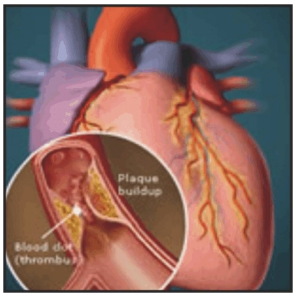
ORIGINAL **PROF-917**

ACUTE MYOCARDIAL INFARCTION



DR. ISHTIAQ AHMED MALIK, FCPS
Cardiologist
AFIC Rawalpindi

DR. KHALID MAHMOOD, MBBS,
PG Trainee Med
CMH Peshawar

DR. M KHALID RAJA, FCPS
Head of Cardiology Department
AFIC/NIHD Rawalpindi

ABSTRACT ... dr_ishtiak@yahoo.com. Acute myocardial infarction is still one of the major killers of mankind. Minute' means muscles i.e earlier the management is started in the form of thrombolytic therapy, better is the prognosis. For this purpose researchers all over the world are striving hard to find the tests, which can be used in making the early diagnosis. Rapid Troponin-T test is a new addition to the better of tests. **Design:** A prospective study. **Setting:** In Armed Forces Institute of Cardiology. **Period:** From Jan 2004 to Jan 2005. To study the comparative efficacy of rapid trop-T test verses conventional biochemical markers like creatine kinase MB (CK-MB) and Lactic Dehydrogenase (LDH). **Material & Methods:** Fifty patients of both sexes and all age groups fulfilling WHO criteria of new onset acute myocardial infarction were included in the study. Rapid Trop-T test, CK-MB and LDH were performed on every patient at 0,2,4,6,12 and 24 hrs on day one, and daily from 2 to 7 days. Rapid Trop-T assay had almost same sensitivity & specificity as CK-MB in early hours after infarction and LDH in the next few days after infarction, this test has few clear advantages of being easy to perform, requiring no special equipment and expertise, and can be a useful tests at peripheral hospitals lacking good laboratory setup.

Key Words: Myocardial Infarction, Troponin-T, Creatinine Kinase, Lactic Dehydrogenase.

INTRODUCTION

The prevalence of Coronary Artery Disease (CAD) has increased to alarming proportion in the last couple of decades. Acute myocardial infarction is one of the commonest diagnoses occurring in hospitalized patients in the world. In the United States 1.5 million myocardial infarction occur each year[1].

Although the disease was thought to be comparatively less common in our part of world, Probably due to changing life style, emergence of new risk factors in causation of coronary artery disease, increasing awareness of disease and better diagnostic aids have been contributory to high prevalence of disease during last decade. In Pakistan 46% of cardiac deaths are due

to myocardial infarction and 27% due to other subsets of ischemic heart disease[2].

Mortality with acute infarction is approximately 25%. A part from the other reasons, one of the very important reasons for this mortality is perhaps delayed diagnosis of the disease. On the other hand, and perhaps equally important is the fact, that out of millions of patient admitted in coronary care units to confirm the diagnosis of acute myocardial infarction, only 30% have confirmed diagnosis of myocardial infarction in the end[3].

The reason for this lack of diagnostic efficiency is the lack of a set of tests with adequate ability to distinguish patients with active ischemia or necrosis from those without these conditions. Currently, the triage of such patients hinges on careful history taking, physical examination and electro cardiographic (ECG) evaluation.

Although the ECG is extremely valuable when it reveals ST- segment elevation, reversible depression, or T-wave inversion, many patients with acute ischemic syndromes do not demonstrate these findings in early hours of attack. Then during early hours after presentation, tests for cardiac enzymes such as creatine kinase (CK) or the CK-MB isoenzymes are associated with inadequate sensitively to be of value in making the critical decision regarding further management[4].

So present research is focused on finding a cardiac marker for acute myocardial infarction, which should confirm the diagnosis in doubtful cases, which is more specific and becomes abnormal/diagnostic very early in the course of infarct, to allow early intervention in the form of thrombolysis or primary angioplasty.

In this regard many biochemical markers are being evaluated. Our study was mainly focused on troponin T (TnT) versus, creatine kinase –MB (CK-MB) and Lactic Dehydrogenase(LDH). By no means it would suffice the significance of the subject, nevertheless an attempt has been made to highlight the more important aspects of the issue.

PURPOSE OF STUDY

The study was carried out to determine the: -

a. Comparison of Tropnin T Rapid Assay with other cardiac markers like serum CK-MB and LDH, in the diagnosis of acute myocardial infarction.

b. To find out the relative sensitivity and specificity of Troponin T in diagnosis of acute myocardial infarction.

