STUDY OF CARDIAC BIOMARKERS IN HEART DISEASE

M.Sc. BIOCHEMESTRY SEMESTER - IV

SUBMITTED TO

DEPARTMENT OF LIFE SCIENCES AND BIOTECHNOLOGY
FACULTY OF SCIENCE

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CERTIFICATE

This is certify that **MR. AMAN KUMAR DURGA PRASAD** has successfully completed the project during the dissertation period from Jan 2023 to Jun 2023 on **STUDY OF CARDIAC BIOMARKERS IN HEART DISEASE** under the guidance of **Dr. PREMLATA PATIL** from **ACE HOSPITAL Kandivali west** .in the partial fulfillment of the requirement for the award of, M.Sc. BIOCHEMISTRY in CHHATRAPATI SHIVAJI MAHARAJ UNIVERSITY, PANVEL, NAVI MUMBAI.

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DECLARATION

I certify that,

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ABSTRACT

Cardiac biomarkers are of great importance in the timely, accurate diagnosis and management of acute coronary syndrome as well as the prognosis. Diagnosis in the golden period is of utmost importance to institute therapy at the earliest and possibly reverse the myocardial damage. Cardiac biomarkers are also a powerful tool for triaging. Among the many biomarkers, the earliest examined were the myocardial enzymes, several myocardial proteins, peptides, and many other molecules. The latest addition to the repertoire is the microRNAs, which are stable molecules detectable in circulation. About four groups are found to be involved in regulation of circulatory system, and some show promise as specific and early markers of acute coronary syndrome and cardiac dysfunction. We review the discovery of key protein biomarkers in the fields of acute coronary syndrome, heart failure, and atherosclerosis, giving an overview of the populations they were studied in and the statistics that were used to validate them. We review statistical approaches that are currently in use to assess new biomarkers and overview a framework for biomarker discovery and evaluation that could be incorporated into clinical trials to evaluate cardiovascular outcomes in the future.

Keywords: cardiology, biomarker development, atherosclerosis, heart failure, acute coronary syndrome, statistical development, acute myocardial infection.

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INTRODUCTION: -

Cardiac biomarkers are endogenous substance (enzymes, proteins, hormones etc.) that are released in blood when heart is damage or stressed. Cardiac biomarkers help healthcare providers know if symptoms are due to a heart attack (myocardial infarction), angina, heart failure or another problem. Increases in cardiac enzymes can also indicate acute coronary syndrome (ACS) or myocardial ischemia. Cardiac biomarkers are central to the new definition of acute myocardial infarction (AMI) biomarker is "a characteristic that is objectively measured and quantified as an indicator of normal biological processes, pathogenic processes or pharmacological response to a therapeutic intervention." Research in this area has broadened our knowledge base, shedding more light on the underlying pathologic mechanisms occurring in patients.

All enzymes–as early as 1954, aspartate amino transferase (AST), followed by lactate dehydrogenase (LDH) in 1955 and creatine phosphokinase (CPK) or creatine kinase (CK) in 1960–from the myocardium were used to diagnose ACS. However, the enzyme assays soon were overtaken by other smaller molecules that were detected much earlier to actual myocardial necrosis and are now mostly obsolete. The isoforms of CK were separated by electrophoresis in 1972 and are very useful in early detection.

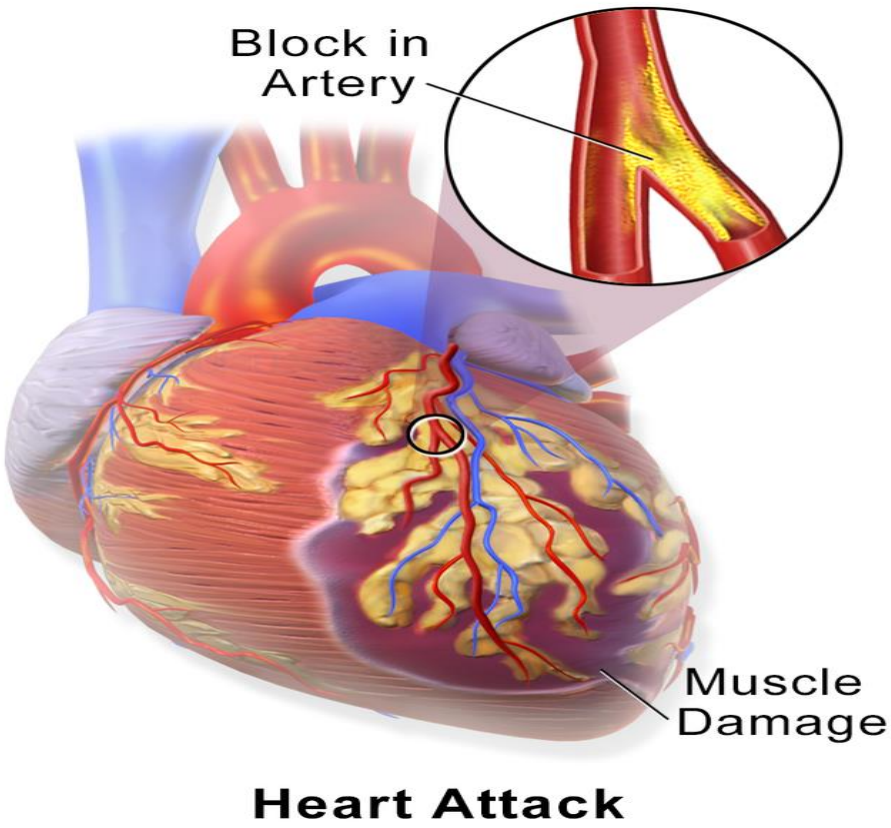


Figure no 1

TYPES: - (A) MARKERS FOR MYOCARDIAL ISCHEMIA.

- CREATINE KINASE (CK)
- CREATINE KINASE MB FRACTION
- MYOGLOBIN – THIS IS SMALL PROTEIN THAT STORE OXYGEN O2
- SGOT (SERUM GLUTAMIC OXALOACETIC TRANSAMINASE)
- LDH (LACTATE DEHYDROGENASE)
- CARDIAC TROPONINS

TYPES: - (B) MARKERS FOR INHALATION OF PROGNOSIS.

- CRP
- HOMOCYSTEINE
- IL-6
- TUMOR NECROSIS FACTOR ALPHA (TNFA)

TYPES: -(C) MARKERS FOR STRESS.

- BNP AND PRO BNP
- APO LIPOPROTEINS
- LIPID PROFILE

HISTORY OF CARDIAC BIOMARKERS

- 1954 - SGOT/AST (Alanine transaminase)
- 1955 - LDH (Lactate Dehydrogenase)
- 1960 - CPK (Creatine phosphokinase)
- 1972 - CPK isoforms by electrophoresis
- 1975 - CK – MB by immune inhibition
- 1975 - Myoglobin
- 1985 - CK – MB Mass immunoassay
- 1989 - Troponin (T)
- 1992 - Troponin (I)

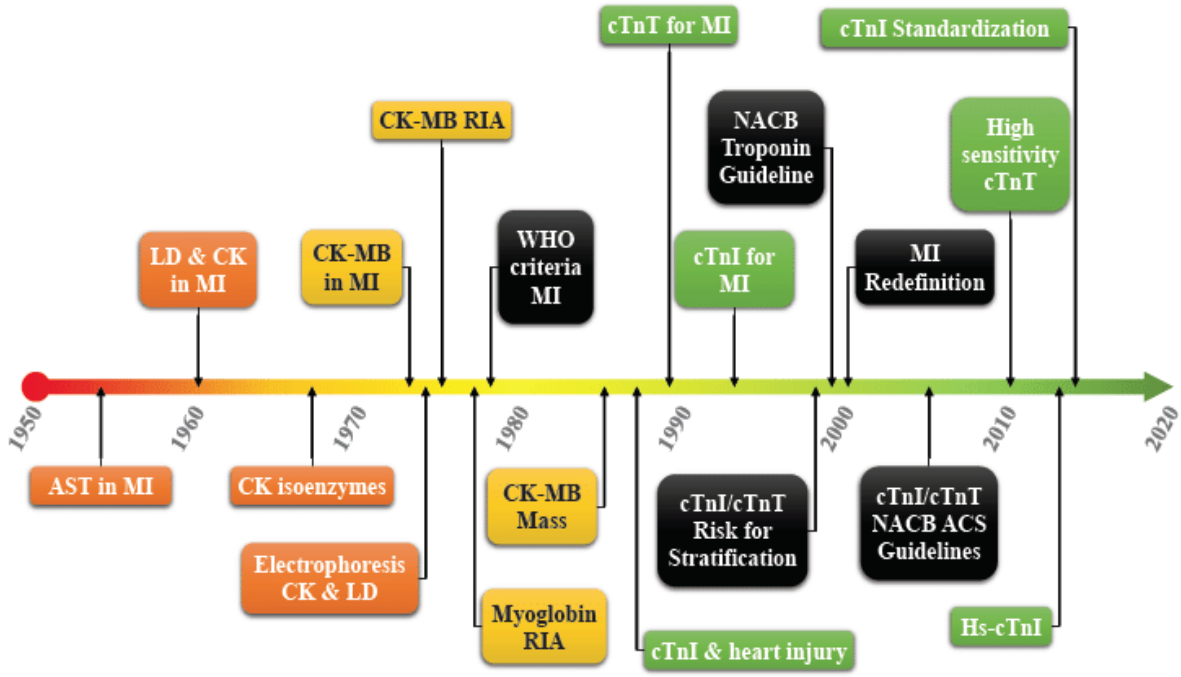


Figure no 2

1954: ASPARTATE AMINOTRANSFERASE (AST)

In 1954, serum glutamic oxaloacetic transaminase (SGOT), now called AST, has been identified as the very first biochemical marker for diagnosis of acute myocardial infection The first method was originally based on paper chromatography and was hence extremely time-consuming. In the same year, a medical student, **Arthur Karmen**, developed a more rapid and practical spectrophotometric method to measure enzyme activity.

Years later, Henry, improved the technique originally introduced by **Karmen**. In the reaction, the oxaloacetate produced by the transaminase serves as substrate for malate dehydrogenase by which it is reduced to malate in the presence of dihydronicotinamide-adenine dinucleotide (NADH), which is simultaneously oxidized. The reaction was monitored by a spectrophotometer as decrease in light absorption at 340 nm. The AST method was then standardized and adapted for use on many automatic analyzers.

AST increases in blood 3–4 hours after acute myocardial infection, reaches the maximum value in blood in 15–28 hours and returns to normal values within 5 days .However, despite the high sensitivity for acute myocardial infection, AST is a non-specific biomarker of cardiac tissue, wherein its activity can also increase in several other conditions including hepatic congestion secondary to congestive heart failure, myocarditis, electrical cardioversion, pericarditis, tachyarrhythmias, pulmonary embolism, and shock.

AST exists in human tissues as two distinct isoenzymes, one located in the cytoplasm (c-AST), and the other in mitochondria (m-AST), which differ in amino acid composition and immunochemical and kinetic properties. In particular, m-AST is infrequently enhanced after myocardial injury, increases later and apparently provides different biological information compared to c-AST . Rabkin *et al*. observed in their study performed on 15 AMI patients evaluated with invasive hemodynamic measurements, that m-AST correlated significantly with the hemodynamic assessment of left ventricular dysfunction of myocardial necrosis.

