMA, and heart fatty acid binding protein (H-FABP) are emerging as clinically useful tools for the diagnosis of CAD. However, still research is progressing to employ these as diagnostic markers for AMI. Hence, there is a requirement of comparing these newer and emerging parameters along with conventional serum markers for their diagnostic ability, sensitivity, and specificity in ischemia and infarction of heart. Apart from this, there is a need to study the pattern of progressive change of these markers in ischemia and infarction.

During myocardial ischemia or infarction, there will be an elevation in the serum biomarkers that are released in a detectable range due to cardiac myocyte damage. The markers of ischemia and infarction may exhibit different patterns; however, much data are unavailable.[2] Several biomarkers are introduced that are specific and sensitive for different stages of cardiac ailments. But, out of huge numbers, it is a challenge to employ the right serum biomarker at the right time to evaluate the status, and a suitable/ideal marker for the early detection and assessment of cardiac damage.

With this background, in the current study, a comparison was made regarding their sensitivities and specificities at the best trade-off (cut-off) values and determining

the diagnostic abilities of the biomarkers in the respective conditions of ischemic and infarction groups.

MATERIALS AND METHODS

Participants

The present study was carried out at Maharajah's Institute of Medical Sciences (MIMS), Nellimarla, Andhra Pradesh. After the written informed consents were obtained, the participants were categorized into three groups i.e., control group, ischemia, and AMI group in the present study.

Inclusion Criteria and Exclusion Criteria

The subjects of both genders with an age group ranging from 31 to 70 were involved in the present study. All documented myocardial ischemia and AMI cases with no prior history and treatment for cardiac ailments were included in the study. The inclusion criteria were based on parameters like age, sex, lifestyle, and family history, and also included risk factors like smoking, obesity, hypertension, and dyslipidemia. The patients with renal failure, diabetes mellitus, pregnancy, arrhythmias, acute heart failure, myocarditis, old AMI patients, patients with left ventricular hypertrophy, muscular dystrophy, and infectious diseases like HIV, and hepatitis were excluded.

The sample size was estimated for a mean difference of 10 units in the biochemical variable (AST and ALT) with a standard deviation of 12 units, a power of 90% and at a significance level of 0.05. The estimated sample size was 32 for each group. SigmaPlot 12.0 (Systat software, USA) software was used for the calculation of sample size. In this comparative cross-sectional study, the control group included healthy subjects (n = 33) of either sex who were not suffering from any sort of cardiac illness. The ischemia group of participants (n = 38) were selected from persons of either sex, who came to the department of General Medicine and Cardiology unit of MIMS. Ischemic subjects (with no past history of ischemia or treatment) were selected for the study.[3] These participants were corroborated by cardiologist as ischemic cases and a sample of 8 mL of blood was collected and analyzed for the cardiac markers.

The infarction group of participants (n = 42) was selected from persons of either sex who were admitted to ICU with the diagnosis of acute myocardial infarction. In this study, multiple samples were collected i.e., at admission, 6th, 12th, 24th, and at 48th hours from the time of admission. However, only the first two time periods (samples at admission period and the 6th hour) were considered for comparative study, as it is crucial to restore the patient with early diagnosis. After meeting the diagnostic criteria of myocardial infarction based on WHO guidelines,[4] 8 mL of blood sample was collected immediately after the admission to ICU of MIMS (within 2–3 hours after the onset of myocardial infarction) and the serum was separated. This serum sample was considered as "0" hour or admission sample. After the "0" hour sample, another sample was taken at the 6th hour and both the samples were analyzed for cardiac biomarkers. Individuals with complaints lasting more than 12 hours before admission were not included in the study because some markers return to normal within 12 to 24 hours of onset of AMI.