MATERIAL AND METHOD

A prospective study carried out in Armed Forces Institute of Cardiology Rawalpindi from January 2004 to January 2005. Fifty patients of all age groups and both sexes presenting with following clinical features were included in study:-

a. Non traumatic chest pain of more than thirty minutes, but less than twelve hours duration.

b. Pain unresponsive to sublingual nitroglycerin.

c. Admission ECG ST segment elevation of more than two mV in anterior chest leads, or more than one mV in limb leads.

Following investigations were performed in every case;

a. ECG, on arrival in cardiology department and six hourly for one day, then once daily.

b. Cardiac Enzymes; On arrival of the patient then at two, four, eight, twelve and twenty four hours on first day and then once daily for seven days.

c. Troponin T rapid Assay which is a qualitative immunological test for the detection of Troponin T in the blood was performed with a test card containing monoclonal antibodies, on bed side according to following protocol:-

1 On arrival of the patient in cardiology

department.

2 At two, four, eight and twenty four hours on first day.

3 Once daily from day two to seven.

Here we would like to mention this test in little detail, with the help of pipette (provided in the kit) 150 micro liter of the patients heparinized Venus blood sample was applied on application well of the test card and the results were read after 20 minutes of blood application, and assessment was made according to following criteria.

1 One line (control line) =Negative
2 Two lines (control & signal line)=Positive
3 No line = Invalid

d. Other investigations performed on every case. Blood CBC, Blood Glucose (Fasting / Random), Blood Lipid Profile, Blood Urea, creatinine, electrolytes, LFTs PTTK- Daily, Urine RE and X Ray chest – PA view

Depending on severity assessed by the killip score every patient was put on a cardiac monitor in the first 24-96 hours of admission. Vital signs were recorded every four hours for the first three days, then thrice daily. Final diagnosis of acute myocardial infarction was made with in forty- eight hours of admission on the basis of WHO criteria.

1 Typical chest pain.
2 Unequivocal ECG changes, i.e., a new pathologic Q wave or evolution of a current of injury (ST segment elevation lasting more than 24 hours, followed by T wave inversion).
3 Characteristic rise and fall pattern of serum enzyme levels, for this study we used the following discrimination limits: -

a Serum CK-MB Activity> 24U/Litre
b Serum LDH > 170/Litre

Any patient suffering from typical chest pain (criteria No.1) and meeting one criterion from 2 and 3 was labeled as a case of acute myocardial infarction. On the basis of this, out of 50 patients included in our study 48 were labeled as suffering from acute myocardial infarction and two from unstable angina.

STATISTICAL ANALYSIS

All the data was entered in computer and receiver operating characteristic curves were constructed to compare the diagnostic performance of rapid Troponin T assay, serum CK-MB and LDH. Level of significance was put at ($P \leq 0.05$).

RESULT

The results of our study are given in the tabulated form as mentioned in the following tables, on the next few pages, with detailed discussion and conclusion in the end of the study.

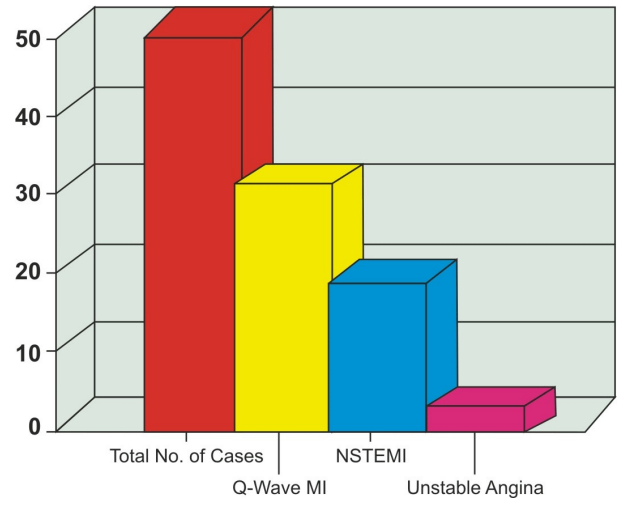


Fig-1. Dfinal diagnosis of patients on the basis of WHO criteria

Table shows that 85% of patients included in our study were between 41-60 years of age. One reason for this comparatively younger age group as compared to other studies may be that majority of patients admitted in military hospital are serving personnel, and therefore relatively young.

