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Rise CKMB and Myoglobin Levels in Non-Cardiac Patients of Ischemic Stroke Presenting to Emergency Department of a Tertiary Care Hospital

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ABSTRACT

***Objective*:** To assess the rise in CKMB and Myoglobin levels and associated factors in non-cardiac patients of ischemic stroke presenting to the Emergency Department of a Tertiary Care Hospital.

Study Design: Cross-sectional study.

Place and Duration of Study: Department of Emergency Medicine, Pak Emirates Military Hospital (PEMH), Rawalpindi Pakistan, from Dec 2020 to May 2021.

Methodology: A total of 150 patients with ischemic stroke diagnosed by the consultant Emergency physician or medical specialist based on clinical and neuro-radiological findings were included in this study. Serum CKMB and myoglobin levels were assessed along with other baseline investigations among the study participants. In addition, the relationship of age, gender, the severity of the stroke and the presence of non-cardiac comorbidities was assessed with the rise in CKMB and myoglobin levels among the target population.

Results: Out of 200 patients with ischemic stroke included in the study, 114(67.0%) were males, while 86(43.0%) were females. 75(37.5%) patients had either raised CKMB or Myoglobin levels, while 125(62.5%) patients had both biomarkers within range. On the National Institutes of Health Stroke Scale, 110(55.0%) patients had mild, 55(22.5%) had mild to moderately severe, 25(12.5%) had severe, and 10(5.0%) had very severe symptoms. Statistical analysis revealed that increased stroke severity had a statistically significant relationship (p-value<0.001) with raised CKMB/Myoglobin levels in the target population.

Conclusion: Raised CKMB or myoglobin levels were found in many patients with acute ischemic stroke. The stroke severity was associated with raised levels of these biomarkers.

Keywords: CKMB**,** Ischemic stroke, Myoglobin, Non-cardiac patients.

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INTRODUCTION

Ischemic stroke has been one of the leading causes of mortality and morbidity among patients of middle and old-age groups in low and middle-income countries.[1] This potentially fatal condition is also equally prevalent in the developed world.[2] Multiple studies have been performed across the globe to look for the factors related to the severity of this disease which disrupts the overall functioning of the human body.[3] A lot of biochemical abnormalities have been noted among these patients, which may have predisposed the patient towards this serious condition or have occurred as a result of the stroke.[4]

It would be interesting to look for relevant biochemical and chemical markers in patients with ischemic stroke. Both ischemia and brain injury may lead to a rise in various chemicals or enzymes in the body among patients suffering from ischemic stroke.[5] CKMB and myoglobin rise has been studied in various physiological and pathological conditions but most have been related to heart, kidneys or musculoskeletal system.[6] Relationship of these chemicals with incidence and severity of stroke would be an interesting phenomenon for clinicians and researchers.

Some research has been done on the rise in cardiac biomarkers among patients suffering from a stroke. Ay *et al*. from Turkey compared CKMG with troponin T levels and concluded that troponin T is more sensitive to cardiac muscle damage and CKMB may be of non-cardiac origin in patients of stroke.[7] Mohamed *et al*. studied the role of biomarkers in diagnosing and predicting the prognosis of embolic stroke. They revealed that the mean levels of biomarkers like BNP, D-dimer, and CK-MB were significantly higher in patients with cardio-embolic stroke than in patients with non-cardio-embolic stroke and were associated with poor short-term outcomes.[8] Xu *et al*. conducted a study on Chinese patients regarding a possible relationship between myoglobin levels and troponin T

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levels and hematoma volume and growth among patients with hemorrhagic stroke. They concluded that serum myoglobin was raised in a significant number of patients presenting with hemorrhagic stroke, and raised myoglobin levels had a statistically significant association with hematoma volume. However, Troponin T levels did not show any such association in their study.[9] existing data suggest that patients with both ischemic and hemorrhagic stroke may present with raised cardiac markers even any cardiac pathology.

Stroke medicine is an evolving speciality in our part of the world. Emergency medicine specialists, internal medicine teams and neurology services share the burden of managing these patients at various levels. Nomani *et al*. conducted a study based on local data concluding that while basic research has gained pace in stroke medicine, advanced research and relevant biochemical studies are extremely limited. The field of stroke neurology needs to grow substantially in Pakistan to be at par with the developed world.[10] We, therefore, designed this study with the rationale to assess the rise of CKMB and Myoglobin levels and associated factors in non-cardiac patients of ischemic stroke presenting to the emergency reception of a tertiary care hospital.

