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Serial Kinetics and Diagnostic Interrelationships of Cardiac Biomarkers in Acute Myocardial Infarction

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ABSTRACT:

Background: *Acute myocardial infarction (AMI) is a major cause of morbidity and mortality worldwide. Cardiac biomarkers are essential for the diagnosis and monitoring of AMI. Although cardiac troponin T (cTnT) is the preferred biomarker, enzymes such as creatine phosphokinase-MB (CPK-MB), aspartate aminotransferase (AST), and lactate dehydrogenase (LDH) are still widely used, especially in resource-limited settings.*

Objectives: *To evaluate the serial kinetics, absolute and percentage delta changes, and interrelationships of cTnT, CPK-MB, AST, and LDH during the first 48 hours after admission in patients with AMI, and to explore their complementary diagnostic roles in a resource-limited healthcare setting.*

Patients and Methods: *This hospital-based observational study included 50 patients with confirmed AMI and 50 age- and sex-matched healthy controls. Serial blood samples were collected from AMI patients at 0, 6, 12, 24, 36, and 48 hours after admission. Biomarker levels were measured using standard laboratory methods. Absolute and percentage delta changes were calculated relative to controls. Pearson's correlation coefficient was used to assess relationships between biomarkers at each time point.*

Results: *All biomarkers were significantly elevated in AMI patients compared with controls. cTnT showed a progressive and sustained rise, reaching over 1100% above control values at 48 hours. CPK-MB and AST demonstrated earlier peaks around 24 hours, followed by a partial decline, while LDH showed a delayed but marked rise. Most biomarker pairs showed no significant linear correlation at any time point; weak negative correlations observed at 12 hours were small in magnitude and likely of limited clinical significance.*

Conclusion: *Cardiac biomarkers in AMI exhibit distinct temporal kinetics with minimal linear correlation. Lack of correlation should not be interpreted as lack of diagnostic utility; rather, it highlights that biomarkers reflect different pathophysiological phases of myocardial injury. cTnT remains the most reliable biomarker, while CPK-MB, AST, and LDH should be interpreted as complementary rather than interchangeable markers.*

KEYWORDS:

Acute myocardial infarction; Cardiac biomarkers; Troponin T; CPK-MB; AST; LDH.

1. Introduction

Acute myocardial infarction (AMI) is one of the leading causes of morbidity and mortality worldwide and remains a major public health challenge, particularly in low- and middle-income countries.[1] Rapid urbanization, sedentary lifestyle, tobacco use, unhealthy diet, and rising prevalence of diabetes and hypertension have all contributed to an increasing burden of ischemic heart disease. In the setting of AMI, time is a critical determinant of outcome: early diagnosis and prompt reperfusion therapy significantly reduce infarct size, preserve left ventricular function, and improve short- and long-term survival. Therefore, the availability of accurate, sensitive, and timely diagnostic tools is central to effective

management of patients presenting with chest pain suggestive of myocardial ischemia.[2]

Cardiac biomarkers have become indispensable in the evaluation of suspected AMI. They provide objective biochemical evidence of myocardial injury, complementing clinical assessment and electrocardiographic changes. Among these, cardiac troponins (including cardiac troponin T, cTnT) are currently considered the gold standard for detecting myocardial necrosis. cTnT is highly specific to cardiac myocytes and is released into the circulation following irreversible damage to the myocardial cell membrane. Its concentration begins to rise within a few hours after the onset of ischemia, typically peaks over 12–24 hours, and remains elevated for several days. This characteristic profile makes cTnT extremely useful not only for confirming the diagnosis of AMI but also for identifying patients who present late, when other markers may already have normalized.[3]

Before the widespread adoption of troponins, enzymes such as creatine phosphokinase-MB (CPK-MB), aspartate aminotransferase (AST), and lactate dehydrogenase (LDH) were widely used as markers of myocardial injury. CPK-MB is relatively more specific for cardiac muscle compared to AST and LDH, and classically shows an early rise, peaking around 12–24 hours and returning to baseline within 2–3 days. This early peaking Pattern makes CPK-MB useful in detecting reinfarction or assessing very early changes after reperfusion. AST and LDH, although less specific to cardiac tissue, are released from multiple organs in response to cell injury and necrosis. Their elevations in AMI reflect the extent of tissue damage but can be influenced by concomitant hepatic, skeletal muscle, or systemic conditions, which may limit their specificity.

