MEDICAL CHANNEL

Original Article

COMPARISON OF IMA VERSUS CTN-I IN ACUTE CHEST PAIN PATIENTS FOR EARLY DIAGNOSIS OF MYOCARDIAL ISCHEMIA IN EMERGENCY DEPARTMENT

1. **JAI PARKASH PANJWANI**
2. **KHEMOMAL A. KARIRA**
3. **JAGDESH**
4. **MUHAMMED ILTAF**
5. **MUHAMMED YOUSIF MEMON**

1. **Assistant Professor**
   Department of Biochemistry
   Baqai Medical University, Karachi, Pakistan.
2. **Professor & Head**
   Department of Biochemistry
   Sir Syed College of Medical Sciences, Karachi, Pakistan.
3. **Associate Prof.**
   Head Department of Biochemistry,
   Bhitai Dental & Medical College, Mirpurkhas, Pakistan.
4. **Medical Technologist**
   Department of Biochemistry,
   Basic Medical Sciences Institute, Jinnah Postgraduate Medical Centre, Karachi, Pakistan.
5. **Associate Professor**
   Department of Biochemistry,
   Liaquat University of Medical & Health Sciences, Jamshoro, Pakistan.

Correspondence:
Dr. Jai Parkash Panjwani
Flat No. 106, Second Floor,
Alwaheed Homes Apartment,
Ferrere Town, Clifton, Karachi,
Pakistan.
Tel: 021-35684305
Mob: 0333-7556474
Email: amanjai22@yahoo.com
aashishjai22@yahoo.com

ABSTRACT

Objective: To evaluate the serum level of ischemia modified albumin (IMA) and cardiac troponin-I in patients with chest pain admitted in emergency department of NICVD for early diagnosis of ischemic heart disease prone to myocardial infarction by observing the sensitivity and specificity of coronary heart disease.

Material and Methods: Present study was carried out in the Department of Biochemistry, BMSI, JPMC; in collaboration of National Institute of Cardiovascular Diseases (NICVD) Karachi. 228 patients out of 1050 were randomly selected who have continuously chest pain for three hours and were divided in three groups. In Group-A patients having chest pain continuously for three hours with normal ECG and Troponin-I (n = 66), Group-B patients with chest pain have developed ECG changes within three hours (n = 72), Group-C patients with chest pain followed by myocardial infarction with increased Troponin-I (n = 90), in addition 54 normal healthy controls subjects were taken from general population for comparison.

Results: The result showed that the mean values of ischemia modified albumin (IMA) in healthy subjects were 22.40 ± 1.46, and in three groups of patients were 40.0 ± 2.79, 85.52 ± 2.10 and 95.31 ± 1.66 respectively. When these values were compared to each other group-A showed statistically significant difference with control, while group-B showed statistically significant difference ($p < 0.01$) with normal control and group-A, where as group-C showed statistically significant difference with normal control and group-A and B. Similarly the mean cTn-I values were 0.12 ± 0.01, 0.13 ± 0.01, 0.41 ± 0.01 and 0.63 ± 0.01 respectively. When these values were compared with each other, group-B showed statistically significant difference ($p < 0.01$) with normal control and group-A, where as group-C showed statistically significant difference with normal control and group-A and B. The sensitivity and specificity among chest pain with normal ECG subjects was 18.2 % and 25.9 %, while chest pain patients with ECG changes showed 62.5 % and 44.2 %; where as in chest pain with M.I. and increased cTn-I subjects was 83.3 % and 58.7 % respectively. Thus sensitivity of IMA > 85 U/ml confirmed that these chest pain patients having angina later will prone ECG changes and may progress to myocardial infarction.

Conclusion: We strongly recommended that serum IMA level should be routinely performed at the time of admission in combination with measurement of cardiac troponin-I and ECG, to confirm or exclude a final diagnosis of ischemic heart disease and to exclude myocardial infarction.

Key Words: IMA, cTn1, ECG, CHD, IHD.