METHODOLOGY

This cross-sectional study was conducted at the Emergency Medicine Department of Pak Emirates Military Hospital, Rawalpindi Pakistan, from December 2020 and May 2021. Ethical approval for the study was obtained from the Ethical Review Board Committee of the Combined Military Hospital, Rawalpindi Pakistan, (A/28/EC/298/2021). The sample size was calculated using the WHO sample size calculator using the population proportion of cardiac biomarkers in stroke at 22.7%,[11] and the margin of error as 10%.

Inclusion Criteria: Patients of both genders between 18 to 70 years presenting with acute ischemic stroke were included in the study.

Exclusion Criteria: Patients with a past or current history of cardiac or skeletal abnormalities or rheumatological conditions were excluded from the study. Patients with cancer, a history of renal or autoimmune disease, or a hemorrhagic stroke were also excluded from the study. In addition, the study did not include patients taking medications that could interfere with CKMB or myoglobin levels. Patients with acute changes on electrocardiogram were excluded as well.

The non-probability consecutive technique was used to gather the sample for the study. Acute ischemic stroke was diagnosed by a consultant medical specialist based on clinical findings and a plain CT scan brain done at the time of presentation.[12]

Myoglobin and CKMB levels were performed on the serum of patients in the Armed forces institute of pathology with raised levels considered as>0.5 mg/dl for myoglobin,[13] and 99th percentile of normal values, 5-25 ng/ml for CKMB.[14] stroke severity was assessed via National Institutes of Health Stroke Scale (NIHSS). The following classes were made based on NIHSS scores Mild<5, Mild to Moderately severe, severe [15-24] and very severe >25.15

Subjects and their caregivers were provided with a detailed description of the study and were inducted into the study after written informed consent. Subjects with confounding variables like the presence of cardiac illness or skeletal conditions were identified by detailed history taking and excluded from the study. The treating physician assessed the severity of the stroke via the National Institutes of Health Stroke Scale (NIHSS). Serum CKMB and myoglobin levels were assessed from the laboratory of their hospital. Variables in the study included age, gender, the severity of the stroke and the presence of non-cardiac comorbidities (HTN/DM).

The characteristics of participants and the distribution of the myoglobin and CKMB levels were described using descriptive statistics. Chi-square was used to determine between-group variances in categorical correlates. In addition, the relationship of age, gender, the severity of the stroke and the presence of non-cardiac comorbidities was assessed with the rise in levels of CKMB/Myoglobin. All statistical analysis was performed using Statistics Package for Social Sciences version 23.0 (SPSS-23.0). Differences between groups were considered significant if p-values were ≤0.05.

RESULTS

Out of 200 patients with ischemic stroke included in the study, 114(67.0%) were males, while 86(43.0%) were females. The mean age of the study participants was 57.6±5.66 years. Out of the study participants, 75(37.5%) had either raised CKMB or Myoglobin levels, while 125(62.5%) had both biomarkers within range. In addition, 39(19.5%) patients had raised myoglobin levels while 42(21.0%) had raised CKMB levels. Table-I summarized the basic demographical

findings of patients included in our study. On the National Institutes of Health Stroke Scale, 110(55.0%) patients had mild, 55(22.5%) had mild to moderately severe, 25(12.5%) had severe, and 10(5.0%) had very severe symptoms. Pearson chi-square analysis revealed that increased severity of stroke had a statistically significant relationship (*p*-value <0.001) with raised CKMB/Myoglobin levels in the target population (Table-II).