1955: LACTATE DEHYDROGENASE (LDH)

Hill and Levi were the first to demonstrate the presence of LDH in human blood serum, and one year later Wróblewski and LaDue observed an increase in LDH activity in serum of patients with acute myocardial infection. Ulmer *et al*. confirmed this observation in a study population of 22 acute myocardial infection patients.

Since LDH is present in nearly all human tissues, LDH isoenzymes, either as a-hydroxybutyrate dehydrogenase (HBD) or lactate dehydrogenase isoenzyme 1 activities (LDH-1), were described as possible biomarkers of acute myocardial infection. by providing more organ specificity than total LDH activity . Moreover, LDH-1 activity can be corrected for *in vivo* or *in vitro* hemolysis by measuring the ratio of LDH isoenzymes 1 and 2: the ratio is over 1.0 in acute myocardial infection patients, whereas it remains below 1.0 in samples of patients with hemolysis.

LDH and its isoenzyme LDH-1 increase in blood 5–10 hours after AMI, reach the maximum value in blood in 60–144 hours and return to normal values in 12 days.

1960: CREATINE KINASE (CK) TOTAL ENZYME ACTIVITY

The first spectrophotometric method for assessment of creatine phosphokinase was developed in 1955 by Oliver. Tanzer *et al*. then developed an enzymatic method for creatine and CK determination, characterized by greater specificity and sensitivity than the previous.

The assay for CK total enzyme activity was finally optimized by Rosalki in 1967, by modifying the Kornberg ATP assay . Interestingly, Rosalki developed this method during a dinner and wrote it on the back of the menu card. This method required the addition of creatine phosphate, ADP, and a thiol, and the combination of all reagents in individual gelatin capsules. The modern fully automated clinical chemistry analyzers use now the same basic reagents, only slightly modified and optimized.

It was only in 1960 that the CK activity was shown to be a potential biomarker of cardiac muscle injury.

Since CK appears in blood 3–9 hours after an acute myocardial infection, reaches the maximum value in blood in 10–20 hours and returns to normal values in approximately 72 hours, the sensitivity of this biomarker is very high when blood is collected early after the onset of disease. Sorensen reported a sensitivity of 98% in the acute myocardial infection diagnosis when blood was collected within 72 hours after the onset of disease. Moreover, he also demonstrated that patients with high CK activity measurement in the third day had a worse prognosis.

Years later, it was shown that total CK activity may be related to the extent of myocardial infarction and prognosis . On the other hand, this biomarker is characterized by low specificity, since its activity increases considerably in liver, biliary tract, kidneys and skeletal muscles diseases.

1972: CREATINE KINASE MB ISOENZYME (CK-MB) ACTIVITY

The enzyme CK is present in humans in three isoenzymes BB, MM and MB, the name of which originates from the various combination of the M (i.e., muscle) and brain (i.e., brain) isoforms. The CK-MB isoenzyme, which is normally undetectable or very low in the blood, increases in both heart and skeletal diseases by showing highest concentration in cardiac muscle (~22% of the total CK content of myocardium compared to ~1–3% in the skeletal muscle). Several studies confirmed that CK-MB subforums provide a reliable and specific diagnosis with high accuracy in the first hours of onset of cardiac symptoms.

In 1972, Roe *et al*. developed a zone electrophoresis method for the identification and quantitation in serum or plasma of the CK-MB isoenzyme. Successively this biomarker was measured by anion-exchange column chromatography and in 1976, Roberts *et al*. developed a radioimmunoassay (RIA) for CK isoenzymes.

The assays for measuring the enzymatic activity of CK-MB isoenzyme represented important advances, especially in terms of improved specificity. In 1979, the World Health Organization (WHO) included in the criteria for AMI diagnosis the demonstration of typical rise or fall patterns of CK, CK-MB, LDH, or AST activities.

However, several preanalytical or analytical variables (i.e., prolonged storage or inadequate preservation, inhibitors or interference from other enzymes or drugs, pH and ionic concentrations used in the analyses and assay temperature) may influence the CK-MB activity. Moreover, the evidence that the activity of CK-MB can be considerably enhanced in many skeletal muscle disorders and that its concentration is characterized by a relatively slow release from the injured muscle cell, lead to way to additional research aimed to identified more reliable biomarkers.

1978: MYOGLOBIN

Myoglobin is a small (17.8 kDa) globular oxygen-carrying protein found in heart and striated skeletal muscle, with an almost identical amino acid sequence. It is a cytoplasmic protein with a low molecular size and it is rapidly released after myocardial injury. It appears in blood 1–3 hours after AMI, reaches the maximum value in blood in 4–7 hours and returns to normal values after 1–1.5 days. However, because of rapid clearance from blood, myoglobin may "miss" late-presenting patients, and it is less cardio specific than CK-MB.

Myoglobin concentration increases in skeletal muscular dystrophy, trauma, inflammation (myositis) or in presence of acute or chronic renal failure. Moreover, increased myoglobin levels can occur after muscle injections or strenuous exercise and in presence of various toxins and drugs.

The first method to detect myoglobin in serum was a RIA developed in 1978. However, this method was time-consuming and not useful for STAT analysis. Following the development of latex-enhanced immunoassays, myoglobin was introduced in the emergency department setting for identification of acute myocardial infection. An automated non-isotopic immunoassay was also successively developed.

Despite myoglobin has been for long considered as the best marker for ruling out AMI in the emergency room from 3 to 6 hours after the onset of cardiac symptoms, the negative predictive value (NPV) reaches only 89%, at best.

On the other hand, since myoglobin is rapidly cleared from plasma after coronary reperfusion, it has been demonstrated that this biomarker may allow the earliest and best discrimination between reperfusion or no reperfusion in patients treated with intravenous thrombolytic therapy. Moreover, rapid kinetic of myoglobin is important for detecting re-infarction in patients with post-infarction angina when troponins are still elevated, or lese during revascularization procedures.

1985: CK-MB MASS

The introduction of immunologic determination of CK-MB mass (i.e., protein concentration) was an important innovation, which virtually replaced the traditional enzymatic assay. The first "mass" immunoassay for CK-MB was developed in the 1985 and was found to be much more sensitive than the measurement of enzymatic activity. One year later, Vaidya *et al*. developed a monoclonal antibody named "Conan MB" (in honor of a movie featuring the story of a barbarian warrior) directed against the CK-MB . This antibody was successively paired with an antibody to the B subunit of CK-MB. This two-site mass immunoassay is that currently used by all automated immunoassay instrumentation.

CK-MB mass measurement has the advantage to be more stable than the enzyme activity after storage and appears to be more sensitive, by increasing in plasma and serum more rapidly than CK or CK-MB activity. However, it is not sufficiently rapid when compared to myoglobin in the early diagnosis of acute myocardial infection, mostly in the first 6 hours after symptom onset. As for the enzymatic activity, the mass value of CK-MB also increases in many conditions other than acute myocardial infection.

In 1986, serum CK-MB mass measurement/total CK activity ratio was proposed to identify false-positive elevations of CK-MB arising from skeletal muscle. A ratio of less than 3 is consistent with a skeletal muscle source, while ratios greater than 5 are suggestive for a cardiac source. Ratios between 3 and 5 represent a gray zone.

In 1990, rapid enzyme immunoassays for direct mass measurement of CK-MB mass as µg/L were developed.

In the same year Delanghe *et al*. suggested that these immunoassays were less vulnerable to analytical interference and that measurement of CK-MB mass concentration is better suited for infarct sizing than measurement of catalytic activity.

1963: THE DISCOVERY OF TROPONINS

The identification, purification, and characterization of troponins should be almost entirely attributed to Professor Setsuro Ebashi, whose landmark contributions in the early 1960s established the molecular basis of the Ca^{2+}-regulation of muscle contraction. Its first contribution was the demonstration that calcium induced the contraction of actin and myosin filaments. Successively he showed that the muscle relaxing component known at that time as the "Marsh factor" was actually made by vesicles, later named sarcoplasmic reticulum, which contained an enzyme that used ATP energy to remove calcium from the medium by transporting it to their lumen. In 1963, he also demonstrated the existence of a third factor (besides myosin and actin) which conferred calcium sensitivity to actomyosin. This factor, tentatively named "native tropomyosin" because of its similarity with tropomyosin, was later shown to be a complex of tropomyosin and a new complex of proteins named troponins. He proved that this complex is the Ca^{2+}-receptive site and proposed the correct scheme for the molecular mechanism of regulation of contraction and relaxation. In the absence of Ca^{2+}, the contractile interaction between myosin and actin is suppressed by troponin-tropomyosin complex. On increasing Ca^{2+} concentrations, this suppression is removed by the binding of Ca^{2+} to the troponin complex which activates the contraction.

Shortly after the discovery of the troponin complex, Ohtsuky, a graduate student working in Ebashi laboratory, showed, by an electron microscopic study, that it is distributed along the thin filament at regular intervals of about 400 A , thus leading to the construction of a model of thin filament as an ordered assembly of troponin, tropomyosin and actin.

1971: TROPONIN ISOFORMS

In 1971, Greaser and Gergely demonstrated that the troponin complex actually consists of three components which were named TnC, TnI, and TnT on the light of their specific properties: Ca^{2+} binding capacity (TnC), inhibition of ATPase activity (TnI) and tropomyosin binding respectively (TnT) . The existence of the three troponin components and the above nomenclature was generally accepted in 1972 in occasion of the Cold Spring Harbor Symposium on muscle, a meeting which would become a hallmark in the history of muscle study. In the follow ten years, many researcher groups became interested in the study of troponins and the knowledge about these proteins increased rapidly. Once the amino acid sequences of troponin isoforms was finally determined , it became possible to search for the regions of functional significance . Such findings were then followed by a number of studies of fluorescence resonance energy transfer, nucleic magnetic resonance and X-ray diffraction which finally led to the definition of the complete structure of troponin . In the meantime, gene expression studies showed that members of the TnC, TnI, and TnT gene families encode muscle-types specific isoforms differentially expressed in adult fast and slow skeletal muscles as well as in heart muscles. These include a fast skeletal and a slow skeletal-cardiac isoform of TnC , and a fast skeletal, a slow skeletal, and a cardiac isoform of both TnT and TnI (cTnT and cTnI). This exquisitely specific pattern of expression supported the use of cTnI and cTnT as biomarkers of cardiac injury.

Subsequent studies revealed that Mutations in the genes that encoding for two human cardiac Tn components, cTnI (TNNI3) and cTnT (TNNT2), are often responsible for cardiomyopathies .