INTRODUCTION

Acute chest pain suggestive of unstable angina (UA) or acute myocardial infarction (AMI) accounts for about six million hospital admissions per annum in the USA. Only

17% of these are finally diagnosed as acute coronary syndromes (ACS) caused by ischemic heart disease[1]. Patients with acute chest pain suggestive of ACS present with a heterogeneous array of conditions, including non-ischemic chest pain (NICP), transient myocardial ischemia, unstable angina, ST segment elevation myocardial infarction (STEMI), and non-ST segment elevation infarction[2].

Ischemia occurs when there is a supply demand mismatch in cardiac blood flow. In unstable angina, this occurs due to partial or total occlusion of a coronary artery due to plaque rupture. In stable angina, there is progressive vascular occlusion resulting ultimately in a stenosis of more than 70% impairing blood flow. If the ischemia is reversible, no myocardial damage occurs where as if the ischemia is prolonged; there will be cellular necrosis and myocardial infarction[3].

Diagnosis of ischemia is difficult in patients presenting with acute chest pain, particularly those with un-interpretable baseline ECGs, normal ECG during pain and/or without evidence of myocardial necrosis. None of the traditional clinical variables, ECG, biochemical markers of necrosis, and imaging techniques can be considered a true ''gold standard'' for the diagnosis of cardiac ischemia[4]. Although cardiac ischemia is highly probable in the presence of ST segment or T wave changes[5].

Ideally, it is essential to identify myocardial ischemia before the onset of irreparable myocardial cell damage. Thus, identification of a biochemical marker that is sensitive and specific for myocardial ischemia and can be rapidly measured in serum would be clinically valuable[6].

Currently, there are no well-defined biochemical markers for identification of myocardial ischemia in non-acute myocardial infarction individuals. Biochemical markers such as CK-MB, Cardiac Troponin-I (cTnI) and myoglobin, used in assessing cellular necrosis, are inappropriate for assessing myocardial ischemia[7]. In cases with cardiac ischemia, rather than necrosis, it may be more difficult to confirm the diagnosis when the patient has acute chest pain, non-diagnostic electrocardiograms (ECG), and normal biomarkers for necrosis. This diagnostic target is still in its infancy and there is no "gold standard" for accurately assessing myocardial ischemia[8].

Ischemia Modified Albumin (IMA) may be a sensitive and early biochemical marker of ischemia in patients presenting with symptoms of acute chest pain[2] and appears to be useful for ruling out acute coronary syndrome in patients attending the emergency department with chest pain suggestive of myocardial ischemia[9]. IMA is produced when ischemia stresses released from hypoxic heart tissue induce modification of circulating albumin[8]. IMA is defined as albumin modified by the free radicals produced in ischemic tissues[10].

Previously there was no gold standard marker for myocardial ischemia and this is one of the main challenges faced in the testing of a marker such as IMA. This marker may improve our ability to identify ischemic patients who are missed by current diagnostic strategies or more confidently rule out non acute coronary syndrome patients. On the contrary IMA has high sensitivity but low specificity in the diagnosis of acute coronary syndrome as compared to troponin which has low sensitivity but high specificity[2]. In relation to Troponin-I albumin cobalt binding, can occur within minutes of an ischemic event via induced endothelial and extracellular hypoxia, acidosis, free radical injury, and sodium and calcium pump disruptions. This effect on albumin could be detectable up to 6 h after the ischemic event[11] and return to base line within 24 hours[12]. Based on this premise, any IMA increase compared to Troponin at the time of admission to an emergency department might be interpreted as an indicator of ischemia before necrosis[13].

SUBJECTS AND METHODS

Present study was carried out in the Department of Biochemistry, BMSI, JPMC; in collaboration of National Institute of Cardiovascular Disease (NICVD) Karachi. 228 patients out of 1050 were randomly selected and included who have continuously chest pain for three hours and classified in three groups. In Group-A patients having chest pain continuously for three hours with normal ECG and Troponin-I (n = 66), Group-B patients with chest pain have developed ECG changes within three hours (n = 72), Group-C patients with chest pain followed by myocardial infarction with increased Troponin-I (n = 90), in addition 54 normal healthy controls subjects were taken from general population for comparison. Statically analysis was obtained through the SPSS-15.