Table-I: Characteristics of Patients Presenting with Acute Ischemic Stroke (n=200)

Characteristics	Frequency(%)
Age (years)	
Mean±SD	57.63±5.669
Range (min-max)	38 years-68 years
Gender	
Male	114 (62.2)
Female	86 (37.8)
Rise in myoglobin	
Yes	39 (19.5)
No	161 (80.5)
Rise in CKMB	
Yes	42 (21.0)
No	158 (79.0)
Severity of stroke	
Mild	110 (55.0)
Mild to moderately severe	55 (22.5)
Severe	25 (12.5)
Very severe	10 (5.0)

Table-II: Association of Different Variables with Rise in Myoglobin/CKMB Levels (n=200)

Factors	CKMB/Myoglobin within range (n=125) n(%)	Raised CKMB or Myoglobin (n=75) n(%)	*p*-value
Age			
50 year or less	53 (42.4)	33 (44.0)	
>50 years	72 (57.6)	42 (66.0)	0.825
Gender			
Male	71 (56.8)	43 (57.3)	
Female	54 (43.2)	32 (42.7)	0.941
Severity of Stroke			
Mild	85 (68.0)	25 (33.3)	
Moderate	26 (20.8)	29 (38.7)	<0.001
Severe	11 (8.8)	14 (18.7)	
Very severe	03 (2.4)	07 (9.3)	
Presence of non-cardiac comorbidities			
No	80 (64.0)	40 (53.3)	0.137
Yes	45 (36.0)	35 (46.7)	

DISCUSSION

The human body adapts various mechanisms to cope with physical or mental stress. Various chemicals in the body are released in response to various types of stresses in different systems. Events like acute ischemic stroke cause serious damage directly to the most important organ of the body and indirectly to the whole body. In this time of acute crisis, the body may adapt via various mechanisms in the form of the release of different biochemicals to overcome this situation. Few biomarkers have been selective to certain systems, but few may not be specific. Limited biomarkers have been studied in relation to acute ischemic stroke. Therefore, we planned this study to assess the rise of CKMB and Myoglobin levels and associated factors in non-cardiac patients of ischemic stroke presenting to the emergency reception of a Tertiary Care Hospital.

Suleiman *et al*.[16] conducted a study from Nigeria with an objective similar to that of ours and concluded that mean values of serum cTnT and CK-MB were higher in acute ischemic stroke patients compared to controls. They performed a case-control study and also included cTnT in addition to CKMB and myoglobin. Despite a slight difference in design, our results supported the findings of Suleiman *et al*., as cardiac markers were significantly raised in patients in our study who presented with acute ischemic stroke.

Xu *et al*.[17] conducted a systematic review and meta-analysis to evaluate the relationship between changes in cardiac biomarkers and stroke. They did an extensive literature search and concluded that several potential mechanisms might be involved in the brain-heart axis. Therefore, clinicians should keep an eye on cardiac function in the treatment of cerebrovascular diseases in order to provide timely and more accurate treatment. We carefully excluded cardiac illnesses from our study participants. However, our study design could still not establish that raised biomarkers were due to brain-heart axis abnormalities or direct stroke damage or underlying cardiac damage.

Another similar study was performed in China by Liu *et al*.[18] regarding the short-term prognostic value of cardiac indicators in patients who had experienced acute ischemic stroke. They studied various cardiac biomarkers and concluded that myoglobin may be an independent predictor of short-term outcomes in patients with acute ischemic stroke. We studied CKMB and myoglobin and concluded that the rise in these biomarkers strongly correlates with stroke severity at the presentation time.

Zeng *et al*.[19] carried out a study to look for the impact of cardiac parameters on the prognosis of patients

with non-large atherosclerotic infarction. They revealed that the rise in CKMB and more severe forms of stroke were independently related to poor prognosis in patients with acute ischemic stroke. We did not study the prognosis or outcome of stroke, but our results revealed that raised cardiac biomarkers were related to stroke severity.

LIMITATIONS OF STUDY

The main limitation of our study was the design of the study. Case-control or cohort study design would have established the cause-and-effect relationship. Moreover, baseline values of these biomarkers in these patients were unknown, so we could not attribute the rise in the levels to the event of a stroke. Future studies with better design may establish the association with more precision.

CONCLUSION

Raised CKMB or myoglobin levels were found in many patients with acute ischemic stroke. In addition, stroke severity was associated with raised levels of these biomarkers.

Conflict of Intrest: None.

Author's Contribution

Following authors have made substantial contributions to the manuscript as under:

MD: Drafting the manuscript, data interpretation, critical review, approval of the final version to be published.

YA: Data acquisition, data analysis, data interpretation, critical review, approval of the final version to be published.

AH & AK: Conception, data acquisition, drafting the manuscript, approval of the final version to be published.

KRB & SR: Study design, data analysis, critical review, drafting the manuscript.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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