1987: CTNI ASSAYS

In the 1980s, several research groups started to look at cardiac troponins as possibly specific cardiac biomarkers. Interest in TnI was prompted by the work of Cummins who developed the first RIA for the measurement of cTnI in serum in 1987 . This RIA methodology which was based on polyclonal rabbit antiserum, required two working days to be performed and had 10 ng/mL as the minimum detectable level. In his pioneer study Cummins showed that serum cTnI was elevated within 4 to 6 hours in patients with AMI, reached a mean peak level of 112 ng/mL (range, 20–550 ng/mL) at 18 hours, and remained above normal value for up to 8 days following myocardial injury. Three years later monoclonal antibodies directed against cTnI were described by two independent groups one of which implemented an enzyme-linked immunoassay (ELISA) for quantification of serum cTnI. The assay developed by Bodor *et al.* had a detectable concentration of 1.9 µg/L and a working range of up to 100 µg/L. It required 3.5 hours to be performed . Such cTnI assay showed high specificity for cardiac injury even in the presence of acute muscle disease, chronic muscle disease, chronic renal failure, and after marathon running . During the following 20 years the cTnI immunoassay has been considerably optimized. Current generations of commercially available assays have an analytical sensitivity almost 100-fold higher (1 *vs*. 100 ng/L) than that of the experimental and commercial assays that were initially described. These assays were not fully standardized at this time and studies have documented substantial differences across

methods . The main factors contributing to the quantitative differences between the cTnI methods include the lack of commutable reference material and difference in the antibody immunoreactivity as well as in the antigen used as calibrators . The analytical characteristics of cTn assays currently on market have been recently described by Jarolim.

1989: CTNT ASSAYS

The first generation immunoassay has been developed by Katus and colleagues in 1989. It was based on an ELISA with two antibodies: the capture antibody conjugated to biotin (M7) and the detection antibody conjugated to horseradish peroxidase (lBIO) . This assay, automatized in 1992 by its incorporation onto the ES-analysers (Boehringer Mannheim TM) , had two problems. The first was due to the assay formulation which comprised a completely cardiac-specific capture antibody (with <0.5% cross-reaction to skeletal muscle) and a detection antibody that was only 78% cardiospecific. The 20% cross-reactivity of the second antibody resulted in falsely TnT levels in patients with massive skeletal muscle damage (rhabdomyolysis). Such problem was soon overcome in 1997 with the introduction of the so-called 'second generation' TnT antibodies (M11.7 as capture antibody and M7 as detection antibody), which completely abolished the non-specific binding to skeletal TnT . With this second generation assay, the normal range of cTnT was between 0 and 0.1 µg/L. The limit of detection (LoD) and linearity of this assay were <0.05 and 12 µg/L, respectively.

The second problem was related to the platform. Although the test on the ES-analyser had been fully automated, it was characterized by a turn-around time of over 90 minutes with assays run daily, which was hence inadequate to fulfil requirements for emergency testing. This problem was also overcome by the introduction of the Elecsys TM analyzers, on which the turn-around time of the cTnT test was comprised between 9 (Elecsys 1010) and 18 (Elecsys 2010) min. At variance with the methodology of the ES analyser the Elecsys analyzers is based on electrochemiluminescence immunoassay (ECLIA) technology and uses a ruthenium labelled component instead of the horseradish peroxidase on the detection antibody .

In 1999, the 'third generation' troponin T assay has been introduced. The difference between the second and the third generation is the use of human recombinant cTnT for calibration (third generation) instead of bovine cTnT (second generation), which considerably improved the assay linearity . The fourth-generation cTnT assay, introduced in 2007, used fragment antigen-binding (FAB) of two cTnT-specific mouse monoclonal antibodies in a sandwich format. The antibodies recognized two epitopes located in the central part of the cTnT molecule. The fourth-generation cTnT assay has a LoD of 10 ng/L and a 10% coefficient of variation (CV) at 30 ng/L .

The new high-sensitivity cTnT (hs-cTnT) assay is a modification of the fourth-generation assay, which was implemented in 2010 . In this fifth generation assay the biotinylated capture antibody was not changed, whereas the detection antibody was genetically re-engineered into a mouse-human chimeric detection antibody to reduce the susceptibility

to interference by heterophilic antibodies. The analytical sensitivity was improved by increasing the sample volume from 15 to 50 µL, increasing the ruthenium concentration of the detection antibody, and lowering the background signal through buffer optimization. As a result, the analytic performance of the hs-cTnT assay had been significantly improved; the LoD was 5 ng/L, the 99th percentile cutoff point was 14 ng/L, and the CV was 10% at 13 ng/L.

Due to patent issues, cTnT assays are only available from one manufacturer (Roche Diagnostic). Therefore, in contrast to cTnI, standardization of the cTnT assay is not seen as a major problem. The only inconvenience is the current coexistence of the less sensitive fourth generation assay in the USA and the hs-cTnT assay in most other countries, since the hs-cTnT has not been licensed for use by the FDA so far.

2012: DIAGNOSTIC VALUE OF CTN IN AMI

According to the international consensus and task force definition of acute myocardial infection established in 2012, the diagnosis of AMI is based mainly on evidence of myocardial ischemia, along with an elevated value of cardiac biomarkers above the 99th percentile and demonstration of an increase or decrease over time.

The continuous improvement of the analytical sensitivity and assay precision at the low measuring range of cTn assays has ultimately led to the development of the so-called “hs” cTn assays which finally satisfy this criterion. In order to label a cTn assay as “hs”, the IFCC task force suggested that cTn should be measurable in more than 50% of healthy subjects, and preferably in more than 95% . The term ultra-sensitive is conventionally reserved to cTnI assay capable to quantify cTn at levels below the lowest concentrations seen in healthy subjects . The interest in this additional sensitivity goes beyond the management of patients with suspected MI and is limited to novel application of cTn assays such as measuring changes in cTn levels after exercise stress testing or after cardio toxic chemotherapy. Nowadays, hs-cTn assays are considered the biomarkers of choice in the early diagnosis of acute myocardial infection being able to detect cTn release at an earlier time point than the previous generations of cTn assays, especially in patients with a recent onset of chest pain . Most patients with an acute myocardial infection, can be reliably identified within 3 h after admission, with nearly 100% sensitivity and 100% NPV using a hs-cTn assay, which indicates that observation time in the emergency department may be reduced for rule out of acute myocardial infection . However, in patients with 3 h values unchanged, but in whom pre-test likelihood of acute myocardial infection is high, additional subsequent sampling (e.g., at 2 or 3 h) may still be advisable.

MARKERS FOR MYOCARDIAL ISCHEMIA.

- Creatinine kinase (CK)
- Creatinine kinase MB fraction
- Myoglobin – this is small protein that store oxygen o2
- SGOT (Serum Glutamic Oxaloacetic Transaminase)
- LDH (Lactate Dehydrogenase)
- Cardiac Troponin

1) CREATININE KINASE (CK): -

Creatine kinase CK is an enzyme that mainly exists in heart and skeletal muscle with small amounts in brain. The cells in skeletal muscles, heart muscles or brain muscles release creatine kinase into blood when they are damaged.

An enzyme is a protein that acts as a catalyst to bring about a specific biochemical reaction.Small amount of ck that's normally in blood mainly comes from skeletal muscles that are attached to bones and tendons.

Any condition injury or event that causes muscle damage and interferes with muscle energy production or use increase level of ck in blood for examples intense exercise can increase ck levels muscle disease myopathies such as muscular dystrophy can also increase ck levels.

There are three types of ck enzymes.

- CK - MB: - Found mostly in heart muscles.
- CK – MM: - Found mostly in skeletal muscles.
- CK – BB: - Found mostly in brain tissue.

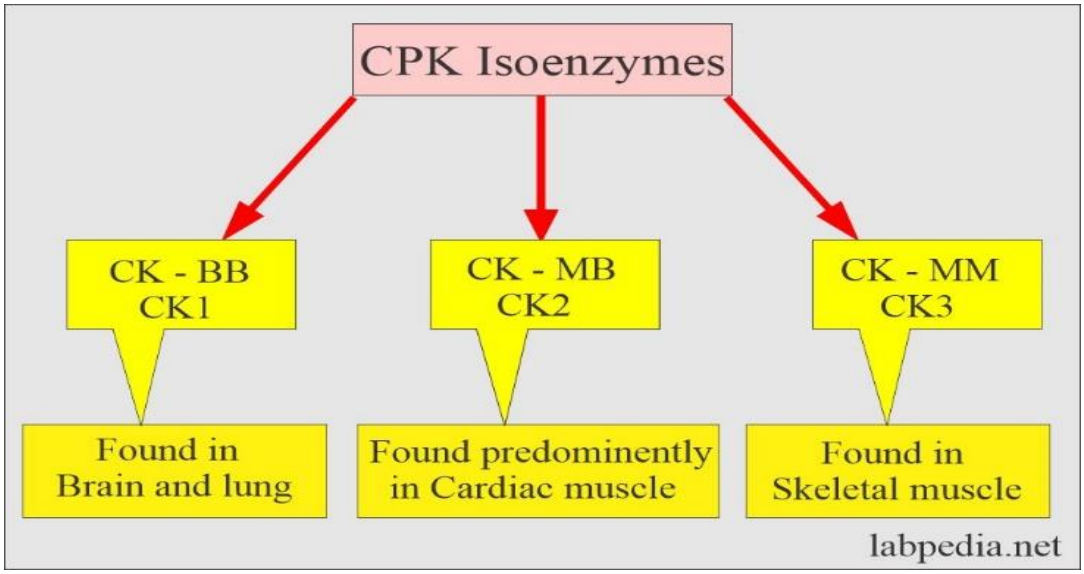


Figure no 3

FUNCTION OF CREATINE KINASE (CK)

The regular function of creatine kinase ck is not really related to what elevated level of it may indicate in blood. Ck's job is to add a phosphate group a group of natural chemical to creatine a substance in muscles cell that helps muscles produce energy. when CK adds phosphates to creatine it turns the creatine into high energy molecules phosphocreatine which body use to generate energy.

CK gets into blood stream when muscles heart or brain experience acute damage or chronic degeneration when muscles are damage the muscles cells brack open and their contents including creatine kinase leak into blood stream.

Creatine kinase to diagnose and monitor the following muscles issues.

- Muscular Diseases.
- Muscular Injuries.
- Muscular Inflammation.

Muscular Diseases: -

Duchene muscular dystrophy (DMD) this is a rare inherited condition that causes weakness, breakdown and less of function of skeletal muscles. It most commonly affects people assigned male at birth.

Rhabdomyolysis : - this condition involves a rapid breakdown of muscle tissue.it can be caused by a serious injury muscle disease or other conditions.

Muscular Injuries:-

Muscular injures can results from the following situation.

- Crushed, compressed torn of strained muscles from accidents or intense exercise.
- Third degree burns.
- Electrocution

Muscular Inflammation:-

Types of muscular inflammation (myositis)

Polymyostis: - this inflammatory muscle disease caused muscle weakness usually in the muscles closest to the trunk of body.

Dermatomycosis's: - this is rare condition that causes muscle weakness and a skin rash.

Pyomyostists :- this is rare bacterial infection of the muscle that often forms an abscess.

CPK release in blood when a muscle is damage CPK leaks into blood stream finding with specific from of CPK is higher determine which tissue has been damage.

2) CREATINE KINASE MB FRACTION (CPK-MB)

This test measures the amount of an isoenzyme of creatine kinase (CK) in blood. It is called CK-MB.

body makes 3 forms of CK, including CK-MB. CK is found in the heart, muscles, and other organs. These include the small intestine, brain, and uterus. If you have a heart attack, injured heart muscle cells release CK-MB into blood.

Because many tissues contain CK, high levels of CK can be a sign of a variety of problems. Higher CK-MB may point more directly to heart damage.

