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Impact of Consistent and Inconsistent Creatine Kinase-MB and Troponin Levels on Hospital lethality in Acute Coronary Disorder

Syed Wajeeh Ur Rehman Shah [1], Hira Shehzadi [2], Neelam Shahzadi [3], Zainab Khalid [4], Muhammad Naeem [4], Raman Latif Qureshi [5], Mubeen Fatima [6]

1- International Medical University, Kyrgyzstan, Bishkek, Kyrgyzstan
2- Hainan Medical University, Haikou, China
3- Karachi Institute of Medical Sciences (KIMS), Karachi, Pakistan
4- University College of Medicine and Dentistry (UCMD), Lahore, Pakistan
5- Fatima Jinnah Medical University, Lahore, Pakistan
6- Department of Forensic Sciences, Lahore University of Biological & Applied Sciences (UBAS), Lahore, Pakistan

***Corresponding Author:** Hira shehzadi **Email:** javeddrhira@gmail.com **Cell:** +923165777883

ABSTRACT

Background: Serum CK-MB and cardiac troponin are important diagnostic predictors used to determine the prognosis of patients with acute coronary disorders (ACD). However, the effects of these biomarkers on hospital lethality remain underexplored.

Objective: This research aimed to determine the effects of consistent and inconsistent CK-MB and troponin levels on hospital mortality in ACD patients.

Methodology: This comparative study was conducted on patients with confirmed ACD admitted to a tertiary care hospital from January 2023 till June 2024. Patients were categorized into two groups based on the consistency of their CK-MB and troponin levels during hospitalization: consistently elevated or normal biomarkers versus those with variable levels. Hospital lethality was defined as mortality occurring during the hospital stay. SPSS version 26 was used for statistical analysis. The study utilized multivariate logistic regression to ascertain independent factors that are associated with hospital death. For continuous variables, t-tests or Mann-Whitney U tests were employed, and for categorical data, chi-square tests.

Results: There were 500 patients in the trial; 250 were in the inconsistent group and 250 were in the consistent group. In the inconsistent group, the hospital fatality rate was 18%, while in the consistent group it was 10% ($p < 0.05$). Variability in biomarker levels was an independent predictor of higher hospital mortality, according to multivariate analysis (OR 2.5, 95% CI 1.5–4.2).

Conclusion: Inconsistent CK-MB and troponin levels were associated with higher hospital mortality in ACD patients. Monitoring and stabilizing these biomarkers may be essential for improving patient outcomes and guiding therapeutic interventions in acute care settings.

Keywords: Myocardial Infarction, Prognosis., Creatine Kinase, MB Form, Troponin, Acute Coronary Syndrome, Biomarkers, Hospital Mortality, Logistic Models.

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INTRODUCTION

Acute coronary disorders (ACD) are conditions which include myocardial infarction (MI) and unstable angina remain major causes of morbidity and mortality globally [1]. It is therefore important that these patients are diagnosed early and as accurately as possible[2]. Among all the diagnostic tools available globally cardiac biomarkers like Creatine kinase-MB (CK-MB) and troponin have become paramount in evaluation of patients with suspected ACD. They help not only in the diagnosis confirmation but also in risk assessment and prediction of patient's outcome[3]. CK-MB is an isoenzyme of creatine kinase that is mainly present in cardiac muscles and its increase is an indicator of myocardial damage[4]. Troponins, that is, tropomyosin I and tropomyosin T, are the proteins which are found in the blood serum in the course of myocardial necrosis and are considered as highly specific for cardiac damage. These biomarkers have been found to progressively increase in ACD and have been associated with adverse prognosis including mortality[5]. However, few studies have been dedicated to assessing the effect of variable levels of these biomarkers which means that their levels can increase and decrease at any time in the prognosis of patients with ACD[6]. In certain stroke patients, there is an elevation in creatine kinase-MB (CK-MB) even in the absence of obvious signs of acute coronary syndrome. Its increases have been proposed as a biological marker for myocardial damage associated with stroke. In comparison to CK-MB, troponin T has higher sensitivity and specificity in detecting mild myocardial damage. In order to ascertain if troponin T rises concurrently with CK-MB, we examined troponin T levels following stroke. For ten days, we measured the levels of troponin T, myoglobin, total creatine kinase (total CK), and CK-MB in thirty patients who had a massive hemispheric infarction but no prior history of coronary heart disease. Following a stroke, there is no rise in troponin T, a more precise biochemical marker of cardiac damage. Elevated CK-MB in conjunction with normal troponin T indicates that CK-MB is not the biological marker for myocytolysis. In stroke patients, CK-MB increases are most likely not cardiac in nature. This study was therefore designed to fill this gap by comparing the rate of consistent and/or inconsistent elevations in CK-MB and troponin during hospitalization and the hospital lethality rate of the patients with ACD. This study may be useful for clinicians when the patients with variable biomarker levels are being managed[7].ECG evaluation, detection of cardiac circulating biomarkers, and clinical sign and symptom assessment are all involved in the diagnosis of acute myocardial infarction (AMI).