Table-I Age incidence in case of acute myocardial infarction		
Agr group	**No**	**% Age**
31-40 Years	4	8.3
41-50 Years	19	39.6
51-60 Years	22	45.7
61-70 Years	3	6.3

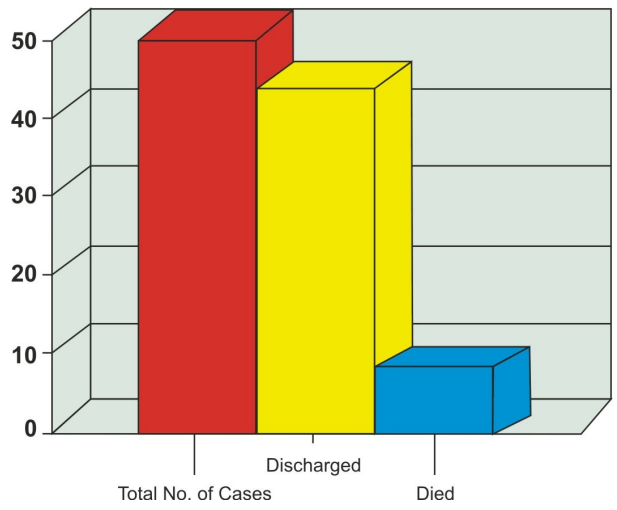


Fig-2. Final outcome of patients, after 7 days

Table-II Sex prevalence in case of acute myocardial infarction		
Sex	**No**	**% Age**
Male	40	83.3
Female	8	16.7

This tables shows that a very high percentage of patients (66.67%) were smoker and equally important is the fact that more than 30% had high blood cholesterol levels.

Total No of Cases were 50, AMI 48 and Unstable Angina were 02.

As shown in the table, out of 48 patients finally diagnosed as suffering from acute myocardial infarction 40 (83.3%) were males and 8 (16.7%) were females, showing much higher incidence in males.

Table-III Past medical history		
Condition	**No**	**% Age**
Smoker*	32	66.67
Hypertension**	8	61.67
Angina pectoris	16	33.33
Previous AMI	3	6.25
Diabetes mellitus	6	12.5
Hypercholesterolemia***	15	31.25

*Smoker at the time of admission.
**Diastolic blood pressure of more than 95 mm of Hg on admission or history of medical therapy for hypertension or both.
***Total cholesterol of more then 6 mmol/ Liter on admission or medical therapy for hyper cholestrolemia or both.

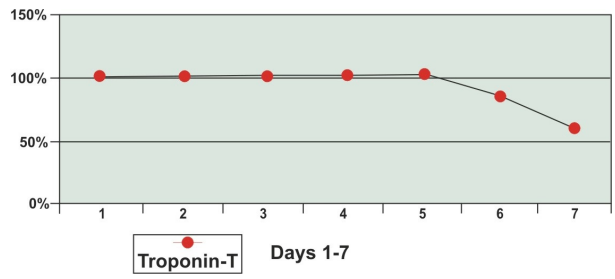


Fig-3. Diagnostic window of individual markers

Table shows that Troponin T rapid Assay was positive in all the 48 cases later diagnosed as AMI according to WHO criteria by the end of 1st day, showing a sensitivity of 100%. In 60% of AMI patients it was positive as early as eight hours after the onset of symptoms, reaching 100% by 12 hours, remaining at this level till day 5, and showing a sensitivity of 54.5% even at day 7.

Table shows that serum CK-MB showed a much earlier sensitivity as compared to Trop T rapid Assay i.e.

became positive in all the 48 patients of AMI 5-8 hours after the onset of symptoms. However, its levels became normal in all patients by the end of 3rd day.

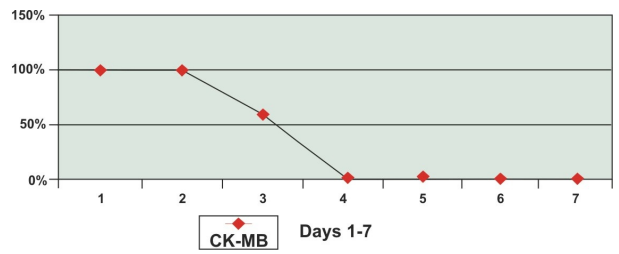
Table-VI Results of Trop-T rapid assay from day 1 - day 7

Time from onset of symptom	No of positive cases		% age of positive cases	
	AMI	Unstable angina	AMI	Unstable angina
0-2 Hours	Nil	Nil	Nil	Nil
3-4 Hours	6	Nil	12%	Nil
5-8 Hours	30	Nil	60%	Nil
9-12 Hours	48	Nil	100%	Nil
12-24 Hours	48	Nil	100%	Nil
2nd Day	43	Nil	100%	Nil
3rd Day	43	Nil	100%	Nil
4th Day	42	Not Done	100%	Not Done
5th Day	42	Not Done	100%	Not Done
6th Day	36	Not Done	81.8%	Not Done
7th Day	24	Not Done	54.5%	Not Done