Despite these limitations, AST and LDH continue to be measured in many clinical laboratories, especially in resource-constrained settings where high-sensitivity troponin assays may not be universally available or may be reserved for selected patients. In such environments, clinicians often rely on a combination of biomarkers to support the diagnosis and to understand the temporal sequence of myocardial injury. Thus, understanding the dynamic behavior of both specific (cTnT, CPK-MB) and non-specific (AST, LDH) markers is important, particularly in settings where patterns over time may provide additional diagnostic and prognostic information.[3]

Although the individual kinetic profiles of these biomarkers are well described, limited data are available on their serial interrelationships and relative delta changes within the same patient population over predefined early time intervals. Understanding these patterns may aid clinical interpretation, particularly in settings where multiple biomarkers are used simultaneously.[4]

Rationale of the Study: Despite widespread guideline endorsement of troponin-based diagnosis, practical constraints in resource-limited environments necessitate continued reliance on traditional cardiac enzymes. Clinicians frequently encounter discordant biomarker results, particularly when patients present at varying times after symptom onset.

This study was designed as an exploratory observational analysis to provide population-specific data on serial biomarker kinetics, absolute and percentage delta changes, and correlation patterns. The aim was not to redefine diagnostic thresholds but to better understand the complementary roles and limitations of commonly used cardiac biomarkers in routine clinical practice.

Aim

To evaluate the serial Pattern and interrelationship of cardiac biomarkers (cTnT, CPK-MB, AST, and LDH) in patients with acute myocardial infarction as compared to healthy controls over the first 48 hours after admission.

Objectives

1. **To measure and compare** the mean levels of cTnT, CPK-MB, AST, and LDH in AMI patients and age- and sex-matched healthy controls at predefined time intervals (0, 6, 12, 24, 36, and 48 hours after admission).
2. **To calculate** the absolute delta (Δ = Cases - Control) and percentage delta (%Δ) for each biomarker at each time point to assess the magnitude and evolution of biochemical changes over time.
3. **To analyze** the correlation between pairs of biomarkers (cTnT vs CPK-MB, cTnT vs AST, cTnT vs LDH, CPK-MB vs AST, CPK-MB vs LDH, and AST vs LDH) at 6, 12, 24, 36, and 48 hours using Pearson's correlation coefficient (r).
4. To assess whether correlation patterns

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support complementary rather than interchangeable clinical use of these biomarkers.

2. MATERIALS AND METHODS

Study Design

A hospital-based observational study with serial biomarker measurements.The study design involved:

- Prospective enrollment of patients presenting with suspected AMI who fulfilled predefined inclusion and exclusion criteria.
- Serial sampling of blood at standardized time intervals after admission.
- Parallel comparison with an age- and sex-matched control group.
- Statistical analysis focusing on temporal trends, delta changes, and correlations between biomarkers.

Study Population

The study included two groups:

- **Cases:**

- Patients diagnosed clinically and biochemically with acute myocardial infarction (**n = 50**). Diagnosis was made by the treating physician based on typical clinical presentation, characteristic ECG changes, and elevated cardiac markers consistent with AMI.

- **Controls:**

- Age- and sex-matched healthy individuals (**n = 50**). with no history of cardiovascular disease, recruited from hospital staff, patient attendants, or individuals attending routine health check-ups. Controls had no acute illness at the time of sampling and no known chronic systemic disease that could influence cardiac biomarker levels.

- Patients were included if they presented within 6 hours of symptom onset to capture early biomarker kinetics.

Inclusion Criteria (Cases)

- Adults aged **≥ 18 years**.
- Confirmed AMI based on:
  - Typical clinical presentation (e.g., chest pain, dyspnea, diaphoresis),
  - ECG changes suggestive of myocardial infarction (e.g., ST elevation/depression, new-onset LBBB, T-wave inversion), and
  - Elevated cardiac markers, as interpreted by the treating physician.

- Presentation within **6 hours of the onset of symptoms**, to ensure the ability to capture the early kinetics of biomarker release.