Methods—Estimation of Cardiac Parameters

Human-N terminal probrain natriuretic peptide (NTproBNP) and heart type fatty acid binding protein (H-FABP) were estimated by enzyme-linked immunosorbent assay method (ELISA). The estimation is based on the principle of double antibody sandwich ELISA with an assay range for NTproBNP 2 to 360 pg/mL and the same for H-FABP is 0.05 to 10 ng/mL. The color that was obtained finally in the corresponding test procedures was measured at 450 nm for both the parameters on Transasia Erba Lisa Scan EM (ELISA reader). The kits, NTproBNP, and H-FABP were provided by SunRed biotechnology company, Shanghai. Ischemia-modified albumin (IMA) is measured by albumin cobalt binding assay, in which a known amount of cobalt is added to the serum sample and then the unbound cobalt is measured by the intensity of colored complex formed after reacting with dithiothreitol by using a colorimeter at 470 nm (Elico CL-157). The values expressed in U/mL are extrapolated from the standard graph and one IMA unit is defined as "gm of free cobalt".[5] The high sensitive cardiac troponin (hscTnI) was estimated by micro-plate enzyme immunoassay, chemiluminescence. This test is performed by CLIA batch analyzer from SFRI – France. The serum sample is used and the adult normal value is ≤1.3 ng/mL and the kit was supplied by monobind inc. (acculite CLIA microwells troponin I (cTnI) test. The estimation of creatine kinase (CK-NAC) was performed by NAC-activated kinetic method and the kit was supplied by Transasia Erba. The measurement was carried out by using random access batch automatic analyzer, Erba smart lab, Transasia. The reference range for this parameter is 15 to 130 IU/L (males) and 15 to 110 IU/L (females).[6] CK-MB was estimated by immuno-inhibition method, Kinetic, based upon the principle; specific antibodies against CK-M inhibit the complete CKMM activity and the CK-M sub unit of CK-MB and only CK-B activity is measured. The kit was supplied by CK-MB Transasia

Erba and analyzed on a random access batch automatic analyzer, Erba smart lab, Transasia with a normal value <25 IU/L. The serum myoglobin was estimated by micro plate immunoenzymometric assay. The final color measured at the wave length of 450 nm on Transasia Erba Lisa scan EM (ELISA reader). The analysis supplied by Monobind inc.[7]

Statistical Method

All the data were expressed as mean ± SE. The means of control, ischemia, and ischemic group were analyzed by one-way analysis of variance (ANOVA) followed by student Newman Keuls test. A probability of <0.05 was taken as statistically significant. All the statistical analyses and graphs plotting were carried out by using Sigmaplot 12.0 (Systat software, USA). The cardiac marker sensitivity and specificity in ischemia and infarction cases against the control group were calculated by DeLong et al[8] methodology using Medcal Version 15.11.4. The Youden index in this version gives the best trade-off (cut-off) between sensitivity (identifying true-positives) and specificity (identifying true-negatives) in the respective conditions.

RESULTS

In the selected list of parameters, the analytical performance of the parameters was evaluated with the help of AUC at 95% confidence intervals (CI) (Table 1). In the ischemic group, the biomarker NTproBNP showed a grater area under the curve (AUC) when compared to other markers. However, IMA and hscTnI closely followed the NTproBNP with less diagnostic significance for ischemia in comparison to NTproBNP. In the infarction group, at the admission period, the serum H-FABP showed more AUC when compared to other parameters. In progression with time from admission i.e., at the 6th hour, the AUC of IMA, H-FABP, and myoglobin remained almost the same as in the admission period. However, the CK, CK-MB,

troponin, and NTproBNP were further elevated and the trend continued in comparison to other markers. The sensitivity and specificity of the markers with trade-off limits of ischemic group in comparison to control group were expressed as percentages. NTproBNP, IMA, and hscTnI showed good sensitivity and specificity and help to rule out and rule in the disease accurately (Table 2). Similarly, Tables 3 and 4 show the data of sensitivity and specificity of the markers at admission and at the 6th hour duration of the infarction group in comparison to the control group. The parameters, such as myoglobin and total CK showed less sensitivity at the admission period, and at the 6th hour, myoglobin showed least sensitivity when compared to other markers.