Table-VII Results of serum-CK-MB levels from day 1 - day 7

Time from onset of symptom	No of positive cases		% age of positive cases	
	AMI	Unstable angina	AMI	Unstable angina
0-2 Hours	Nil	Nil	Nil	Nil
3-4 Hours	20	Nil	41.66%	Nil
5-8 Hours	48	Nil	100%	Nil
9-12 Hours	48	Nil	100%	Nil
12-24 Hours	48	Nil	100%	Nil
2nd Day	43	Not Done	100%	Not Done
3rd Day	25	Not Done	58.14%	Not Done
4th Day	Nil	Not Done	Nil	Not Done
5th Day	Nil	Not Done	Nil	Not Done
6th Day	Nil	Not Done	Nil	Not Done
7th Day	Nil	Not Done	Nil	Not Done

Table-VIII Results of serum - LDH levels from day 1 - day 7				
Time from onset of symptom	No of positive cases		% age of positive cases	
	AM	Unstable angina	AMI	Unstable angina
0-2 Hours	Nil	Nil	Nil	Nil
3-4 Hours	Nil	Nil	Nil	Nil
5-8 Hours	Nil	Nil	Nil	Nil
9-12 Hours	Nil	Nil	Nil	Nil
12-24 Hours	5	Nil	10.24%	Nil
2nd Day	10	Nil	23.25%	Nil
3rd Day	36	Not Done	83.72%	Not Done
4th Day	42	Not Done	100%	Not Done
5th Day	42	Not Done	100%	Not Done
6th Day	40	Not Done	96.25%	Not Done
7th Day	38	Not Done	90.47%	Not Done



Fid-4. Diagnostic window of individual markers

Tables shows that serum LDH was last to rise, showing a sensitivity of only 10.24% on day-1 and 23.25% on day 2, gradually achieving 100% sensitivity on day 4 and 5, dropping to about 90 % on day 7.

DISCUSSION

In this small study, we observed the role of Troponin T rapid assay as marker for the diagnosis of acute myocardial infarction, and its comparison with other markers like serum CK – MB, and LDH. Here it would be worth mentioning that although there are too many studies done on Troponin T, apart from one study conducted by Antman et al in 1995[5], on Troponin T rapid assay there was no other study specifically based on this test.

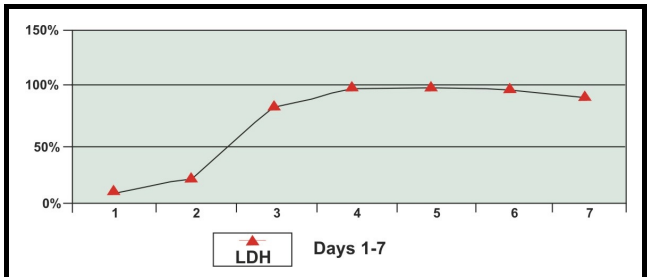


Fig-5. Diagnostic window of individual markers

In the coming few pages we would first discuss few positive aspect of this test observed in our study and then equally important negative aspects of the test in the end.

A. EASY AVAILABILITY, READY TO USE:

Troponin T rapid assay was the most easily available test

in terms of time during our study. For example it took about 60-70 minutes to take the patients blood samples, send it to the laboratory and get the results of serum CK – MB and LDH, while on the other hand only 20-25 minutes were spent in performing/ getting the results of Troponin T rapid assay, thus a saving a 40-45 minutes every time in performing the test.

Secondly it required no special equipment or clinical expertise to perform this test, while a comprehensive laboratory set up is required to perform the CK- MB and LDH levels, making it worth while to use in those emergency departments or small hospitals where these standard tests are not available.

B. LARGE DIAGNOSTIC WINDOW

If we look back at the results of individual markers in our study especially table 6,7 and 8 for a while, it is clear that serum CK –MB has a definite edge over Tropnin T rapid assay in early hours of infarction showing a sensitivity of 100% at 8 hours, as compared to only 60% sensitivity for Troponin T at same time. But on the other hand Troponin T showed a large diagnostic window being positive in 100% of cases till day 5 and 54% of cases till day 7. Whereas CK – MB was normal in all the cases by the end of 3rd day.

Now looking back at the diagnostic window of LDH, although it has equally large diagnostic window as Troponi-T but it has very poor sensitivity in the first twenty four hours. In other words Troponin T rapid assay perform the role of two conventional cardiac markers at the same time i.e. as an early marker as well as late marker of myocardial infarction, again in situations where these conventional markers are not available.