Each year millions of Americans go to the emergency room with chest pain, but only a small amount of those people are having a heart attack or other serious, sudden heart problem. This test helps healthcare provider figure out if you're having a heart attack.

Measuring CK-MB used to be a common tool for diagnosing heart attacks, but healthcare providers use it less often today. Cardiac troponin is now the blood test of choice for finding a heart attack. This is because cardiac troponin is more specific and more sensitive than CK-MB.

Symptoms of a heart attack often include:

- Pain or discomfort in the chest, such as a squeezing sensation or feeling of fullness
- Pain in the neck, back, left arm, or jaw
- Shortness of breath
- Light headedness or dizziness
- Nausea or vomiting
- Sudden sweating
- Tiredness

Although the abovementioned symptoms may be indicative of heart attack.

Levels of CK – MB rise in the serum within 4-6 hours of myocardial infarction and reach a peak in 16-30 hours ,however they also disapper faster than they appear in the bloodstream heance the test needs to be repeated after 48 hours.

CK-MB released any process that disrupts cardiac sarolemmal membrane e.g. myocarditis cardiac trauma or cardiac surgery including endmyocardial biopsy can release cytosolic CK-MB.

It is the most sensitive and the most specificity to indicate available for the diagnosis of an acute myocardial infection.

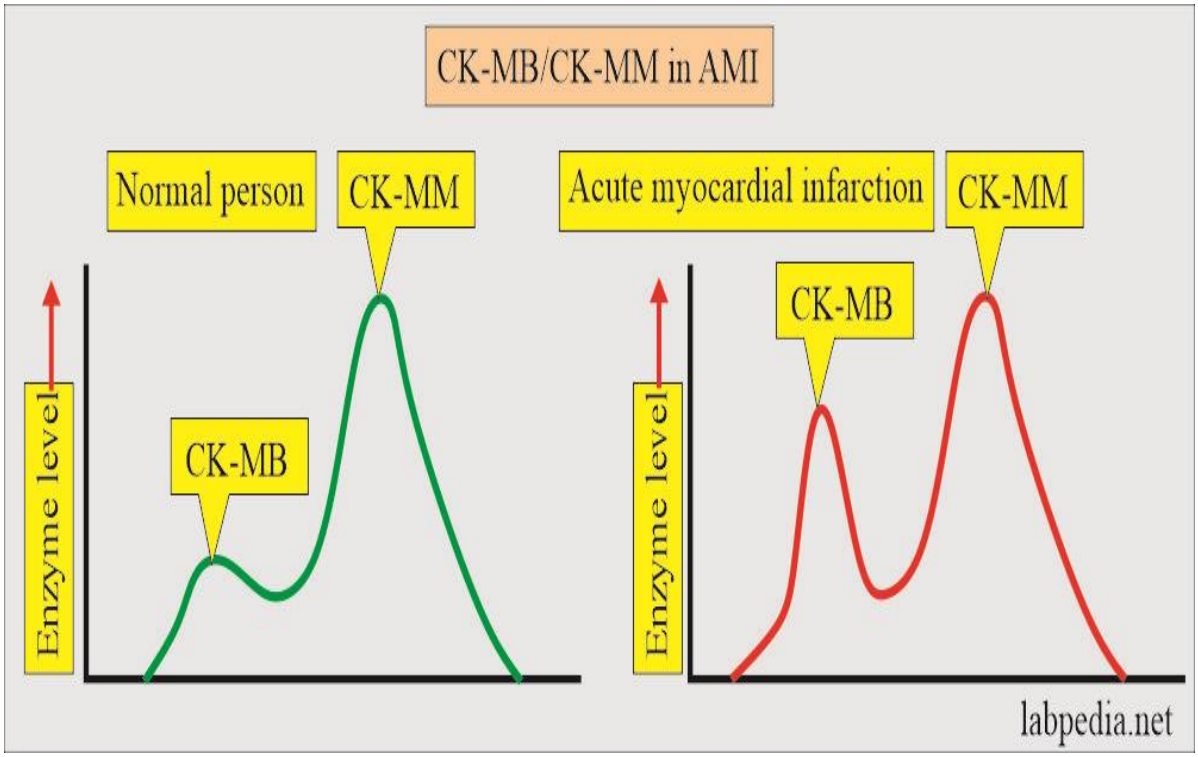


Figure no 4

3) MYOGLOBIN TEST

A myoglobin test measures the amount of myoglobin, a protein found in skeletal muscles (the muscles attached to tendons and bones) and heart muscles, in blood or urine (pee).

All cells in body need oxygen in order to function. They use oxygen to convert stored energy. skeletal muscles and heart muscles require a lot of oxygen and energy due to their constant use.

Healthcare providers may use a myoglobin blood test to detect muscle damage. When heart or skeletal muscles experience an injury, muscle cells release myoglobin into bloodstream. The level of myoglobin in blood can rise very quickly with severe muscle damage, and healthcare providers typically measure it within a few hours following an injury.

kidneys filter out myoglobin from blood and release it into urine. Healthcare providers sometimes use a urine test to evaluate myoglobin levels if you've had extensive damage to skeletal muscles (rhabdomyolysis). Urine myoglobin levels reflect the degree of muscle injury — the more myoglobin in urine, the more severe the injury. Since myoglobin is toxic to kidneys, a urine test can also assess the risk of kidney damage.

Function of myoglobin:-

Myoglobin is a protein that's found in striated muscles, which includes skeletal muscles (the muscles attached to bones and tendons) and heart muscles. Its main function is to supply oxygen to the cells in muscles (myocytes).

All cells in body need oxygen in order to function. They use oxygen to convert stored energy. skeletal muscles and heart muscles require a lot of oxygen and energy due to their constant use.

When would I need a myoglobin test?

healthcare provider may order a myoglobin blood test if you're experiencing symptoms of severe damage to muscles, such as from accidents that result in muscle trauma, or muscular dystrophy.

Symptoms of muscle injury or damage include:

- Muscle pain(cardiac)
- Dark-colored urine.
- Fever.
- Fatigue.
- Nausea and vomiting.
- Abdominal pain.

While healthcare providers have used myoglobin blood tests along with troponin tests to help detect a heart attack early in the past, they now use myoglobin testing less frequently for this purpose. More recent studies have revealed that newer markers, such as troponin, are better for detecting heart attacks.

healthcare provider may order a urine myoglobin test if you have extensive damage to skeletal muscles, resulting in the rapid breakdown of muscle (rhabdomyolysis), and if they suspect that you may have damage to kidneys from excess myoglobin.

The BioCheck Myoglobin Enzyme Immunoassay provides a rapid, sensitive, and reliable assay for the quantitative measurement of myoglobin in serum. The antibodies developed for the test will determine a minimal concentration of 5.0 ng/ml, and there is no cross-reactivity with related cardiac or skeletal enzymes.

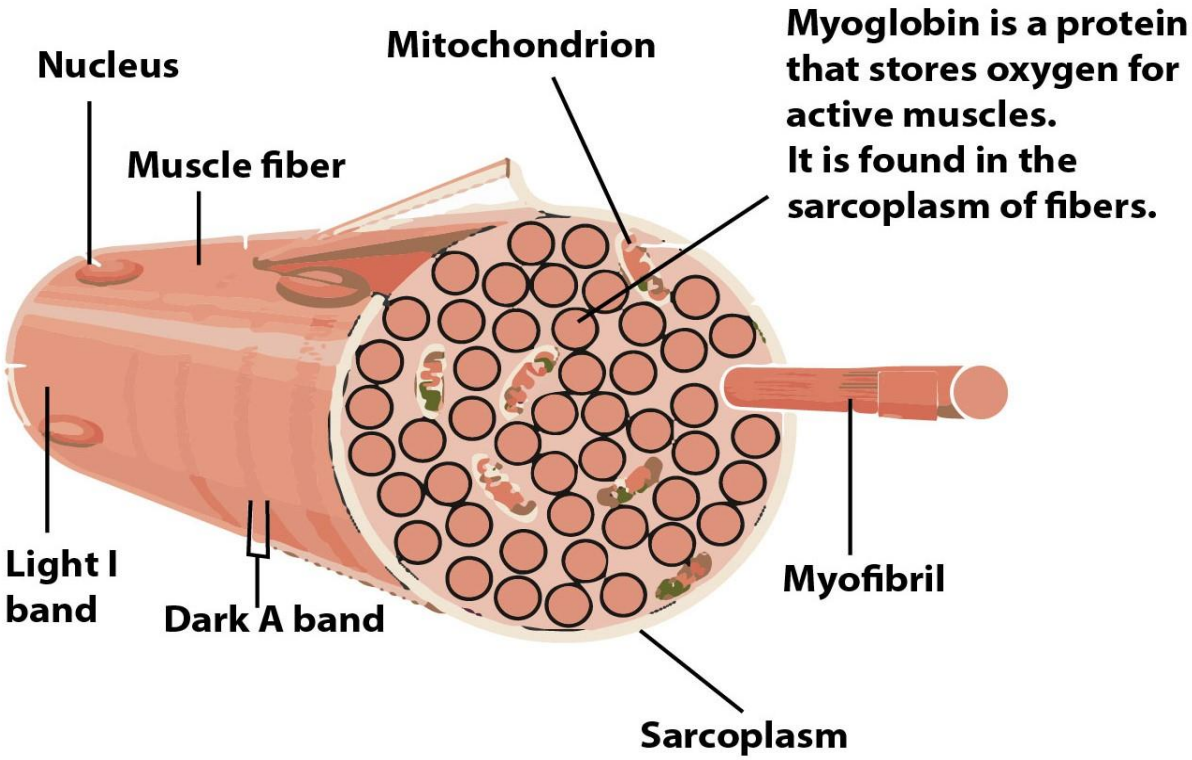


Figure no 5

4) SGOT (SERUME GLUTAMATC OXALOACETATE TRANSAMINASE)

SGOT is an enzyme liver makes. Other organs, like heart, kidneys, brain, and muscles, also make smaller amounts. AST is also called SGOT (serum glutamic-oxaloacetic transaminase).

Normally, AST levels in blood are low. When liver is damaged, it puts more AST into blood, and levels rise.

A high AST level is a sign of liver damage, but it can also mean you have damage to another organ that makes it, like heart or kidneys. That's why doctors often do the AST test together with tests of other liver enzymes. It is commonly referred to as AST, which stands for aspartate aminotransferase**.**

It is an enzyme that is found in tissues apart from bones, including the tissues of the liver, heart, kidneys, skeletal muscles as well as other tissues. The SGOT is an enzyme that liver produces it. Other organs also generate smaller quantities, such as kidney, heart, brain & muscles.

In a healthy man's blood, SGOT levels are low. The standard blood SGOT level is approximately 5 to 40 units per liter of serum. Whenever there is harm to the heart tissues, liver tissues, kidneys tissues, and other tissues, SGOT or AST is released into the blood. A high level of AST is a sign of liver harm, but it could also mean that you have harmed another organ, like kidney or heart, that causes it. This is why doctors also conduct AST tests along with other liver enzyme examinations.