Table 2: The sensitivity and specificity of the cardiac markers of ischemic group

Parameter	Trade off	Sensitivity %	Specificity %
NTproBNP (pg/mL)	>86.7	73.4	92.9
IMA (Ku/mL)	>78	89.47	93.94
CK (IU/L)	>126	63.24	69.71
CK-MB (IU/L)	>24.13	63.16	97.0
Myoglobin (ng/mL)	>99.3	26.32	98.08
H-FABP (ng/mL)	>4.2	39.47	90.91
hscTnI (ng/mL)	>0.9	97.37	93.75

The sensitivity and specificity of markers in ischemic in comparison to control and values are expressed as percentages

Table 3: The sensitivity and specificity of the markers at the time of admission in Infarction group

Parameter	Trade off	Sensitivity %	Specificity %
NTproBNP (pg/mL)	>94.8	97.8	97.0
IMA (Ku/mL)	>74	95.2	84.8
CK (IU/L)	>126	59.5	69.7
CK-MB (IU/L)	>24.27	94.4	99.0
Myoglobin (ng/mL)	>96.37	76.2	93.9
H-FABP (ng/mL)	>4.66	95.8	99.2
hscTnI (ng/mL)	>0.9	98.3	93.9

The sensitivity and specificity of markers in infarction group at the time of admission in comparison to control and values are expressed as percentages

Table 1: A consolidated table of area under the curve for the serum cardiac parameters in ischemia and infarction subjects (admission period and 6th hour)

Test result variables	Area under the curve (with 95% confidence interval)		
	Ischemia	Infarction	
		At admission	At 6th hour
NTproBNP	0.80 (0.74–0.96)	0.83 (0.72–0.89)	0.93 (0.90–0.96)
IMA	0.79 (0.77–0.88)	0.83 (0.74–0.90)	0.84 (0.75–0.91)
CK	0.71 (0.57–0.78)	0.78 (0.71–0.82)	0.89 (0.76–0.93)
CK-MB	0.75 (0.74–0.82)	0.77 (0.69–0.80)	0.92 (0.89–0.96)
Myoglobin	0.65 (0.56–0.79)	0.86 (0.73–0.93)	0.90 (0.89–0.94)
H-FABP	0.76 (0.64–0.78)	0.89 (0.72–0.92)	0.91 (0.89–0.94)
hscTnI	0.79 (0.70–0.87)	0.85 (0.75–0.92)	0.94 (0.92–0.94)

The values present in the parenthesis are upper and lower bounds

Table 4: The sensitivity and specificity of the markers at the time of 6th hour from admission period in infarction group

Parameter	Trade-off	Sensitivity %	Specificity %
NTproBNP (pg/mL)	>94.8	98.4	97.2
IMA (Ku/mL)	>78	92.9	93.9
CK (IU/L)	>171	71.4	96.0
CK-MB (IU/L)	>24.27	98.1	97.0
Myoglobin (ng/mL)	>99.3	95.2	92.0
H-FABP (ng/mL)	>4.66	98.6	97.4
HscTnI (ng/mL)	>1.1	99.1	98.0

The sensitivity and specificity of markers in infarction group at 6th hour from the time of admission in comparison to control and values are expressed as percentages

Study of Pattern of Serum Cardiac Biomarkers in Control, Ischemia, and Infarction Groups

The pattern shift of serum biomarker levels in the form of percent changes in ischemia and infarction in comparison to control is depicted in Graph 1. The mean values of the biomarkers in the control group were taken, as fold of rise of variations of these markers in ischemia and infarction was calculated. The CK levels when compared with control, the ischemia, the "0" hour, and 6th hour of infarction groups showed a significant increase. In comparison to control, in ischemia, the CK was raised by 1.19 fold and in infarction at 0 hour 1.15 fold, and the 6th hour, 1.68 fold. The upward trend in the percentage of mean values continued, and the fold of rise in the subsequent periods at 12, 24, and 48 hours was (3.24, 4.40, and 3.61) F = 22.9; p < 0.001. In comparison to the control, the CK-MB at the 6th hour of infarction showed a significant rise rather than "0" hour of infarction and ischemic group. In ischemia, the level was raised about 1.19 fold and in infarction at 0 hour, 1.15 fold and at the 6th hour, 1.68 fold in comparison to control. The upward trend continued and the fold of rise in infarction at 12, 24 and 48 hours was (3.24, 4.40, and 3.61), F = 47.5; p < 0.001.