MATERIALS AND METHODS:

This comparative study was conducted at Ghurki Trust Teaching Hospital, Lahore, Pakistan, University of Lahore Teaching Hospital, Lahore, Pakistan, and International Medical University, Kyrgyzstan, between January 2023 till June 2024, after receiving ethical approval from the institutional review board (Approval No. ERC/2023/16A). The study included patients aged 18 years or older who had a confirmed diagnosis of acute coronary disorder (either myocardial infarction or unstable angina) and presented with elevated CK-MB and/or troponin levels at admission. Exclusion criteria included patients with end-stage renal disease, those with troponin elevations unrelated to myocardial ischemia (such as those due to sepsis or chronic renal disease), and patients who did not have at least two serial CK-MB and troponin measurements during hospitalization. A systematic sampling technique was used, with every nth eligible patient selected until the target sample size was achieved. The sample size calculation was

conducted using G*Power, with an 80% power (β = 0.20) and a 5% significance level (α = 0.05). Preliminary data suggested an expected hospital mortality difference of 8% between the consistent and inconsistent biomarker groups. The minimum sample size required was 480 patients, but a total of 500 patients were included to account for potential dropouts. Patients were divided into two groups based on the variability of their CK-MB and troponin levels. The consistent group(n=250) included patients whose CK-MB and troponin levels remained consistently elevated or consistently normal throughout hospitalization. The inconsistent group(n=250) comprised patients with fluctuating CK-MB and/or troponin levels. Biomarker levels were measured at admission and at 24-hour intervals during hospitalization to assess the consistency or variability of the biomarker levels.The primary outcome of the study was in-hospital mortality, defined as any death occurring during the hospital stay. Secondary outcomes included the length of hospital stay and ICU admission rates. Data analysis was performed using SPSS version 26.0. Continuous variables were compared using t-tests or Mann-Whitney U tests, and categorical variables were compared using chi-square tests. A multivariate logistic regression model was used to identify independent predictors of in-hospital mortality, adjusting for age, gender, diabetes, hypertension, mechanical ventilation, and CK-MB/troponin variability. The proportional hazards assumption was tested to ensure model validity, and p-values ≤0.05 were considered statistically significant.

RESULTS

The table-1 presents the baseline demographic and clinical characteristics of patients. There were no statistically significant differences between the two groups in terms of age, gender, or prevalence of comorbidities such as diabetes, hypertension, and smoking history. The p-values indicate that both groups were comparable, ensuring that any differences in outcomes are not due to demographic or baseline clinical disparities.