Purpose of the SGOT test

The serum glutamic-oxaloacetic transaminase or SGOT test is mainly done to check the condition of the liver. The primary function of the SGOT or AST enzyme is to help in amino acid metabolism. While the enzyme can be found in the cells of other vital organs, the AST or SGOT test is part of the liver panel tests. The SGOT test is usually prescribed when a person shows the following symptoms:

- Cardiac
- Weight loss
- Nausea
- Weakness
- Yellowing of skin and whites of the eyes
- Pain and swelling in the abdomen, where the liver is present
- Dark color urine
- The stool is pale in color
- Visible swelling in ankles
- Frequent skin itching
- Loss of appetite

The test is also prescribed for people who:

- Have a family history of liver diseases
- Have recently been to a place with a high hepatitis contraction rate
- Are alcoholic, or were alcoholic
- Have diabetes
- Are obese
- Have non-alcoholic fatty liver disease
- Are undergoing treatment for existing liver diseases.

5) LACTED DEHYDROGENASE TEST (LDH)

Lactate dehydrogenase (LDH) is an important enzyme that helps with cellular respiration, the process through which body transforms glucose (sugar) from the food you eat into energy for cells.

Enzymes are proteins that help speed up metabolism, or the chemical reactions in body. They build some substances and break others down. You have LDH in almost all of the tissues in body. Its highest concentrations are in muscles, liver, kidneys and red blood cells.

As new cells form in tissues, body gets rid of older or "dead" cells. This normal process causes tissues to release LDH into bloodstream or other body fluids. Because of this, it's normal to have some LDH in a blood or fluid sample at all times.

An LDH (lactate dehydrogenase) test measures the amount of LDH in blood or other body fluid to check for tissue damage.

While it's normal to have some LDH in blood or body fluids, when tissues in body experience damage or injury, they release excess LDH into bloodstream or other body fluids. If LDH blood or fluid levels are elevated, it may indicate that certain tissues in body have been damaged by a chronic (long-term) or acute (short-term) disease or injury.

LDH tests can't determine which tissues in body are damaged. Because of this, healthcare providers often order other tests alongside LDH tests to help diagnose conditions.

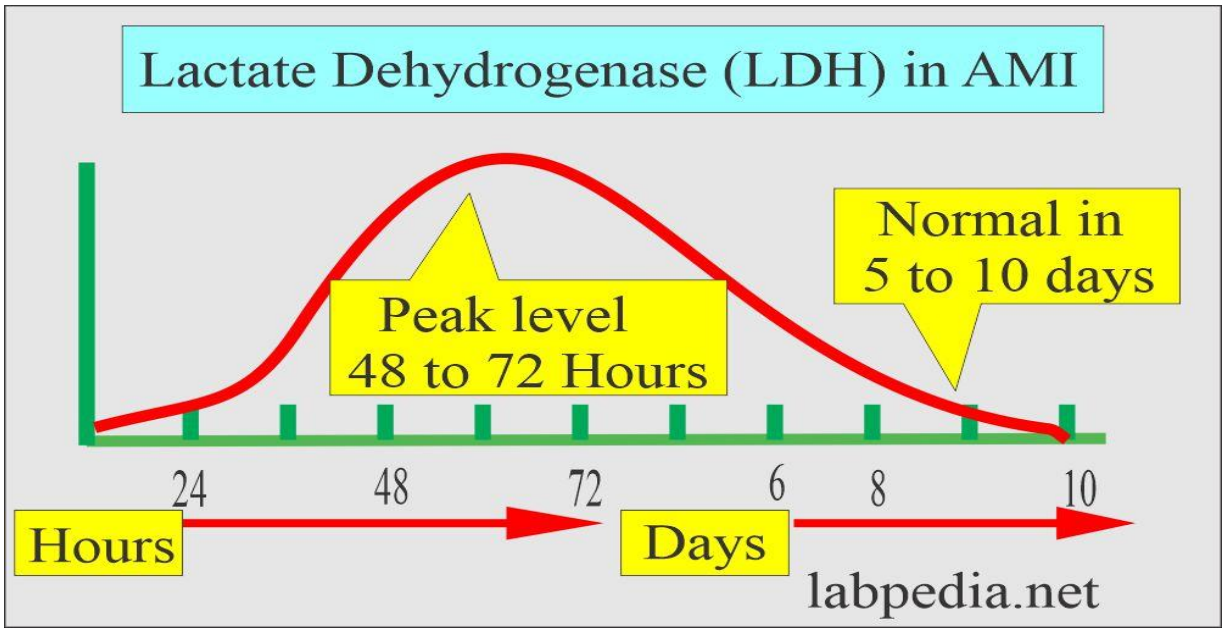


Figure no 6

6) CARDIAC TROPONINE TEST

A troponin test looks for the protein troponin (there are two forms related to heart, troponin I and troponin T) in blood. Normally, troponin stays inside heart muscle's cells, but damage to those cells — like the kind of damage from a heart attack — causes troponin to leak into blood. Higher levels of troponin in blood also mean more heart damage, which can help healthcare providers determine the severity of a heart attack.

Newer versions of this test are much more sensitive and can pick up far smaller amounts of this protein in blood than before. That can speed up the process of diagnosing a heart attack. This test is also useful when other tests are inconclusive or when you have vague symptoms. This test is also known as a cardiac troponin test, or uses the abbreviations cTn, cTnI or cTnT, depending on the specific type of test. Some versions of this test can only detect one type of troponin, while others can detect both.

Troponin is a protein, a complex chemical molecule, found in certain types of muscle in body. Under normal circumstances, it exists inside muscle cells and only freely circulates in bloodstream in tiny amounts. However, damage to certain types of muscle cells can cause more troponin to escape into blood.
There are two types of troponin that are more detectable after heart muscle damage, which use the letters I and T to tell them apart.

- **Troponin I (cTnI).** This kind of troponin is unique to heart muscle.
- **Troponin T (cTnT).** Troponin T does exist in other types of muscle, but the amounts are very limited. The Troponin T in heart muscle also has a slightly different structure, which doesn't occur anywhere else in body.

Troponin levels usually increase sharply within three to 12 hours after a heart attack and peak about 24 hours after the heart attack. They will also remain high for several days.

The most common use of troponin tests is to confirm or rule out a heart attack. However, any kind of damage to heart muscle can potentially cause the release of this chemical into bloodstream. Other conditions that can cause troponin levels to increase include:

- Chronic kidney disease.
- Pulmonary embolism (a blood clot in lungs).
- Congestive heart failure.
- Heart surgery.
- Heart valve diseases.
- Irregular heart rhythms (arrhythmias).
- Sepsis.
- Exercising too much or too strenuously.
- Extreme emotional strain, such as grief or stress.

Other heart conditions that can contribute to high troponin levels include:

- myocarditis, which is inflammation of the heart muscle

- pericarditis, which is inflammation of the sac of the heart
- endocarditis, which is inflammation of the inner layer of the heart
- cardiomyopathy, which is a weakened heart
- heart failure
- stable angina, which is a type of chest pain caused by poor blood flow to the heart

Other possible causes of high troponin levels include:
intense exercise

- burns
- medications, like metoprolol (Toprol XL, Lopressor)
- stroke
- diabetes
- kidney disease
- pulmonary embolism, which is a blood clot in lungs
- hypothyroidism, which is an underactive thyroid
- intestinal bleeding

an extensive infection, like sepsis

7) TROPONIN I TEST (cTnI)

Troponin I is present in both cardiac and skeletal muscles. It is important in the process of muscle contraction. As it is present in the cardiac muscle, it has a value as a cardiac marker as well. Troponin I is a part of the muscle contraction apparatus. This protein is about 24kDa in weight. The main function of troponin I is to aid the formation of the actin-tropomyosin complex. Troponin I binds to the actin molecules to hold the actin-tropomyosin complex in place. The binding of the troponin I to the actin protein result in a conformational change in the protein. This prevents the binding of myosin in the relaxed muscle.

Troponin I can be further categorized based on the distribution of the troponin I. Thus, troponin I can be skeletal muscle-specific troponin I or cardiac Troponin I. Separate genes code for each of the troponins. Therefore, the identification of different troponin levels is possible. The most widely studied troponin I type is the Cardiac Troponin I. This is due to the vital role it plays as a cardiac marker during ischemic heart disease conditions. The cardiac troponin I levels are important in diagnosing myocardial infarction. During infarction, the cardiac troponin I levels go high.

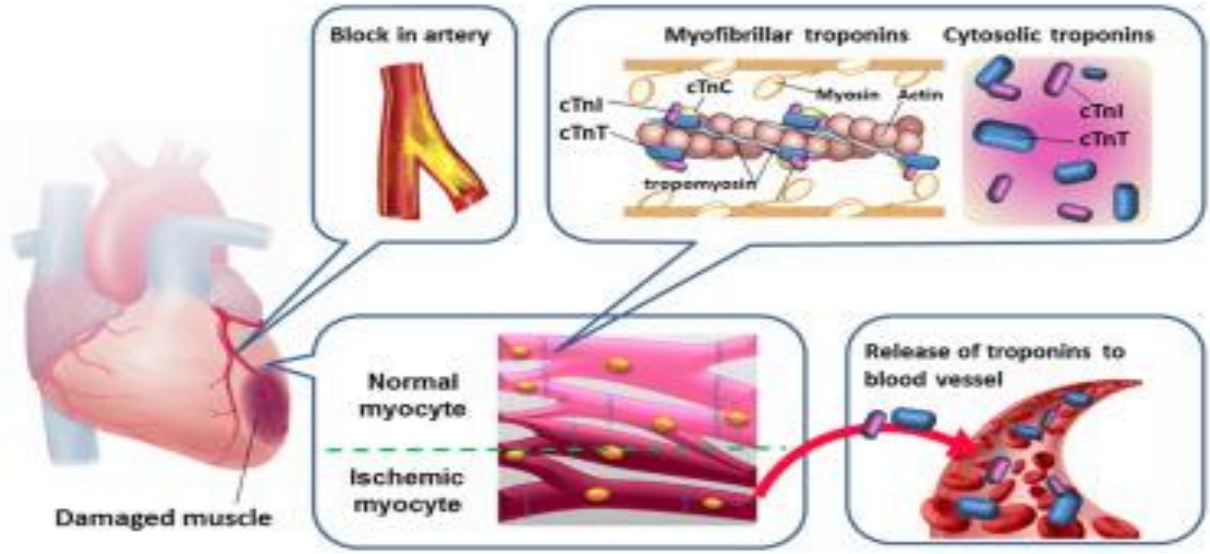


Figure no 7

8) TROPONIN T TEST (cTnT)

Troponin T is also a protein present in both skeletal and cardiac muscles. Similar to troponin I, Troponin T also aids in muscle contraction. Thus, the primary function of troponin T is to bind to the tropomyosin protein and help in the contraction process. The binding of troponin T to tropomyosin cause a conformational change which facilitates the binding of tropomyosin to actin. This initiates the muscle contraction process.
Troponin T protein is also subcategorized based on their distribution. Troponin T is mainly of two types, the skeletal troponin T and the cardiac troponin T. Cardiac troponin T is a widely used cardiac marker for myocardial infarction. The level of cardiac troponin T increases during cardiac conditions. This makes Troponin T a good cardiac marker.