Exclusion Criteria

Patients were excluded if they had any of the following conditions known to alter biomarker levels independently of acute coronary occlusion:

- **Chronic kidney disease** (which may cause persistently elevated troponin and affect the clearance of markers).

- **Chronic liver disease or skeletal muscle disorders** (which can elevate AST, LDH, and CPK-MB independently of cardiac injury).

- **Known myocarditis or heart failure**, which may cause chronic or intermittent elevations of cardiac biomarkers.

- **Recent trauma or surgery**, or any acute condition (e.g., severe myopathy, hemolysis), is likely to influence biomarker levels.

- **Hemolysed or inadequate blood samples** can spuriously alter enzyme measurements and compromise assay reliability.

Sample Collection and Biomarker Measurement

Timing of Sample Collection

Blood samples were collected from cases at predefined time intervals to capture the dynamic changes in biomarker levels:

- **Baseline (0 hours):** At admission, as soon as possible after presentation.
- **6 hours** after admission.
- **12 hours** after admission.
- **24 hours** after admission.
- **36 hours** after admission.
- **48 hours** after admission.

These time points were selected to cover the

early, peak, and declining phases of biomarker release following AMI.

For the control group, blood samples were obtained once, at a corresponding baseline time point for comparison of mean values.

Pre-analytical Procedures

- Venous blood samples were collected using standard aseptic techniques.
- Samples were drawn into appropriate vacutainers (e.g., plain or serum-separating tubes) and allowed to clot, then centrifuged to separate serum.
- All samples were processed promptly according to laboratory protocol to minimize pre-analytical variability.
- Samples showing visible hemolysis or inadequate volume were discarded, and re-sampling was done wherever feasible.

Biomarkers and Analytical Methods

The following biomarkers were measured using standard laboratory techniques:

1. **Cardiac Troponin T (cTnT)**

- Measured by an **immunoassay (chemiluminescence-based)** on an automated analyzer.
- The assay used manufacturer-recommended reagents, calibration standards, and internal quality control procedures.

2. **Creatine Phosphokinase-MB (CPK-MB)**

- Estimated by an **enzymatic immunoinhibition method**, which selectively measures the MB isoenzyme fraction of creatine kinase.

3. **Aspartate Aminotransferase (AST)**

- Determined by the **kinetic UV method**, measuring the rate of change in absorbance due to the enzymatic reaction.

4. **Lactate Dehydrogenase (LDH)**

- Measured by an **enzymatic spectrophotometric method**, based on the catalytic conversion of lactate to pyruvate (or vice versa) with associated change in absorbance.

Quality control was maintained by running appropriate internal control sera with each batch of tests and following standard operating procedures for instrument maintenance and calibration.

3. Data Analysis

1. Biomarker Comparison

- For each biomarker (cTnT, CPK-MB, AST, LDH), **mean ± standard deviation (SD)** values were calculated separately for cases and controls.
- For cases, mean values were calculated at each time point (0, 6, 12, 24, 36, and 48 hours).
- **Absolute delta (Δ)** and **percentage delta (%Δ)** were calculated using control values as reference:

- **Absolute delta (Δ):**

Δ=Mean value in cases-Mean value in controls

- **Percentage delta (%Δ):**

%Δ=(Mean value in cases-Mean value in controlsMean value in controls)×100. Where appropriate, inferential statistical tests (e.g., Student's t-test for normally distributed data or non-parametric equivalents) could be used to compare means between cases and controls at each time point (you can specify these exactly in your thesis depending on what you actually used).

2. Correlation Analysis

To evaluate the linear relationships between different biomarkers at various time points, **Pearson's correlation coefficient (r)** was calculated for the following pairs:

- cTnT vs CPK-MB
- cTnT vs AST
- cTnT vs LDH
- CPK-MB vs AST
- CPK-MB vs LDH
- AST vs LDH

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Correlation analysis was performed at **6, 12, 24, 36, and 48 hours** after admission (time points at which substantial biomarker changes are expected).

The strength of correlation was interpreted as:

- **r = ±0.00–0.19** → No correlation
- **r = ±0.20–0.39** → Weak correlation
- **r = ±0.40–0.59** → Moderate correlation

A **p-value < 0.05** was considered statistically significant.