Table-1: Baseline Demographic and Clinical Characteristics of Patients

Characteristic	Consistent Group (n=250)	Inconsistent Group (n=250)	p-value
Mean Age (years)	64.8 ± 11.2	65.2 ± 12.4	0.45
Male Gender (%)	58%	62%	0.32
Diabetes Mellitus (%)	28%	30%	0.61
Hypertension (%)	40%	42%	0.78
Smoking History (%)	22%	25%	0.49

*For continuous variables (e.g., mean age): Student's t-test was used for comparison between groups.
*For categorical variables (e.g., gender, diabetes, hypertension, smoking history): Chi-square test was used.
**p-values* indicate the statistical significance of differences between the consistent and inconsistent groups.

The baseline clinical and demographic characteristics of the patients in the consistent and inconsistent groups are contrasted in the fig-1.It shows the average age, the proportion of men to women, and the frequency of diabetes, hypertension, and smoking history. The average age of both groups is comparable: 64.8 years for the consistent group and 65.2 years for the inconsistent group. In the inconsistent group, the percentage of men is marginally greater (62%) than in the consistent group (58%). With 28% in the consistent group and 30% in the inconsistent group, the prevalence are comparable between the two groups. With 40% in the consistent group and 42% in the inconsistent group, the rates in both groups are similar. Compared to the consistent group (22%), a somewhat higher percentage of patients in the inconsistent group (25%) had a history of smoking.

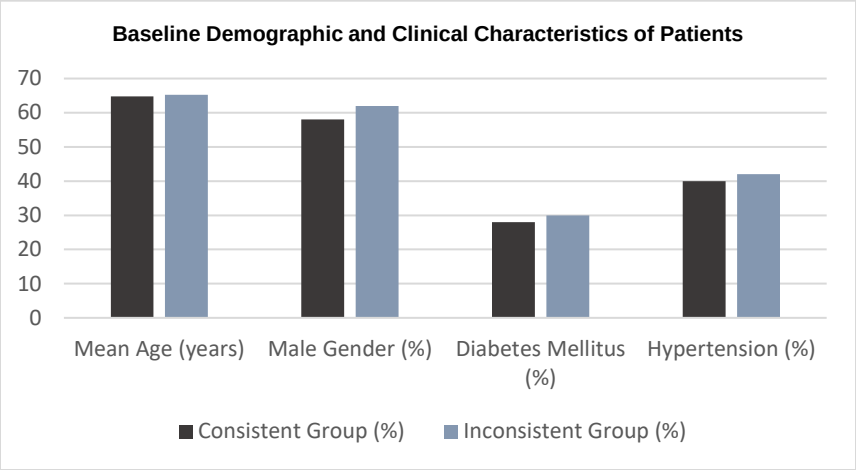

Fig-1: Baseline Demographic and Clinical Characteristics of Patients

Table-2 shows percentage of mortality in Hospital was higher in the inconsistent group, 18% as compared to the consistent group 10%; p = 0.02. The inconsistent group also had a longer median hospital stay of 8 days as compared to 5 days of the consistent group (p=0.01) and a higher proportion of patients admitted to the ICU 35% as compared to 25% (p=0.04). These findings indicate that fluctuations in biomarker concentration could be indicative of a more aggressive form of the disease and poorer prognosis.

Table 2. Hospital Outcomes of Patients

Outcome	Consistent Group (n=250)	Inconsistent Group (n=250)	p-value
Hospital Lethality (%)	10%	18%	0.02
Median Length of Stay (days)	5	8	0.01
ICU Admission (%)	25%	35%	0.04

For hospital lethality and ICU admission (categorical variables): Chi-square test was used.
For length of stay (continuous variable): Mann-Whitney U test was used due to the non-normal distribution of data.
p-values indicate statistical significance.

The multivariate analysis found that different pattern of CK-MB and troponin was an independent predictor of hospital lethality with OR of 2. 5 (95% CI 1.5–4.2, p<0.01). Other significant predictors were age more than 70 years, diabetes mellitus and use of invasive mechanical ventilation. These observations emphasize the role of biomarkers' stability as one of the most crucial indicators of the patients' outcomes.