Troponins are the proteins required for the contraction of the skeletal and cardiac muscles. Skeletal muscles help move the limbs and other parts of the body, while cardiac muscles form the wall of the heart and are the part that suffers most damaged during a heart attack. During a heart attack, the flow of blood through the coronary arteries is blocked or limited, which makes the heart muscle cells starve for oxygen. This is when troponin proteins are released into the bloodstream, acting as a biomarker that indicates cardiac injury.

A high-sensitive troponin T test is a very useful diagnostic tool that allows for the detection of even very low levels of troponin T in the blood, which can help diagnose heart attacks more quickly and accurately. The troponin T test can also be used to diagnose other heart-related conditions, like coronary artery disease, angina, congestive heart failure, and cardiomyopathy.

Troponin I

- 90% sensitivity for myocardial infarction 8 hours after onset of symptoms (1); 95% specificity (1)
- low specificity for unstable angina - 36% - note however that there is evidence that (2)
- troponin I elevation is useful for predicting in-hospital risk for unstable angina patients admitted to a community hospital. The association of ECG changes and high troponin I identifies a population at very high risk; however, the absence of both variables in patients with a diagnosis of unstable angina does not preclude the development of events
- rises after 3-6 hours (1)
- peaks at about 20 hours (1)
- general advantages (3)
- troponin T (cTnT) and troponin I (cTnI) are released only following cardiac damage

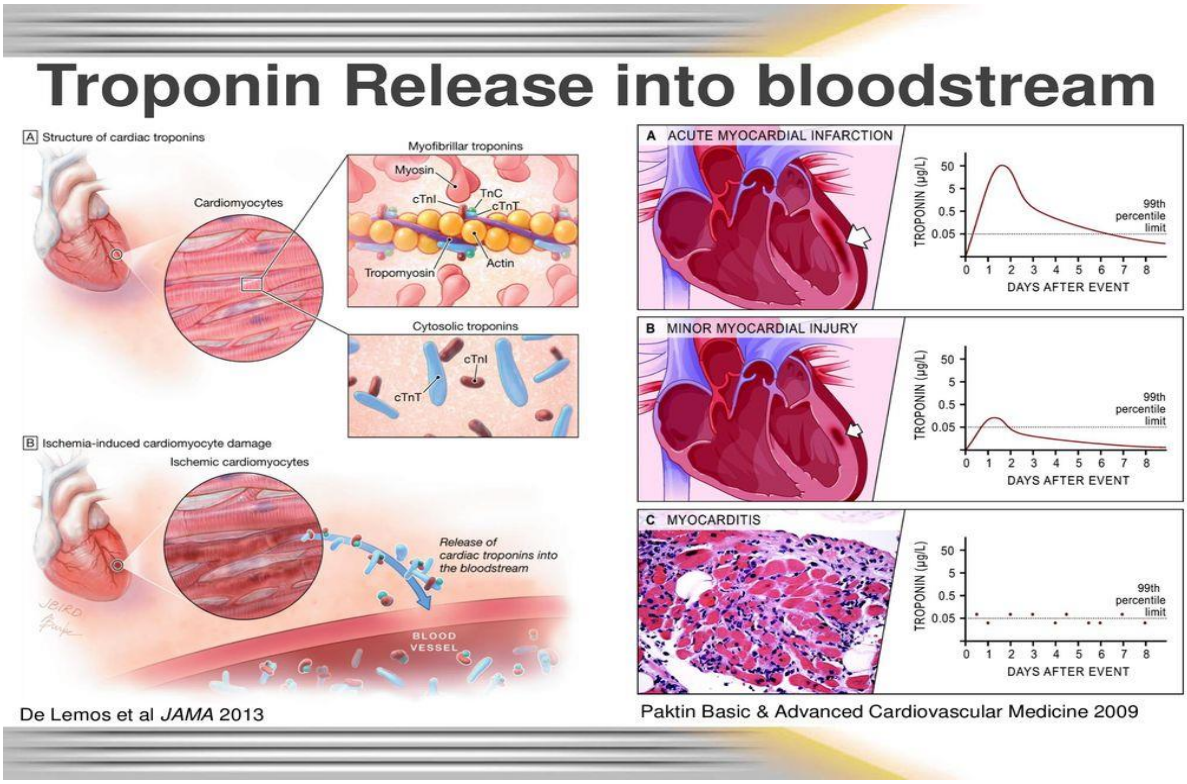


Figure no 8

STUDY OF CARDIAC BIOMARKERS IN HEART DISEASE

Cardiac markers are biomarkers measured to evaluate heart function. They can be useful in the early prediction or diagnosis of disease. Although they are often discussed in the context of myocardial infarction, other conditions can lead to an elevation in cardiac marker level.

Most of the early markers identified were enzymes, and as a result, the term "cardiac enzymes" is sometimes used. However, not all of the markers currently used are enzymes. For example, in formal usage, troponin would not be listed as a cardiac enzyme.

INTRODUCTION:-

Heart releases cardiac enzymes (cardiac biomarkers) when there's heart damage or stress due to low oxygen. Troponin and creatinine phosphokinase (CPK) levels rise after a heart attack. Elevated heart enzyme levels can also indicate acute coronary syndrome or ischemia. Healthcare providers use enzyme marker tests (blood tests) to measure cardiac enzymes. Cardiac biomarkers help healthcare providers know if symptoms are due to **a heart attack (myocardial infarction), angina, heart failure** or another problem. Increases in cardiac enzymes can also indicate **acute coronary syndrome (ACS) or myocardial ischemia**. Treatments for these conditions vary. An accurate diagnosis is critical to ensuring you receive the appropriate care. : The present study was done in patients **ACUTE CARDIAC CARE (ACE) HOSPITAL KANDIVALI west** from the period of JAN 2023 to JUNE 2023. Samples are drawn from OPD patients/ Admitted patients.

Results: Out of total 100 samples collected during this duration 65 samples were from male patients and 35 from female patients. Out of 65 male samples, 39 were found to have a positive cardiac patient. Similarly out of 35 samples from females 21 were found to have a positive cardiac patient.

SIGNS AND SYMPTOMS FOR CARDIAC DISEASE

1. Chest pain

Figure no 9

It's the classic sign of a heart attack, yet many people don't realise this could be a medical emergency.

Professor Newby says: "If you have chest pain and you feel extremely unwell, you should dial 101 and get an ambulance as soon as possible. If it's a heart attack, it's usually described as a heaviness, tightness or pressure in the chest; people will often describe it as 'an elephant sat on my chest' or 'it felt like a tight band around my chest,' that sort of constricting feeling.

"If chest pains occur when you are exerting yourself, but go away when you stop, that would suggest it's more likely to be angina. That would still mean you should go and see a doctor, but you don't have to call 101."

Professor Newby advises that chest pains accompanied by feeling extremely unwell, mean it is probably the right time to call 101 and request an ambulance.

2. Feeling sick

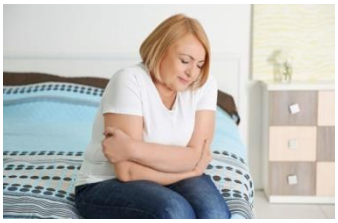


Figure no 10

Obviously not every bout of nausea equals a heart attack – but if you're getting pain as well, alarm bells should ring. Professor Newby says: "If you experience intense chest pain even when you are just sitting around doing nothing and you are also feeling sick, that is the time to call for an ambulance."

If you're getting some discomfort, but not intense pain, as well as feeling sick, call 101 for advice.

3. Stomach pain or indigestion

Figure no 11

An indigestion-type pain or a burning sensation in your chest or stomach can be a sign of a heart attack or related heart problem. Professor Newby says: "Because the heart, the gullet [the passage between your mouth and stomach] t

4. Feeling sweaty

Figure no 12

Working up a sweat when you've been to the gym or because it's a really hot day, is nothing to worry about. But feeling hot and clammy along with chest pains is a sign that you should call an ambulance.

5. Arm pain

Figure no 13

You might not associate arm pain with your heart, but it can be a sign of a heart attack. Professor Newby says: "If your pain is going down the arm, especially the left arm, or into the neck that makes it more likely to be heart-related than indigestion. If it doesn't go away, or if you know you have heart disease and have used your GTN (glyceryl trinitrate) spray two or three times to no discernible effect, you should be seeking emergency medical advice." Call 101 for an ambulance.

6. Jaw or back pain

Figure no 14

Professor Newby says: "With heart attacks, it can even happen that the pain is felt in the jaw, or the back. Again, if it doesn't go away, call 101 and ask for an ambulance." There is some evidence that women's symptoms are more likely to vary from 'classic' chest pain, and we know that women are less likely to seek medical attention and treatment.

7. Choking sensation

Figure no 15

Professor Newby says: "The word 'angina' actually means 'choking', and sometimes the tightness or pain can be up in the throat. People tend to describe a 'restricting' or 'choking' sensation."

08. Extreme fatigue

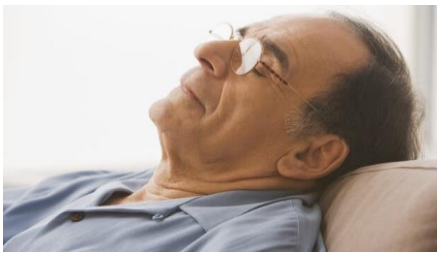


Figure no 16

Feeling tired all the time can be a symptom of heart failure, as well as of other conditions. Professor Newby says: "Many of my patients tell me they're tired, whether they've got heart failure or not, whether they've got angina or not! It's a difficult one, because it's so non-specific."

09. Irregular heartbeat

Professor Newby says: "This is a hot topic at the moment, there's a lot of focus on diagnosing irregular heartbeats. I did an audit of the heart monitors we give out to people for investigation and from about 700 people, we found only about 20 that had atrial fibrillation [which can increase your risk of stroke]. The vast majority of people just had extra ectopic beats, which are usually harmless.