The IMA showed a significant variation among all the groups. In comparison to control, the fold of rise of IMA was 1.44 (144%) and in infarction at "0" hour and the 6th hour, it was 1.49 and 1.54, respectively. Similarly, at 12, 24, and 48th hours, the fold of elevation was 1.55, 1.42, and 1.32, respectively, F = 39.2; p < 0.001. H-FABP in the control group showed variation with the infarction group, but not significant with ischemia, as the fold of rise was very less, 1.2. In infarction, the fold of elevation was 3.97, 8.61, 10.21, 4.14, and 2.39 in the respective time periods, starting from admission to 48th hour, and showed good, significant variation, F = 84.7; p < 0.001. The serum NTproBNP variation in the ischemia and infarction groups was significant in comparison to control. The fold of increase in the marker level of ischemia was 1.65, and in the infarction group, it was 3.3, 4.69, 6.49, 7.60, and 9.07 in the respective time periods, F = 206.2; p < 0.001. The troponin also showed a very high significance in ischemia at "0" hour and 6th hour of infarction in comparison to the control. All values were highly significant. The ischemia showed a 3.6 fold increase compared to the control. While at "0" hour it was 6.83 and at the 6th hour, there was an 11.10 folds rise. The trend showed at other time periods was 16.93, 28.14, and 33.95 folds in 12th, 24th, and 48th
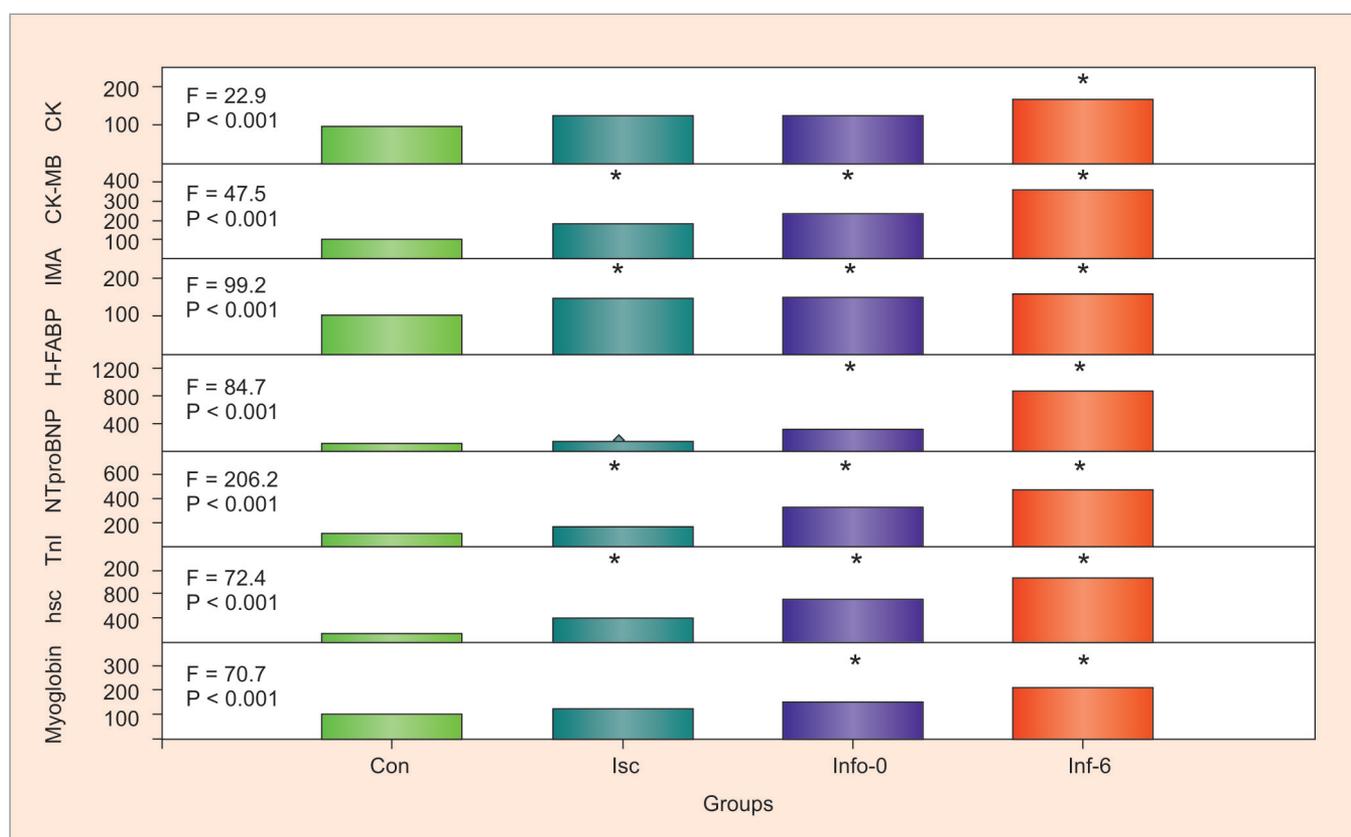
Graph 1: The percent of elevations in the levels of serum cardiac biomarkers in control (con), ischemia (Isc), 0 and 6 hours infarction (Inf). Control = 100%