Table 3. Multivariate Analysis of Predictors of Hospital Lethal

Variables	Odds Ratio (OR)	95% Confidence Interval (CI)	p-value
Inconsistent Biomarkers	2.5	1.5–4.2	<0.01
Age > 70 Years	1.8	1.2–2.9	0.02
Diabetes Mellitus	1.6	1.1–2.7	0.03
Mechanical Ventilation	2.2	1.4–3.5	<0.01

Multivariate logistic regression was used to identify independent predictors of hospital lethality.
The model adjusted for age, diabetes mellitus, mechanical ventilation, and biomarker inconsistency.
p-values indicate the statistical significance of the variables in the model.

The multivariate analysis of hospital lethality predictors is depicted in the graph, which also includes the odds ratios (OR) and 95% confidence intervals (CI) for each variable. Hospital lethality risk was considerably greater in patients with inconsistent biomarker levels (OR of 2.5 (CI: 1.5–4.2), meaning they were 2.5 times more likely to die in the hospital than those with consistent biomarkers. In comparison to younger patients, older patients (over 70 years old) had an OR of 1.8 (CI: 1.2–2.9), indicating an 80% higher chance of hospital lethality. Individuals with diabetes were 60% more likely than non-diabetic patients to experience hospital lethality, with an OR of 1.6 (CI: 1.1–2.7). An OR of 2.2 (CI: 1.4–3.5) indicated a notably increased risk of mortality in the presence of mechanical ventilation.

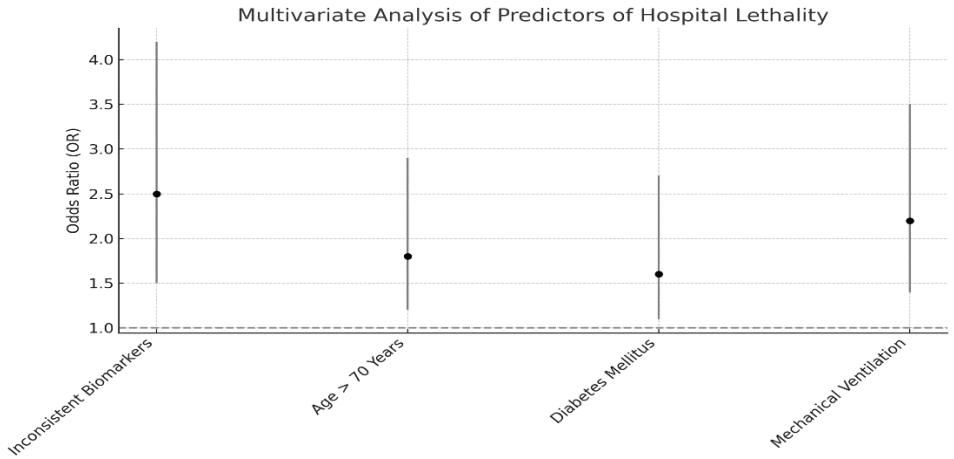

Fig-2: multivariate analysis of hospital lethality predictors

DISCUSSION

This study demonstrates a significant association between inconsistent CK-MB (Creatine Kinase-MB) and troponin levels and higher in-hospital mortality in patients with acute coronary disorders (ACD) [8]. The results indicate that variations in these biomarkers may reflect a worsening cardiac status, associated with poor prognosis. The fluctuation in biomarker levels could be linked to intermittent ischemic episodes, fluctuations in myocardial oxygen demand and supply, or other pathophysiological processes that are not fully captured by single measurements of biomarkers[9].The higher mortality rates noted among the group of subjects with biomarker fluctuation are useful to demonstrate the realities of treatment in patients with irregular values. These patients may need greater care, close supervision and more aggressive interventions to reduce the risk or deterioration of the cardiac state [10]. Biomarker fluctuations probably indicate a less stable environment within the cardiac context which warrants increased monitoring. According to Pelletier *et al.* (2016) investigations, patients with inconclusive troponin or CK-MB values should undergo early invasive intervention, including revascularization or medical management that includes beta-blockers or antiplatelets, to reduce subsequent myocardial infarction [11]. Furthermore, patients having varying levels of biomarkers were found to be having a longer length of stay in the hospital and they are more prone to be admitted in the ICU than patients