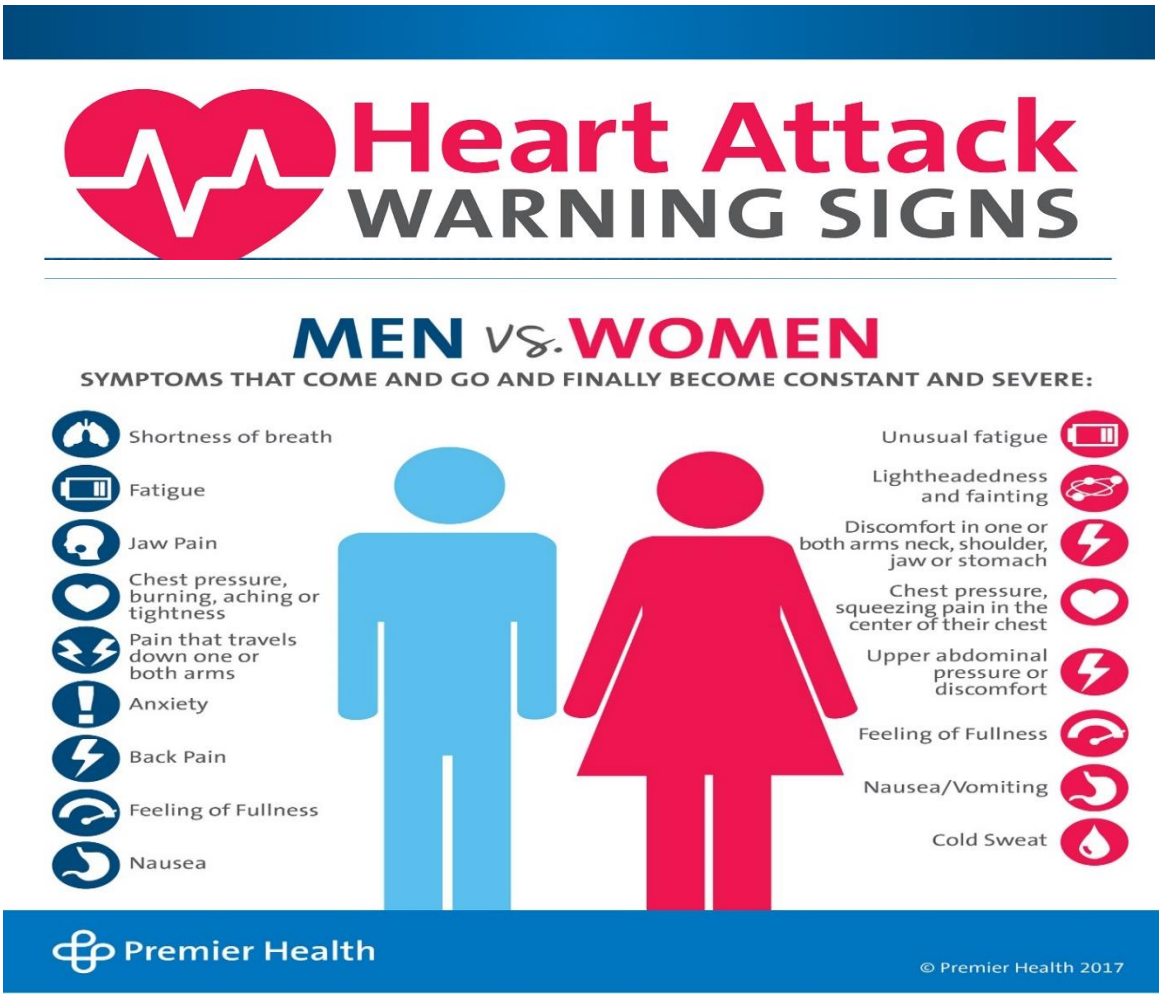

Heart Attack
WARNING SIGNS
MEN vs. WOMEN
SYMPTOMS THAT COME AND GO AND FINALLY BECOME CONSTANT AND SEVERE:
Shortness of breath
Fatigue
Jaw Pain
Chest pressure, burning, aching or tightness
Pain that travels down one or both arms
Anxiety
Back Pain
Feeling of Fullness
Nausea
Unusual fatigue
Lightheadedness and fainting
Discomfort in one or both arms neck, shoulder, jaw or stomach
Chest pressure, squeezing pain in the center of their chest
Upper abdominal pressure or discomfort
Feeling of Fullness
Nausea/Vomiting
Cold Sweat
Premier Health
© Premier Health 2017

Figure no 17

MATERIALS AND METHODS

LABORATORY DIAGNOSIS METHODS

TEST	METHODS	RESULT TIMING	NORMAL RANGE
CREATININE KINASE (CK)	SPECTROPHOTOMETRY /LFA	15 MIN / 10 MIN	< 150
CREATININE KINASE MB FRACTION	SPECTROPHOTOMETRY / LFA	15 MIN / 10 MIN	< 24
MYOGLOBIN	SPECTROPHOTOMETRY /CLIA	15 MIN / 20 MIN	
SGOT (AST)	SPECTROPHOTOMETRY	10 MIN	< 45
LDH (LACTATE DEHYDROGENASE)	SPECTROPHOTOMETRY	10 MIN	230 - 460
CARDIAC TROPONIN (T,I,)	CLIA METHOD / CHROMATOGRAPHY/ LFA	17 MIN / 15 MIN / 10 MIN	Trop i <0.3 ng/ml Trop t <0.3 ng/ml

BIOCHEMICAL ANALYZER XL640

SPECTROPHOTOMETRY MACHINE

Figure no 18

ERBA XL640

Figure no 19

Fully automated Clinical Chemistry analyzer with throughput of 640 tests/hr with I.S.E (Na/K/Cl/Li) and diffraction grating for high resolution measurement. On board are 50 samples and 56 refrigerated reagent positions with STAT facility. XL 640 features extensive quality control, user friendly and low consumption service.

DISPENSING OF SAMPLES AND REAGENTS

- Sample volume: 2-70µl (0.2 µl step)
- Reagent volume: R1 50-300 ul (1 µl step), R2 10-300 ul (1 µl step)
- 3 dispensing probes (sample, R1, R2) equipped with liquid -level sensor and crash detector
- Auto-dilution of samples and calibrators
- Clot detection

ECONOMY

- Minimum reaction volume: 180 µl
- Reusable reaction cuvettes

MIXING SYSTEM

- 2 independent stirrers
- 3 user selectable mixing speeds

QUALITY CONTROL

- 4 levels of control material can be used
- Levey-Jennigs graphs
- Twin Plot diagrams for monitoring of systematic and random error

REACTION UNIT WITH WASH STATION

- 72 reusable hard glass cuvettes
- Possibility of replacement of individual cuvette
- Wash station – cuvette rinsing and drying in eight-step procedure
- Automatic cuvette blank measurement before analysis

SAMPLE TRAY

- 80 positions for samples, blanks, standards, calibrators, controls and ISE solutions
- Primary tubes 5, 7 and 10 ml, vacuum system tubes and cups
- STAT sample with priority in any position
- Additional tray for 80 samples included

REAGENT TRAY

- 56 positions, 20 ml, 50 ml reagent containers, 5 ml tube with adaptor
- Reagent compartment with Peltier/air cooler (8-12°C)
- Option to use one reagent for several test simultaneously

MEASUREMENT MONITORING

- Colour indication of sample analysis
- Possibility of monitoring the reaction in real time
- Reagent volume monitoring
- Informative reports on ongoing analyzer status

RANDOX IMOLA (BIOCHEMISTORY ANALYZER)

SPECTROPHOTOMETRY MACHINE

Figure no 20

TEST LIST FOR CARDIAC DONE ON THIS MACHINE

- CREATININE KINASE (CK)
- CREATININE KINASE MB FRACTION
- MYOGLOBIN
- SGOT (SERUM GLUTAMIC OXALOACETIC TRANSAMINASE)
- LDH (LACTATE DEHYDROGENASE)

I CHROMAII (FLUORESCENCE-BASED LATERAL FLOW IMMUNOASSAY)

Figure no 21

Figure no 22

I Chroma™ II

A compact and easy-to-use, fluorescence based POCT(Point-of-care testing) immunoassay analyser ichroma™ II is a compact, easy-to-use diagnostic immuno-analyzer to measure the presence of various biomarkers for cardiac, cancer, hormones, infectious diseases, autoimmune diseases, and metabolic diseases.

Diagnosis method

Fluorescence-based Lateral Flow Immunoassay

TEST LIST FOR CARDIAC DONE ON THIS MACHINE

- CREATININE KINASE (CK)
- CREATININE KINASE MB FRACTION
- CARDIAC TROPONIN I
- CARDIAC TROPONIN T

ADVIA CENTAUR XP - SIEMENS

Figure no 23

ADVIA CENTAUR XP MACHINE

POWERFUL PRODUCTIVITY

- High throughput, up to 240 tests per hour, to keep pace with peak workload times
- High-resolution touch screen for easy interaction
- Expanded ancillary reagent and fluid capacity
- Data archive feature reduces time for administrative tasks
- Universal sample rack design eliminates manual tasks

PRINCIPLE

- CLIA (Chemiluminescence Immunoassay)

TEST LIST FOR CARDIAC DONE ON THIS MACHINE

- CREATININE KINASE MB FRACTION
- CARDIAC TROPONIN I
- CARDIAC TROPONIN T
- MYOGLOBIN

RESULTS ANALYSIS

MALE PATIENTS RESULT ANALYSIS

SR.NO	TEST	RESULT	NORMAL RANGE / UNIT	DIAGNOSIS
1	Troponin I Level	**15.0**	<0.3 ng/ml	**CHEST PAIN(+)**
	CPK MB	**218**	3-100 ng/ml	
	CPK TOTAL	**301.1**	<171 u/l	
	LDH	238.1	230 – 460 u/l	
	SGOT/AST	22.5	<45 u/l	
2	Troponin T Level	**8.07**	<0.3 ng/ml	**LEFT VENTRICULAR EJECTION FRACTION (LVEF)50-50%**
	CPK MB	**143**	3-100 ng/ml	
	CPK TOTAL	**206.1**	<171 u/l	
	LDH	**311.7**	230 – 460 u/l	
3	Troponin I Level	**9.45**	<0.3 ng/ml	**EFFORT ANGINE ON AND OFF SEEN YESTERDAY EVENING**
	CPK MB	**241.7**	3-100 ng/ml	

	CPK TOTAL	**379.1**	<171 u/l	
	LDH	399.1	230 – 460 u/L	
	SGOT/AST	34.1	<45 u/l	
4	Troponin I Level	**12.5**	<0.3 ng/ml	**LEFT VENTRICULAR FAILURE**
	CPK MB	**388.4**	3-100 ng/ml	
	CPK TOTAL	**187.9**	<171 u/l	
	LDH	299.4	230 – 460 u/l	
	MYOGLOBIN	**118.9**	28-72 ng/ml	
5	Troponin T Level	**2.89**	<0.3 ng/ml	**EFFORT ANGINE ON AND OFF SEEN YESTERDAY EVENING**
	CPK MB	**131.7**	3-100 ng/ml	
	CPK TOTAL	**387.1**	<171 u/l	
	LDH	**556.1**	230 – 460 u/l	
	SGOT/AST	**77.1**	<45 u/l	
6	Troponin I Level	**4.59**	<0.3 ng/ml	**HISTORY OF CHEST PAIN(+)**
	CPK MB	**157.1**	3-100 ng/ml	
	CPK TOTAL	**346.2**	<171 u/l	
	LDH	**610.1**	230 – 460 u/l	
	SGOT/AST	**79.2**	<45 u/l	

	MYOGLOBIN	59.4	28-72 ng/ml	
7	Troponin I Level	**3.01**	<0.3 ng/ml	**LEFT VENTRICULAR EJECTION FRACTION (LVEF)45%**
	CPK MB	**310.1**	3-100 ng/ml	
	CPK TOTAL	**421.0**	<171 u/l	
	LDH	**599.2**	230 – 460 u/l	
	SGOT/AST	**124.1**	<45 u/l	
	MYOGLOBIN	39.2	28-72 ng/ml	
8	Troponin I Level	<0.01	<0.3 ng/ml	**ARM PAIN**
	CPK MB	50.1	3-100 ng/ml	
	CPK TOTAL	100.7	<171 u/l	
	LDH	312.1	230 – 460 u/l	
	SGOT/AST	25.2	<45 u/l	
	MYOGLOBIN	44.1	28-72 ng/ml	
9	Troponin I Level	**9.68**	<0.3 ng/ml	**CHEST HEAVINESS /BREATHLESSNESS**
	CPK MB	**271.1**	3-100 ng/ml	
	CPK TOTAL	**210.1**	<171 u/l	
	LDH	**476.2**	230 – 460 u/l	