3. Graphical Representation

To visually assess relationships between biomarkers:

- **Scatter plots** were generated for each biomarker pair at each time interval.
- The plots allowed visualization of:
  - Direction of association (positive/negative),
  - Degree of scatter around any apparent line of best fit,
  - Presence or absence of linear trends and potential outliers.

These graphical representations support the numerical correlation analysis and help in an intuitive understanding of how biomarker levels move together over time.

4. Statistical Software

Data entry and analysis were performed using standard statistical software such as **SPSS**, **R**, or **Microsoft Excel**.

- Descriptive statistics were used to summarize biomarker levels. Absolute and percentage delta values were calculated using mean control values as a fixed reference.
- Pearson's correlation coefficient was applied as an exploratory method to assess linear relationships between biomarkers. Formal normality testing and data transformation were not performed, which is acknowledged as a limitation.
- Multiple correlation analyses were conducted without adjustment for multiple comparisons; therefore, isolated statistically significant findings were interpreted cautiously.

Table 1: Cardiac Biomarkers – Control vs Cases with Delta (Cases - Control)

Group	Marker	Time	Value	Δ (Cases - Control)
Control	cTnT	0 h	0.4734	
Cases	cTnT	6 h	1.3872	1.3872 - 0.4734 = **0.9138**
Cases	cTnT	12 h	2.1962	2.1962 - 0.4734 = **1.7228**
Cases	cTnT	24 h	3.5166	3.5166 - 0.4734 = **3.0432**
Cases	cTnT	36 h	5.09	5.09 - 0.4734 = **4.6166**
Cases	cTnT	48 h	5.748	5.748 - 0.4734 = **5.2746**
Control	CPK-MB	6 h	29.9452	
Cases	CPK-MB	6 h	100.0588	100.0588 - 29.9452 = **70.1136**
Cases	CPK-MB	12 h	110.4162	110.4162 - 29.9452 = **80.4710**
Cases	CPK-MB	24 h	193.4552	193.4552 - 29.9452 = **163.5100**
Cases	CPK-MB	36 h	104.6802	104.6802 - 29.9452 = **74.7350**
Cases	CPK-MB	48 h	124.656	124.656 - 29.9452 = **94.7108**
Control	AST	0 h	38.242	
Cases	AST	6 h	75.4474	75.4474 - 38.242 = **37.2054**
Cases	AST	12 h	89.8944	89.8944 - 38.242 = **51.6524**
Cases	AST	24 h	180.3238	180.3238 - 38.242 = **142.0818**
Cases	AST	36 h	104.2618	104.2618 - 38.242 = **66.0198**
Cases	AST	48 h	128.6026	128.6026 - 38.242 = **90.3606**
Control	LDH	0 h	184.5122	
Cases	LDH	6 h	512.4012	512.4012 - 184.5122 = **327.8890**
Cases	LDH	12 h	602.5992	602.5992 - 184.5122 = **418.0870**
Cases	LDH	24 h	1019.8852	1019.8852 - 184.5122 = **835.3730**
Cases	LDH	36 h	1559.2512	1559.2512 - 184.5122 = **1374.7390**
Cases	LDH	48 h	1837.2454	1837.2454 - 184.5122 = **1652.7332**

Table 1 highlights distinct temporal patterns of biomarker elevation in AMI. While all biomarkers showed significant increases compared with controls, cTnT and LDH exhibited sustained and progressively increasing delta values, whereas CPK-MB and AST peaked earlier and showed partial declines. These findings underscore the differing release kinetics and clinical utility of individual cardiac biomarkers in the early evolution of acute myocardial infarction.

Table 2: Cardiac Biomarkers – Control vs Cases with Absolute and Percentage Delta Over Time