with constant biomarkers. This also means that elevated and then falling CK-MB and troponin levels may be an indicator of increased resource utilization in hospital[12]. The identification of these high-risk patients at an early stage could help clinicians manage hospital resources better and perhaps enhance the ICU capacity, and ultimately reduce hospital mortality rates[13]. Amoras *et al.* (2023) stated that cardiac biomarkers, such as myoglobin, cardiac troponin I (cTnI), cardiac troponin T (cTnT), and total creatinine kinase (CK), play a pivotal role in the risk assessment and clinical management of patients with acute coronary syndrome (ACS)[14]. However, the current study adds to the literature by looking at variability of these biomarkers instead of peak or baseline values. A more dynamic approach to longitudinal biomarker monitoring can offer critical insights into the evolving condition of a patient, which may be missed when using static measurements[15] .In patients with chronic renal failure (CRF), elevated biomarkers such as CK-MB and troponin can be observed even in the absence of overt signs of myocardial ischemia, making it challenging to interpret the clinical relevance of these markers. Raffee *et al.* (2022) stated that reducing the coefficient of variation (COV), a statistical measure that reflects the reliability of a diagnostic tool, could lead to more frequent and accurate diagnoses of acute myocardial infarction (AMI) in these populations, allowing for earlier treatment and improved outcomes[16] .The findings of this study have several important clinical implications. First, routine monitoring of CK-MB and troponin levels in ACD patients should not only focus on initial or peak values but also consider biomarker trends over time. This would enable the early detection of worsening myocardial injury or unstable ischemic episodes[17]. Patients with fluctuating biomarker levels should be flagged as high-risk and may benefit from more aggressive interventions, including early invasive strategies, continuous hemodynamic monitoring, and closer follow-up after hospital discharge [18].The relationship between inconsistent biomarker levels, longer ICU stays, and extended hospitalization durations underscores the need for better hospital resource management. Patients with variable biomarkers may require closer surveillance and more frequent assessments to prevent adverse outcomes. Early identification of this high-risk group will help ensure that hospital and ICU resources are used more efficiently and that patients receive the level of care necessary to improve outcomes [19].There are several limitations to this study. First, the study was conducted at only three hospitals, which may affect the generalizability of the findings. Larger, multi-centre studies are needed to validate these results. Second, although the study adjusted for key clinical factors such as age, diabetes, and mechanical ventilation, other relevant confounders like medication use (e.g., aspirin, beta-blockers, antiplatelet agents), previous cardiac history, and socioeconomic status were not included in the analysis[20]. These factors could potentially influence the association between biomarker variability and outcomes. Future studies should incorporate a broader range of clinical and demographic variables to strengthen the conclusions [21].However, this work contributes to the existing knowledge by looking at the effects of biomarker variability in a way that has not been done comprehensively before. The findings of the study imply that biomarkers should be monitored longitudinally rather than this short study to improve the clinician's understanding of patients' risk and their subsequent clinical management[16, 22].

CONCLUSION

This study demonstrates that variability in CK-MB and troponin levels is significantly associated with higher in-hospital mortality in patients with acute coronary disorders (ACD). Patients with inconsistent biomarker levels are at greater risk of adverse outcomes, including prolonged hospital stays and increased ICU admissions. These findings highlight the need for continuous monitoring of CK-MB and troponin levels throughout hospitalization, rather than relying solely on initial or peak values. Tailored, individualized treatment strategies targeting patients with fluctuating biomarker levels may improve clinical outcomes and reduce mortality. Further research is warranted to explore the mechanisms underlying biomarker variability and the potential benefits of early, aggressive interventions in these high-risk patients.

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Conflicts of Interest:

The authors did not disclose any conflicts of interest.

Data Availability:

The data supporting the findings of this study are available upon reasonable request from the corresponding author.

Authors' Contribution:

All authors contributed equally.

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