TABLE # 1

Comparison of IMA and Troponin-I of Normal healthy Subjects with study groups

(Values are expressed ± s.e.m. as mean)

Parameters	**Normal Control**(n =54)	**Group-A**(n =66)	**Group-B**(n =72)	**Group-C**(n =90)
IMA (u/ml)	22.40 ± 1.46	40.0 ± 2.79 °	85.52 ± 2.10 ● °	95.31 ± 1.66 ° Δ
Troponin-I (ng/ml)	0.12 ± 0.01	0.13 ± 0.01	0.46 ± 0.01 ● °	0.63 ± 0.01 ° Δ

° **%** Significant as compared to Controls p<0.01; ● Significant as compared to Group A p<0.01; Δ Significant as compared to Group A and B p<0.01.

Group-A = Patients having chest pain continuously three hours with normal ECG and Troponin-I.

Group-B = Patients with chest pain and developed ECG changes.

Group-C Patients with chest pain followed by myocardial infarction with increased Troponin-I.

FIGURE # 1
Comparison of IMA and Troponin-I of Normal healthy Subjects with study groups

FIGURE # 2
Distribution of patients according to chest pain, ECG and Tropinin-I

COLLECTION OF SERUM SPECIMENS

After all aseptic measures, about 8 milliliters of blood was taken from the antecubital vein and was centrifuged for 5 – 10 minutes at a speed of 2500 – 3000rpm. The serum obtained was stored at -70°C till analyzed. Before analyzing serum was thawed and allowed to attain room temperature.

LABORATORY ASSAYS

Ischemia Modified Albumin (IMA) assayed by using kit— # obtained by——-

Troponin-I was determined by using kit——# obtained by ——

RESULTS

Table # 1 shows the comparison of ischemia modified albumin (IMA) and troponin-I (cTn-I) among control and patients A, B & C groups, the mean values of IMA in controlled was 22.40 ± 1.46, while in patient A,B&C groups were 40.0 ± 2.79, 85.52 ± 2.10 and 95.31 ± 1.66 respectively. When these values were compared to each other group-A showed statistically significant difference with control while group-B showed statistically significant difference ($p < 0.01$) with normal control and group-A, where as group-C showed statistically significant difference with normal control and group-A and B. Similarly the mean cTn-I values were 0.12 ± 0.01, 0.13 ± 0.01, 0.41 ± 0.01 and 0.63 ± 0.01 respectively. When these values were compared with each other, group-B showed statistically significant difference ($p < 0.01$) with normal control and group-A, where as group-C showed statistically significant difference with normal control and group-A and B.

As a whole this table indicates progressive rise in IMA level followed by ECG changes and developed M.I in some chest pain patients within three hours. The result of table # 1 & represented in figure # 1.

Table # 2 shows the distribution of patients with sensitivity and specificity according to the chest pain, ECG and troponin-I level. Out of sixty six chest pain with normal ECG patients (Group-A),

TABLE # 2

Distribution of patients according to chest pain, ECG and Tropinin-I

Parameters	Chest pain with normal ECG (n=66)	Chest pain with ECG changes (n=72)	Chest pain with MI and ↑ cTn-I (n=90)	P-value
IMA				
> 85 U/ml	12 (18.2 %)	45 (62.5%)	75 (83.3%)	0.001 *
d” 85 U/ml	54 (81.8 %)	27 (37.5%)	15 (16.7%)	
Sensitivity	18.2%	62.5%	83.3%	0.001 *
Specificity	25.9%	44.2%	58.7%	

twelve (18.2%) patients had IMA levels more than 85 U/ml and fifty four (81.8%) patients had IMA levels equal and or less than 85 U/ml, while out of seventy two chest pain patients with ECG changes (Group-B), forty five (62.5%) subjects had IMA levels more than 85 U/ml and twenty seven (37.5%) patients had IMA levels equal and or less than 85 U/ml. Meanwhile out of ninety chest pain with M.I. and increased cTn-I patientts (Group-C), seventy five (83.3%) patients had IMA levels more than 85 U/ml and fifteen (16.7%) patients had IMA levels equal and or less than 85 U/ml.