Group	Marker	Time	Value	Δ (Cases - Control)	%Δ vs Control
Control	cTnT	0 h	0.4734		
Cases	cTnT	6 h	1.3872	0.9138	193.0%
Cases	cTnT	12 h	2.1962	1.7228	363.9%
Cases	cTnT	24 h	3.5166	3.0432	642.8%
Cases	cTnT	36 h	5.09	4.6166	975.2%
Cases	cTnT	48 h	5.748	5.2746	1114.2%
Control	CPK-MB	6 h	29.9452		
Cases	CPK-MB	6 h	100.0588	70.1136	234.1%
Cases	CPK-MB	12 h	110.4162	80.4710	268.7%
Cases	CPK-MB	24 h	193.4552	163.5100	546.0%
Cases	CPK-MB	36 h	104.6802	74.7350	249.6%
Cases	CPK-MB	48 h	124.656	94.7108	316.3%
Control	AST	0 h	38.242		
Cases	AST	6 h	75.4474	37.2054	97.3%
Cases	AST	12 h	89.8944	51.6524	135.1%
Cases	AST	24 h	180.3238	142.0818	371.5%
Cases	AST	36 h	104.2618	66.0198	172.6%
Cases	AST	48 h	128.6026	90.3606	236.3%
Control	LDH	0 h	184.5122		
Cases	LDH	6 h	512.4012	327.8890	177.7%
Cases	LDH	12 h	602.5992	418.0870	226.6%
Cases	LDH	24 h	1019.8852	835.3730	452.7%
Cases	LDH	36 h	1559.2512	1374.7390	745.1%
Cases	LDH	48 h	1837.2454	1652.7332	895.7%

Table 2 demonstrates distinct temporal and quantitative differences in biomarker behavior following AMI. cTnT and LDH showed the greatest and most sustained percentage increases over time, whereas CPK-MB and AST exhibited earlier peaks followed by partial declines. These findings emphasize the differing release kinetics and complementary clinical roles of cardiac biomarkers in the early evolution of acute myocardial infarction.

Figure 1: Correlation Heat Map Analysis of cardiac Biomarkers

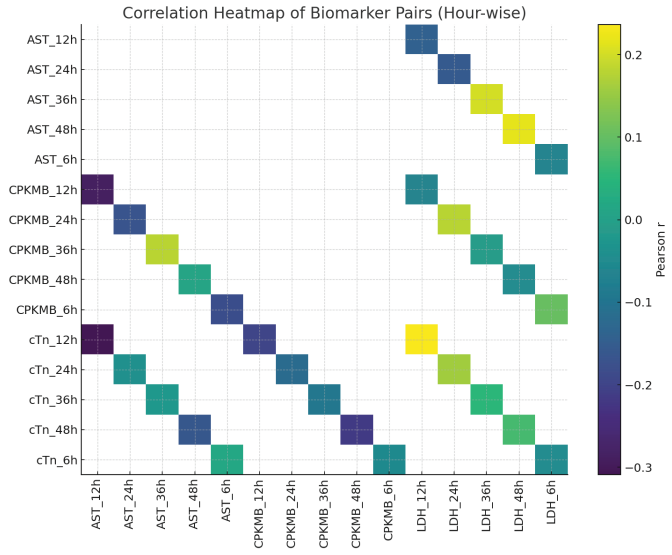

Figure 1: The correlation heat map depicting pairwise relationships among cardiac biomarkers at different time points demonstrated an overall lack of meaningful linear association between the studied parameters. Across all time intervals (6, 12, 24, 36, and 48 hours), cardiac troponin T (cTnT) showed negligible correlation with CPK-MB, with correlation coefficients consistently close to zero and no statistically significant associations (all $p > 0.05$). This Pattern indicates that variations in CPK-MB levels are largely independent of cTnT concentrations throughout the first 48 hours following myocardial injury.

Similarly, the heat map revealed weak to near-zero correlations between CPK-MB and AST at all measured time points. The correlation coefficients were small and inconsistent in direction, with no time point demonstrating statistical significance. Notably, at 48 hours, the correlation between CPK-MB and AST was virtually absent ($r \approx 0.01$, $p = 0.05$), reinforcing the lack of a linear relationship.

Overall, the heat map visualization confirms that while these biomarkers are all associated with myocardial injury, they exhibit **distinct temporal release kinetics and biological behavior**, resulting in minimal linear correlation with one another. This supports the concept that cTnT, CPK-MB, and AST provide **complementary rather than interchangeable diagnostic information** during the evolution of acute myocardial infarction.