Mean ± SE (n – control = 33; ischemia = 38 and infarction = 42; CK (creatine kinase; IU/L); CK-MB (creatine kinase – MB; IU/L); IMA (ischemia modified albumin; U/mL); H-FABP (heart type fatty acid binding protein; ng/mL); NTproBNP (N-terminal probrain natriuretic peptide; ng/mL); hscTnI (high sensitive cardiac troponin; ng/mL); *significantly different from control

hours of infarction, F = 72.4; p < 0.001. Myoglobin did not show significance in ischemia in comparison to the control. There is a significant variation in infarction when compared with the control. The ischemic group showed 1.05 folds, and infarction 1.39, 2.05, 2.64, 1.56, and 1.13 in the respective time periods, F = 70.7; p < 0.001.

DISCUSSION

From Table 1, it is evident from the area under the curve (AUC) of the ischemic subjects, the parameters NTproBNP, IMA, and hscTnI are having more area under the curve, hence more diagnostic ability to detect ischemia during the initial stages and can predict the future outcome of the disease. In AMI, at the time of admission period, the observations of AUC for the markers myoglobin, hscTnI, H-FABP, IMA, and NTproBNP showed a significant diagnostic ability to detect myocardial infarction at the earliest period after the onset of the symptoms. The area under the curve for all the parameters which showed more than 0.80 indicated as having a better diagnostic ability in the detection of AMI when compared to other parameters.[9] It was observed that our results supported previous claims that, apart from other potential markers included in this study, H-FABP (AUC 0.89) showed more area under the curve and can be treated as earliest and more efficient marker for ruling out the disease. These results indicate the fact that H-FABP is well suited for an early detection of ACS. Chen et al[10] reported that the area under the ROC curve of H-FABP was significantly greater than that of cTnI, CK-MB and Mb within 3 hours and can be used as a sensitive marker for AMI in the early stage.

One study by Hjortshoj et al[11] showed that the sensitivity of IMA at admission with an AUC for IMA was 0.73 and claims that IMA is not supposed to be considered as a standard marker. Our results do not corroborate the study of Hjortshoj et al[11] and the ROC curve analysis clearly showed that AUC was 0.83 (with 95%CI). In case of myoglobin, the ROC analysis in one study revealed the diagnostic accuracy of myoglobin concentration as indicated by the area under the ROC curve (AUC) that increased significantly from 3 to 5 hours after onset of symptoms (0. 96 ± 0.014; p = 0.0040). This stated that myoglobin is an early and efficient marker within 5 hours from the onset of infarction.[12] In our study, myoglobin proved as a potential marker in the early stages of AMI, but the diagnostic efficiency is not superior to H-FABP.