Now lets have a brief look at the other side of picture which is not very bright due to following reasons;

A. COST EFFECTIVENESS

In our laboratory set-up it cost Rs. 200 to perform the serum CK – MB, Rs. 150 to perform the serum LDH and Rs. 650 is the cost of Troponin T rapid assay, making it about three times costlier as compared to conventional markers. In cases where one has to make repeated test to rule out or rule in the myocardial infarction it increases the burden on the pockets of already poor patients of a very poor society.

B. POOR SENSITIVITY IN EARLY HOURS OF INFARCTION: Despite the repeated claims of manufacturer regarding very early sensitivity of Troponin T rapid assay in acute myocardial infarction, it could not be verified in our study rather it showed a sensitivity of only 60% at the end of 8 hours.

In the conditions like acute myocardial infarction where every minute is important in terms of reducing morbidity and mortality, It sounds unwise to recommend such tests if markers like Ck – MB are available which show a sensitivity of 100% at the same time.

The 86% sensitivity was reported in Antman et al 1995, study for Troponin T rapid assay, perhaps one reason for the lowest sensitivity reported in our study may be, that as per the manufactures instruction, Troponin T rapid assay kits should be stored at a temperature of +2˚ to 8˚ C.

In our country most of our chemists do not adhere to or they are unaware of significance of such instructions. Then due to lack of education, our patients are not very reliable historians. These may be the reasons for reduced sensitivity of test observed in our study.

The incidence of ischemic heart disease leading to myocardial infarction is the major cause of cardiac deaths in the world and we are no more an exception from this, rather it has increased manifold because of increase in average age.

Although most of the research today is directed towards prevention of the disease, by identifying the correctable risk factors. But still no one can deny the importance of early diagnosis of this deadly condition where minutes means muscles, because sooner the thrombolytic therapy, or primary intervention is offered, better is the chance for patient to live a normal life.

The fifty patients included in our study were the true reflection of a cross section of Pakistani population drawn from the serving / retired army personals, their families, and civilians attending this institute, so there was diversity of ethnic groups.

To recommend a new biochemical marker for diagnosis of myocardial injury it should have some additional qualities, which the older markers lack.

In this regard as for as Troponin T rapid assay is concerned, we failed to find any additional benefits or qualities of this test apart from those few mentioned in the last paragraph of this section. This statement is based on two reasons:

First of all if we look back at the table 6 and table 7 for the comparison of earlier sensitivity of Troponin T and CK-MB. It is clear that CK-MB possesses much better earlier diagnostic value as compared to Troponin T rapid assay.

For example CK-MB had much superior sensitivity in first few hours of myocardial infarction, where definite therapy is dependent upon earlier diagnosis and indeed the highest priority in the thrombolytic treatment of myocardial infarction is to minimize the delay in the initiation of therapy, regardless of the agent used.

So in the setting of a coronary care unit where CK-MB is usually available, it should be regarded as biochemical marker of choice during early hours of infarction. Another possibility is that, may be in future by reducing the present cut-off value of 0.2ng/ml, Troponin -T rapid assay sensitivity may be increased in early hours to improve its diagnostic efficiency,

Now in case of those patients who present late and whom a retrospective diagnosis of AMI must be made, at a time when CK-MB levels have returned to normal. We are left with two choices i.e. serum LDH and Troponin-T in our study. If we again look back at table 6 and 8, we see that the results of LDH and Troponin-T are not very different from each other, from the 2nd day onwards. So again in a coronary care unit which already has the availability of serum LDH and CK-MB, we do not recommend adding Troponin-T rapid assay in routine cases because it would put extra burden both on the patient (in terms of cost) and the doctors (in terms of work) to perform this additional test.

Another disadvantage of Troponin – T rapid assay is that it cannot be used as a prognostic test, like Troponin-T quantitative immune assay, measured by enzyme linked immunosorbent assay (ELISA) with an ES-300 immune assay analyzer[6], but so for its availability in limited to few selected centers in the country.

CONCLUSION

In the end we would like to list its main advantages observed in our study. These are;

- Bedside availability.
- Easy to perform.
- No special equipment required.
- Quick results.

Although Troponin-T rapid assay was not very sensitive in our study in contrast to the claims of manufacturers. We are of the view that at remote places where advance laboratory services are not available, Troponin-T rapid assay can play a very useful role in combination with history of the patient and ECG findings to segregate the patients, presenting with chest pain of cardiac origin from those of non-cardiac origin, and on the basis of similar findings it has been approved by FDA[7].

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When we are flat on our backs;
there is no way to look but up.

Roger W. Babson