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Table 3: Pearson Correlation Between Myocardial Infarction Biomarkers (cTnT, CPK-MB, AST, LDH) at Different Time Intervals (6h, 12h, 24h, 36h, 48h)

Time	Bio-marker 1	Bio-marker 2	n	r (Correlation)	p-value	Interpretation
6h	cTnT	CPK-MB	50	-0.055	0.704	No correlation
6h	cTnT	AST	50	0.017	0.905	No correlation
6h	cTnT	LDH	50	-0.046	0.751	No correlation
6h	CPK-MB	AST	50	-0.179	0.213	No correlation
6h	CPK-MB	LDH	50	0.103	0.479	No correlation
6h	AST	LDH	50	-0.066	0.651	No correlation
12h	cTnT	CPK-MB	50	-0.196	0.172	No correlation
12h	cTnT	AST	50	-0.309	**0.029**	Weak negative correlation (significant)
12h	cTnTT	LDH	50	0.237	0.098	Trend, not significant
12h	CPK-MB	AST	50	-0.288	**0.043**	Weak negative correlation
12h	CPK-MB	LDH	50	-0.063	0.666	No correlation
12h	AST	LDH	50	-0.142	0.326	No correlation
24h	cTnT	CPK-MB	50	-0.118	0.415	No correlation
24h	cTnT	AST	50	-0.037	0.801	No correlation
24h	cTnT	LDH	50	0.159	0.270	No correlation
24h	CPK-MB	AST	50	-0.170	0.237	No correlation
24h	CPK-MB	LDH	50	0.177	0.218	No correlation
24h	AST	LDH	50	-0.155	0.283	No correlation
36h	cTnT	CPK-MB	50	-0.094	0.516	No correlation
36h	cTnT	AST	50	-0.022	0.879	No correlation
36h	cTnT	LDH	50	0.053	0.713	No correlation
36h	CPK-MB	AST	50	0.180	0.211	No correlation
36h	CPK-MB	LDH	50	-0.007	0.962	No correlation
36h	AST	LDH	50	0.201	0.162	No correlation
48h	cTnT	CPK-MB	50	-0.217	0.130	No correlation
48h	cTnT	AST	50	-0.163	0.259	No correlation
48h	cTnT	LDH	50	0.073	0.614	No correlation
48h	CPK-MB	AST	50	0.009	0.951	No correlation
48h	CPK-MB	LDH	50	-0.048	0.740	No correlation
48h	AST	LDH	50	0.217	0.130	No correlation

Table 3 Correlation analysis revealed no consistent linear association between most biomarker pairs. Weak negative correlations observed at 12 hours were small in magnitude and not sustained at later time points.

4. DISCUSSION

The present hospital-based observational study evaluated the serial behavior and interrelationship of four cardiac biomarkers—cTnT, CPK-MB, AST, and LDH—in patients with acute myocardial infarction, compared with age- and sex-matched healthy controls. The analysis focused both on **absolute and percentage delta changes** over time and on **correlation patterns** between biomarkers at 6, 12, 24, 36, and 48 hours after admission.

Overall, three key findings emerged:

1. All four biomarkers showed substantial elevation in AMI cases compared with controls, but with distinct temporal kinetics, consistent with their known biological behavior.

2. cTnT and LDH exhibited the greatest and most sustained percentage increases over 48 hours, while CPK-MB and AST showed earlier peaks followed by partial declines.

3. Despite clear rises in all markers, there was no significant linear correlation between most biomarker pairs at any time point, except for a weak negative correlation between cTnT and AST and between CPK-MB and AST at 12 hours.

These findings have important implications for understanding biomarker dynamics and for their practical use in clinical settings, particularly where resources are limited.

Serial Pattern of cTnT and Comparison with Literature

In this study, cTnT showed a marked and progressive rise over time**,** from approximately 193% above control at 6 hours to more than 1100% above control at 48 hours. The absolute delta increased from 0.91 ng/mL at 6 hours to 5.27 ng/mL at 48 hours, indicating a sustained and steadily increasing release of troponin into the circulation. This Pattern reflects ongoing or evolving myocardial necrosis and the prolonged release and slow clearance of cTnT from injured cardiomyocytes.

This temporal profile is consistent with established literature, which shows that cardiac troponin levels rise within a few hours of symptom onset, peak around 12–24 hours, and remain elevated for up to 7–10 days following AMI.[2] The Third Universal Definition of MI emphasizes the importance of detecting a rise and/or fall of troponin, with at least one value above the 99th percentile, to diagnose AMI.[6] Our findings align with this concept of dynamic change: the progressive increase over 48 hours demonstrates clear biochemical evidence of acute myocardial injury.