The hscTnI in the 1st hour of its presentation yielded a diagnostic accuracy for AMI as shown by the area under the receiver-operating characteristics curve of 0.85. One study reported that the hscTnI assays effectively distinguish patients with AMI and those with cardiac non-CAD.[13] Another study supports the view of this author where troponin showed large window periods in the serum. So, serial sampling and assessment of cardiac troponin are not required, but only sampling at admission and at a later stage will be adequate in clinching the diagnosis. Regarding NTproBNP, the combination with cTn increases the diagnostic capability and assists the clinicians in differentiating between MI, unstable angina, and non-cardiac causes of chest pain.[14]

To summarize, according to the data which are evident from the previous information in the current study, hscTnI, NTproBNP, and IMA in ischemia, and during the early hours of AMI, the H-FABP followed by myoglobin and IMA showed the best diagnostic ability. In AMI, these three markers can be considered as early markers; however, after initial hours i.e., 6 hours, the other markers showed more diagnostic ability. Early detection is more crucial rather than later stages of AMI in saving the patient's life by accurate diagnosis by the clinicians. Apart from this, throughout the entire episode of AMI, hscTnI is considered as a reliable marker. NTproBNP follows closely at the heels of hscTnI in serving as a reliable marker. This study also suggests that CK-MB can also contribute in clinching the diagnosis for the entire period. The markers that are commonly elevated or showing good AUC in both ischemia and infarction were NTproBNP, hscTnI, and IMA respectively. Therefore, these markers may be treated as common diagnostic tools in both the conditions of ischemia and infarction (Table 1). It is evident from Graph 1 the pattern of markers in respective conditions; compared to the control, it was evident that the fold of rise was accordingly for hscTnI > NTproBNP > IMA > H-FABP in ischemia. In infarction, the fold of rise accordingly at "0" hour was hscTnI > H-FABP > NTproBNP > IMA > myoglobin > CK-MB and CK, and at 6th hour, hscTnI > H-FABP > NTproBNP > myoglobin > CK-MB and CK> and IMA in the infarction group. In comparison to control, when the pattern of markers was constructed in ischemia, the NTproBNP and IMA in ischemia could be treated as differentiating/distinguishing biomarker from that of infarction. This conclusion is based on the data that hscTnI is commonly elevated in all the respective conditions of ischemia and infarction. Therefore, for the distinguishing of ischemia and infarction, the next two markers (NTproBNP and IMA) that were increased in ischemia were considered (where these two markers exhibited different patterns in infarction). The pattern that was shown in ischemia, able to predict the future infarction as these markers (hscTnI, NTproBNP, and IMA) significantly correlated with the pattern of infarction.

Regarding the sensitivity and specificity of the cardiac markers, in the early stages of infarction, all the markers showed good sensitivity and specificity which are included in the current study regardless of the marker used as the standard. In the ischemic group, the IMA, hscTnI, and NTproBNP showed good sensitivity when compared to other markers (Table 2). Overall, the sensitivity of troponin I in ischemia and infarction is more when compared to other markers. IMA and NTproBNP closely follow troponin. Ross et al,[15] found that troponin I level more than 0.6 ng/mL can be used as a positive value in the detection of AMI and in comparison to CK-MB and ECG, the estimation of troponin using in the early hours (within 6 hours) can bring the sensitivity to 94% and specificity to 81%. Hence, it can be claimed as the best marker. Patil et al[16] claimed that the sensitivity and the specificity of IMA (with an AUC of 0.90) in the diagnosis of AMI were 88 and 93% as compared to 87 and 75%, respectively, for troponin I. The combination of IMA and troponin enhances the sensitivity to 96% i.e., a precise diagnostic biomarker. However, our study demonstrated hscTnI with good diagnostic sensitivity in both ischemia and infarction. Studies showed that among the same patients, the myoglobin–CK-MB–TnI triad had a sensitivity of 57%. The combination of IMA–myoglobin–CK-MB–TnI increased the sensitivity for detecting ischemia up to 97%, with a negative predictive value of 92%.[17] The serum myoglobin in the early of AMI showed good sensitivity, but exhibits poor performance in the suspected ischemic cases. Studies reported that 4 hours after the onset of symptoms, the serum myoglobin (the sensitivity was 93% and specificity, 89%) concentration distinguished easily those patients with myocardial infarction from those without, whereas when creatine kinase values were used, the sensitivity was poor, but the specificity was high.[18]