	SGOT/AST	**69.5**	<45 u/l	
10	Troponin T Level	0.01	<0.3 ng/ml	
	CPK MB	**249.5**	3-100 ng/ml	**BODY PAIN LAST 2 DAYS**
	CPK TOTAL	**541.1**	<171 u/l	
	LDH	**623.1**	230 – 460 u/l	
	SGOT/AST	**142.3**	<45 u/l	
	MYOGLOBIN	57.2	28-72 ng/ml	

FEMALE PATIENTS RESULT

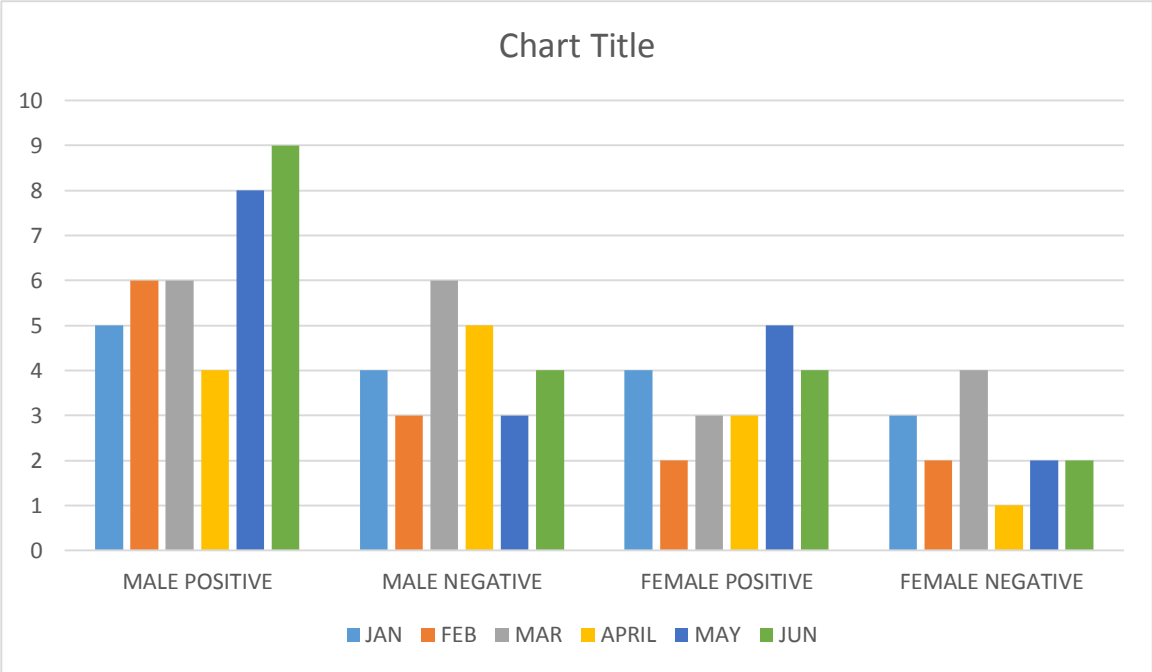
SR.NO	**TEST**	**RESULT**	**NORMAL RANGE**	**DIAGNOSIS**
1	Troponin I Level	**11.4**	<0.3 ng/ml	**ALLERGE BREATHLESS(+)**
	CPK MB	**310.1**	3-100 ng/ml	
	CPK TOTAL	**298.1**	<145 u/l	
	LDH	**510.1**	230 – 460 u/l	
	SGOT/AST	**77.1**	<45 u/l	
2	Troponin T Level	**7.90**	<0.3 ng/ml	**CHEST HEAVINESS /BREATHLESSNESS**

	CPK MB	**212.1**	3-100 ng/ml	
	CPK TOTAL	**324.1**	<145 u/l	
	LDH	323.1	230 – 460 u/l	
	SGOT/AST	22.8	<45 u/l	
3	Troponin I Level	<0.01	<0.3 ng/ml	**FEELING SWEATY**
	CPK MB	36.5	3-100 ng/ml	
	CPK TOTAL	112.1	<145 u/l	
	LDH	346.2	230 – 460 u/l	
	SGOT/AST	29.1	<45 u/l	
	MYOGLOBIN	39.8	25-58 ng/ml	
4	Troponin I Level	**2.07**	<0.3 ng/ml	**CHEST HEAVINESS /BREATHLESSNESS**
	CPK MB	**355.2**	3-100 ng/ml	
	CPK TOTAL	**421.1**	<145 u/l	
	LDH	**669.6**	230 – 460 u/l	
	SGOT/AST	**114.1**	<45 u/l	

THE STUDY OF CARDIAC BIOMARKERS TABLE SHOWING TOTAL NUMBER OF PATIENTS OBTAINS DURING 6 MONTHS IN CARDIAC AND AVERAGE OF TOTAL MONTHS.

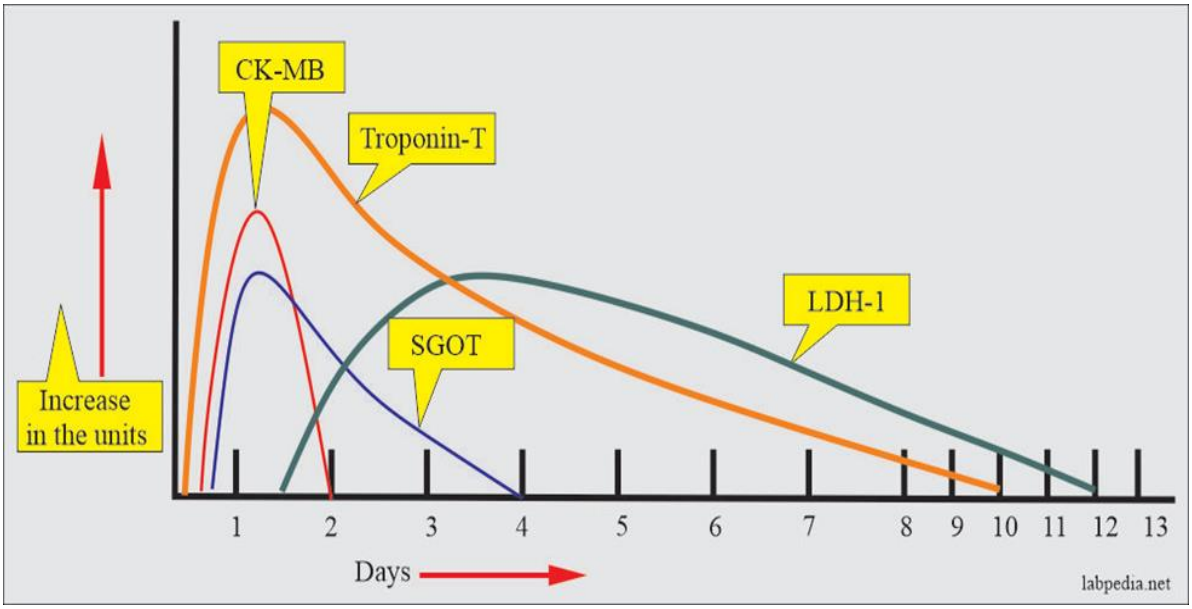
	NO OF CARDIAC POSITIVE/NEGATIVE PATIENTS					
Months	TOTAL PATIENTS	POSITIVE MALE	POSITIVE FEMALE	NEGATIVE MALE	NEGATIVE FEMALE	AGE DURATION 30 TO 80
January	16	05	04	04	03	55-80
February	15	06	02	03	02	55-70
March	19	06	03	06	04	47-80
April	13	04	03	05	01	40-70
MAY	18	08	05	03	02	50-80
JUNE	19	09	04	04	02	55-80
MEAN	**16.2%**	**6.3%**	**3.5%**	**4.1%**	**2.3%**	

6 MONTHS DATA ANALYSIS OF CARDIAC PATIENTS



COMPARISON GRAPH OF MALE AND FEMALE AND POSITIVE AND NEGATIVE CARDIAC PATIENTS.

CARDIAC BIOMARKERS RELEASING FLOW CHART



CARDIAC BIOMARKERS RELEASING TIME TABLE

Marker	Time of release after MI	Mean peak time	Time of return to normal
CK-MB	3–12 h	18–24 h	48–72 h
Myoglobin	2–3 h	9–12 h	24 h
CTnI	3–12 h	24 h	5–10 days
CTnT	3–12 h	12–48 h	5–14 days
IMA	0–30 min	6 h	12–24 h
LDH	12–24 h	24–48 h	10–14 days
AST	12–24 h	24–48 h	10–14 days
HFABP	1–5 h	5–10 h	24 h

DISCUSSION

Advantages and disadvantages of cardiac biomarkers, proteins, and some peptides in diagnosis of AMI

AST currently has no place in the diagnosis of AMI. Peptide-structured molecules have not yet found any place in the diagnosis of AMI. If CK-MB is used in the diagnosis of AMI, serial increase and decrease should not be seen in the level of CK-MB. CK-MB should be at least 10–14 U/L. In monitoring at 4-hour intervals, CK-MB should be increased by 50%. If viewed in a single time period, it should be twice the normal level. If it is analyzed after 72 hours, it is important that CK-MB is seen to be higher than troponins and LDHs. Cardiac enzymes are superior to ECG in the diagnosis of AMI. Myoglobin, are early biomarkers in the diagnosis of AMI. TnT and TnI are late markers. CK-MB is a remarkable AMI biomarker in the first 10–12 hours. An increase in TnI is an indicator of myocardial injury if CK-MB is within normal limits. For the diagnosis of AMI, TnI is more specific. While CK-MB levels return to normal within 72 hours after MI, and as cardiac troponins are released in the troponin complex, their level can be high in the blood even 7–14 days later. In other words, the analysis of troponins can be used to diagnose an individual's past AMI within 7–14 days. TnT is not specific to the heart. TnT shows biphasic release during AMI. The first peak occurs within 24 hours of symptoms, and the second one is on the fourth day. TnT levels are high in the blood for a few days and return to normal values after 10–14 days. TnI is specific to the heart. After 9–12 hours, the sensitivity for the diagnosis of AMI is 100% and has monophasic release kinetics. In patients with chronic renal failure, TnT may increase without myocardial damage. Therefore, TnI is a more reliable biomarker in the diagnosis of AMI in patients with chronic renal failure.4 Multiple cardiac biomarkers are recommended, as they increase specificity and sensitivity in the diagnosis of AMI. The properties of some dispensable cardiac biomarkers used in the diagnosis of AMI are summarized.

CONCLUSION

AMI has a high mortality rate worldwide, but fast and reliable diagnosis can reduce mortality. Biomarkers are elevated because of cell death in the myocardium. Therefore, many biochemical parameters of heart-tissue origin have been used in the diagnosis of AMI from past to present. A biomarker that meets the definition of an ideal cardiac biomarker, as we previously described, has yet to be discovered. In other words, there is no consensus on the best cardiac biomarker. There is no doubt that a better one will always exist. Analysis of a single biomarker is not recommended, since there is no ideal and specific single biomarker. It should also be noted that cardiac biomarkers do not make for a diagnosis, but do help in reaching one.

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