Modern reviews have consistently shown that troponin, especially high-sensitivity assays, outperforms older markers (CK-MB, AST, LDH) in both sensitivity and specificity for AMI diagnosis. [7] The large percentage deltas observed in our study reinforce the central role of cTnT as the primary diagnostic and monitoring biomarker in AMI and support guideline recommendations that troponin be used as the preferred marker, with other enzymes relegated to supportive roles. [6]

Behavior of CPK-MB: Early Peak and Partial Decline

CPK-MB in our study showed a pattern typical of an early peaking biomarker. Relative to control values at 6 hours, CPK-MB increased by about 234–269% at 6–12 hours, reached a maximum percentage delta of ~546% at 24 hours, and then declined slightly to 249–316% above control by 36–48 hours. This Pattern reflects the earlier release and faster clearance of CPK-MB, which historically made it useful for detecting early infarction and reinfarction.

These findings are in line with classic descriptions that CPK-MB rises within 3–6 hours, peaks at around 12–24 hours, and returns toward baseline within 2–3 days. [6,10] Previous comparative studies have shown that although CK-MB can be diagnostically useful, troponin generally has equal or superior diagnostic accuracy and better prognostic value for infarct size and adverse outcomes. [8]

Our data demonstrate that while CPK-MB does rise substantially in AMI, its profile differs from the sustained rise of cTnT. The partial decline by 36–48 hours means that late presenters might have near-normal or falling CK-MB despite still markedly elevated cTnT. This supports current practice where CK-MB is considered adjunctive at best and primarily useful when evaluation of reinfarction or very early dynamic changes is needed, rather than as a standalone diagnostic marker.[9]

AST and LDH: Supportive, Less Specific, and Late Markers

AST in this study showed a **moderate early rise** (~97–135% above control at 6–12 hours), peaking at **~371% above control at 24 hours**, followed by a partial decline at 36–48 hours (172–236% above control). **LDH**, by contrast, showed a **delayed but very large rise**, from ~178% at 6 hours to almost **900% above control at 48 hours**, with especially large deltas from 24 hours onward.

Historically, AST and LDH were the first enzymes used for AMI diagnosis, with AST introduced in the 1950s and LDH soon after.[11] AST typically rises within 3–4 hours of infarction, peaks around 15–28 hours, and then declines, while LDH levels

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increase within 6–12 hours, peak at 1–3 days, and return to baseline within 8–14 days.[12] Our findings mirror these classical kinetics, with the prominent late rise in LDH reflecting its role as a **late marker** of tissue injury.

However, both AST and LDH are **non-specific**, being released from the liver, skeletal muscle, and other tissues, and modern guidelines no longer recommend them as primary diagnostic markers for AMI.[2] In our study, although they clearly increased in AMI cases, their interpretive value is limited by this lack of specificity and by their delayed peaks. The patterns we observed support their role, at most, as **supportive or historical markers** rather than as first-line tests.

Lack of Significant Correlation Between Biomarkers

One of the most striking findings of this study is that, despite clear elevations in all biomarkers, **most pairwise correlations were not statistically significant** at any time point. Specifically:

- At **6 hours**, all correlations among cTnT, CPK-MB, AST, and LDH were in the "no correlation" range ($|r| < 0.20$, $p > 0.05$).
- At **12 hours**, there was a **weak but statistically significant negative correlation** between cTnT and AST ($r = -0.309$, $p = 0.029$) and between CPK-MB and AST ($r = -0.288$, $p = 0.043$). All other correlations at this time point were non-significant.
- At **24, 36, and 48 hours**, none of the biomarker pairs showed significant correlation ($p > 0.05$), with most r values close to zero.

Thus, even though each marker rises in AMI, **they do not move in a parallel or linearly related fashion** in individual patients across the time points studied. The absence of strong correlations does not imply a lack of clinical usefulness. Instead, it reflects differing biological behavior, timing of release, and specificity of each biomarker. Weak correlations observed at isolated time points are likely incidental and should not be over-interpreted.