H-FABP showed good diagnostic sensitivity and specificity at the admission period and at the 6th hour from admission in the AMI group; however, it does not show much potential sensitivity in ischemic cases. Chen et al[10] reported that H-FABP is the best sensitive marker in the early stages of AMI when compared to CK-MB, cTnI, and myoglobin i.e., in the early hours (within 3 hours from the onset of symptoms). The diagnostic sensitivity for AMI was 64.29% and within 6 hours, it was 84.38%.[6] In the present study, NTproBNP exhibited reliable diagnostic sensitivity and specificity and can be relied in both ischemia and infarction as a diagnostic marker. Palladini et al[19] claimed that NT-proBNP is the reliable sensitive marker in ACS with a sensitivity (93.33%) and specificity (90.16%) and considered it as superior to other markers. Therefore, it was observed in the current work, hscTnI followed by NTproBNP holds its potentiality and superiority in diagnosing the condition,

rather than other markers in the panel. Our study observed that the diagnostic sensitivity of CK and CK-MB were not superior to other markers; however, it can be the potential marker in infarction and suspected ischemia. CK-MB sensitivity significantly increases over 3 hours of observation of stable chest discomfort patients in the ED; it also increases as a function of the total interval from onset less than 3 hours from the onset (38%). 6 to 12 hours (92%) and more than 12 hours 100% of sensitivity (Tables 3 and 4).[20] In view of multi-marker strategy, as the release kinetics of the markers were different, it is evident from our study that the combination of hscTnI, NTproBNP, and IMA would increase the sensitivity in the detection of ischemia. The H-FABP and myoglobin showed a lesser role in the detection of ischemia. It was clearly shown in the ischemic group that the levels of markers in the serum showed a significant variation, especially for hscTnI, NTproBNP, and IMA. These markers may be released in the pre-infarction condition or ischemia due to transient damage of myocardium.

CONCLUSION

Instead of using a single marker, employing multi-markers will be helpful for the right diagnosis of AMI. H-FABP in the early stages and hscTnI, NTproBNP, IMA, and CKMB in the later stages of ACS contribute immensely for the diagnosis of AMI. In ischemia, hscTnI and NTproBNP are the reliable markers in the diagnosis. NTproBNP and IMA may be considered as differentiating markers in ischemia from infarction because of the definitive patterns observed.

ACKNOWLEDGMENTS

REFERENCES

1. Vasan RS. Biomarkers of cardiovascular disease molecular basis and practical considerations. Circulation 2006 May;113(19):2335-2362.
2. Jaffe AS, Ravkilde J, Roberts R, Naslund U, Apple FS, Galvani M, Katus H. Its time to change to a troponin standard. Circulation 2000 Sep;102(11):1216-1220.
3. Heras M, Bueno H, Bardaji A, Fernández-Ortiz A, Martí H, Marrugat J; DESCARTES Investigators. Magnitude and consequences of under treatment of high risk patients with non ST segment elevation acute coronary syndromes: insights from the DESCARTES Registry. Heart 2006 Nov;92(11):1571-1576.
4. Thygesen K, Alpert JS, White HD; Joint ESC/ACCF/AHA/ WHF Task Force for the Redefinition of Myocardial Infarction.

Universal definition of myocardial infarction. Eur Heart J 2007 Oct;28(20):2525-2538.

5. Behera S, Mangaraj M, Chandra Mohapatra P. Diagnostic efficacy of ischemia modified albumin and its correlation with lipid profile, oxidative stress in acute myocardial infarct patients on admission. Asian Pac J Trop Dis 2012 Feb;2(1): 62-65.

6. Teitz NW, editor. Specimen collection and processing: sources of biological variation. In: Text book of clinical chemistry. 2nd ed. Philadelphia (PA): W.B Saunders Co.; 1994.