The sensitivity and specificity among chest pain with normal ECG patients was 18.2 % and 25.9 %, in chest pain patients with ECG changes was 62.5 % and 44.2 %; where as in chest pain with M.I. and increased cTn-I patients was 83.3 % and 58.7 % respectively. Thus sensitivity of IMA > 85 U/ml confirmed that these chest pain patients have angina, later will prone ECG changes and may progress to myocardial infarction. In summary it is concluded that patients with chest pain having high serum value of IMA > 85 U/ml were the patients of coronary artery disease suggested that these patients should be monitored with proper treatment at early stage to care from myocardial infarction. The result of table # 2 is also shown in figure # 2.

DISCUSSION

The symptoms of patients with myocardial ischemia and/or infarction can be diverse. Although not specific for myocardial ischemia / infarction, chest pain is one of the earliest and most common symptoms in patients presenting to the emergency department [14].

The results of our study showed that IMA is a useful marker for the diagnosis of ACS. There is a significant relationship between the results of cTn-I, a measure of myocardial necrosis and IMA, and a measure of ischemia, in evaluating patients with ACS.

Our study showed that IMA level in group-A, B and C were found very significantly higher than in normal healthy individuals. Significant difference was seen in chest pain with ECG changes when compared with chest pain patients with normal ECG, this is justified according to many research studies. Bar-Or *et al*.,[7] observed the same results and stated that IMA is a useful marker for the early diagnosis of myocardial ischemia. Similarly Sinha *et al*., [2] and Bar-Or *et al*.,[15] described higher levels of IMA in chest pain with ECG changes than in normal ECG patients and control. In present study we observed increased IMA as a diagnostic factor for early diagnosis of myocardial ischemia and observed significant elevated levels of IMA in most of the chest pain patients. These findings are in agreement with the study of Sameer *et al*., [14] who found high level of IMA in chest pain patients.

In our study IMA and cTn-I was correlated positively with age in chest pain with ECG changes (Group-B) and chest pain and diagnosed MI patients (Group-C), is in agreement with Sameer *et al*.,[14] and Kim *et al*.,[16]. Although the underlying mechanism remains unknown, it has been suggested that the association between age and IMA could be related to age-induced changes and life style.

Sinha *et al.,* (2004)[2] stated that a very high sensitivity (85%) of IMA can help the cardiac emergency room to identify the cardiac and non-cardiac chest pain cases. In our study we also observed (83%) sensitivity of IMA in chest pain. Our results are in complete agreement with the studies of Bar-Or *et al*.,[15] and Christenson *et al*.,[11] where the sensitivity of 82% for the IMA assay has been reported. IMA appears to establish itself as the marker for cardiac ischemia where as cTn-I should be used to follow up the cases with overt infarction.

CONCLUSION

In summary our study showed for the first time that the sensitivity of IMA for the diagnosis of acute ischemic chest pain is greater valuable than with ECG and cTn-I. Our hypothesis may propose that measurement of IMA can be used at admission, in combination with measurement of cardiac troponin-I and ECG, to confirm or exclude a final diagnosis of ischemic heart disease and to exclude myocardial infarction.

RECOMMENDATION

This study is being conducted 1st time in Pakistan, which isolate cardiac from non-cardiac patients admitting with chest pain in cardiology department. Therefore we strongly recommend serum IMA as a diagnostic biochemical tool for diagnosing cardiac ischemia and must be routinely done in the emergency unit of Cardiology Department.

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