Comparison with Other Studies

Several studies have documented **moderate to strong correlations** between peak CPK-MB and peak troponin values or infarct size in AMI, especially when peak values or area-under-the-curve (AUC) measures are used.[13] In contrast, more recent or differently designed studies (e.g., single-time-point measurements, different populations, or small sample sizes) have reported **weak or non-significant correlations** between troponin and CK-MB, suggesting that these biomarkers may reflect partly distinct physiological aspects of myocardial injury and may not always behave in parallel.[11,13]

Our findings fall closer to the latter group, showing **the absence of meaningful linear correlation** between cTnT and CPK-MB at all studied time points (r ranging from -0.055 to -0.217, all $p > 0.05$). This suggests that, in our cohort:

- Individual variability in infarct size, timing of presentation (even within the ≤6 h inclusion window), reperfusion status, and comorbidities may have led to **asynchronous release and clearance** of different biomarkers.
- Non-cardiac factors (e.g., subclinical hepatic or muscle involvement) may have influenced AST and LDH levels independently of the degree of myocardial necrosis, weakening correlations with cardiac-specific markers.
- The relatively smaller sample size (n = 50) may have limited the power to detect modest correlations.

The weak negative correlation between cTnT and AST at 12 hours, although statistically significant, is **small in magnitude** and unlikely to have major clinical implications. It may reflect random variability, differential timing of peak release, or confounding by extracardiac AST sources. A similar argument applies to the weak negative correlation between CPK-MB and AST at 12 hours.

Overall, the lack of robust correlation in this study reinforces the idea that:

- **Each biomarker has its own kinetic profile and influencing factors**, and
- Absence of correlation does not negate their individual diagnostic value, particularly for cTnT.

Pathophysiological and Clinical Implications

1. **Troponin as the Central Marker**

2. The very large and sustained percentage increases in cTnT compared with controls, coupled with its well-established cardiac specificity, support its role as the **primary biomarker** for diagnosis and risk stratification in AMI.[2]

3. **Timing Matters More Than "Panel Parallelism"**

4. The absence of strong correlations between markers suggests that clinicians should interpret them **in the context of timing** rather than expecting them to rise and fall together. For example:

- In the early hours, CPK-MB may rise earlier while cTnT is still rising.
- In late presenters, CK-MB may have started to decline while cTnT and LDH remain markedly elevated.

5. **Limited Interchangeability of Non-troponin Markers**

6. Our correlation data suggest that **CPK-MB, AST and LDH cannot reliably substitute for cTnT** at any time point, since their values do not show consistent linear relationships with troponin. This aligns with current guideline recommendations to use non-troponin markers only as adjuncts or for specific purposes (e.g., suspected reinfarction, historical comparison). [9]

7. **Resource-limited Settings**

8. In settings where only some markers are available, our findings highlight that:

- CPK-MB may still help in early diagnosis, but its interpretation must consider its early peak and decline.
- AST and LDH elevations should be interpreted with caution, given their poor specificity and lack of reliable correlation with cTnT.
- Whenever possible, **troponin assays should be prioritized**, even if the frequency of sampling has to be reduced, as the most informative test.

Strengths and Limitations

Strengths

- Serial measurement of four biomarkers at multiple time points (0, 6, 12, 24, 36, 48 hours) allowed a detailed description of **dynamic changes** and **delta values** over the first 48 hours of AMI.
- Inclusion of a control group enabled calculation of **absolute and percentage deltas**, providing a more meaningful context than raw values alone.
- Relevance to real-world, resource-limited settings

Limitations

- The modest sample size may have limited statistical power to detect moderate correlations.
- Patients were not stratified by STEMI/NSTEMI, infarct size, or reperfusion status.
- Use of a single control mean may exaggerate percentage delta values, especially for low-baseline biomarkers such as cTnT.
- Lack of adjustment for multiple comparisons increases the risk of type I error.

Conclusion: This study highlights that cardiac biomarkers in AMI show distinct and time-dependent kinetic patterns with minimal linear correlation. cTnT remains the cornerstone biomarker, while CPK-MB, AST, and LDH provide complementary information. Correlation alone should not be used to judge clinical interchangeability; timing, specificity, and biological behavior are more important determinants of diagnostic value.

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