7. Apple FS, Christenson RH, Valdes R Jr, Andriak AJ, Berg A, Duh SH, Feng YJ, Jortani SA, Johnson NA, Koplen B, et al. Simultaneous rapid measurement of whole blood myoglobin, creatine kinase MB, and cardiac troponin I by the triage cardiac panel for detection of myocardial infarction. Clin Chem 1999 Feb;45(2):199-205.

8. DeLong ER, DeLong DM, Clarke-Pearson DL. Comparing the areas under two or more correlated receiver operating characteristic curves: a non parametric approach. Biometrics 1988 Sep;44(3):837-845.

9. Zhu W, Zeng NN, Wang N. Sensitivity, specificity, accuracy, associated confidence interval and ROC analysis with practical SAS® implementations. In: Northeast SAS User Group proceedings, Section of Health Care and Life Sciences, Baltimore (MD). 2010. pp. 1-10.

10. Chen L, Guo X, Yang F. Role of heart-type fatty acid binding protein in early detection of acute myocardial infarction in comparison with cTnI, CK-MB and myoglobin. J Huazhong Univ Sci Technolog Med Sci 2004 Oct;24(5):449-451.

11. Hjortshoj S, Kristensen SR, Ravkilde J. Diagnostic value of ischemia-modified albumin in patients with suspected acute coronary syndrome. Am J Emerg Med 2010 Feb;28(2):170-176.

12. De Winter RJ, Koster RW, Sturk A, Sanders GT. Value of myoglobin, troponin T, and CK-MB mass in ruling out an acute myocardial infarction in the emergency room. Circulation 1995 Dec;92(12):3401-3407.

13. Haaf P, Drexeler B, Reichilin T, Twerenbold R, Reiter M, Meissner J, Schaub N, Stelzig C, Freese M, Heinzelmann A, et al. High-sensitivity cardiac troponin in the distinction of acute myocardial infarction from acute cardiac non-coronary artery disease. Circulation 2012 Jul;126(1):31-40.

14. Christenson E, Christenson RH. The role of cardiac biomarkers in the diagnosis and management of patients presenting with suspected acute coronary syndrome. Ann Lab Med 2013 Sep;33(5):309-318.

15. Ross G, Bever FN, Uddin Z, Hockman EM. Troponin I sensitivity and specificity for the diagnosis of acute myocardial infarction. J Am Osteopath Assoc 2000 Jan;100(1):29-32.

16. Patil SM, Banker MP, Padalkar RK, Pathak AP, Bhagat SS, Ghone RA, Phatake AS. The clinical assessment of ischaemia modified albumin and troponin I in the early diagnosis of the acute coronary syndrome. J Clin Diagn Res 2013 May;7(5): 804-808.

17. Anwaruddin S, Januzzi JL, Baggish AL, Lewandrowski EL, Lewandrowski KB. Ischemia modified albumin improves the usefulness of standard cardiac biomarkers for the diagnosis of myocardial ischemia in the emergency department setting. Am J Clin Pathol 2005 Jan;123(1):140-145.

18. McComb JM, McMaster EA, MacKenzie G, Adgey AA. Myoglobin and creatine kinase in acute myocardial infarction. Br Heart J 1984 Feb;51(2):189-194.

19. Palladini G, Campana C, Klersy C, Balduini A, Vadacca G, Perfetti V, Perlini S, Obici L, Ascari E, d'Erill GM, et al. Serum N-terminal pro–brain natriuretic peptide is a sensitive marker of myocardial dysfunction in AL amyloidosis. Circulation 2003 May;107(19):2440-2445.

20. Young GP, Gibler WB, Hedges JR, Hoekstra JW, Slovis C, Aghababian R, Smith M, Rubison M, Ellis J. Serial creatine kinase-MB results are a sensitive indicator of acute myocardial infarction in chest pain patients with non diagnostic electrocardiograms: the second Emergency Medicine Cardiac Research Group Study. Acad Emerg Med 1997 Sep;4(9):869-877.