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Indications and Clinical Utility of Cardiac Biomarkers in the Emergency Room of a Nigerian Tertiary Hospital

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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Original Research Article

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ABSTRACT

Background: The prevalence of acute coronary syndrome (ACS) in Nigeria is on the rise with dire morbidity and mortality risks. Cardiac biomarkers are rapid and sensitive tools used as adjunct in the diagnosis of ACS. The clinical utility of cardiac biomarkers is yet to be well explored in Nigerian setting.
Objectives: To determine the indications and clinical utility of cardiac biomarkers as well as their electrocardiographic (ECG) changes.

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Methods: This study is a retrospective review of all patients who had point-of-care serum Troponin-I, Creatine kinase MB isoenzyme and myoglobin done at the medical emergency department of LASUTH over a three year period (January 2017 to December 2019). Their records were retrieved; demographics, indications for testing and ECG findings were recorded. Data was analyzed using SPSS version 20.0 software.
Results: 593 tests were done in the 3 years period of study. Only 397 patients had complete records. 48.6% were male. The mean age of the study population was 55.02 ± 16.64 years (range 13-94 years). Chest pain was the commonest indication for test (91%). Other indications are loss of consciousness, palpitations, seizures and unexplained dyspnea. Mean duration of chest pain prior to presentation was 9 days. 16.1% (64 patients) of patients tested had elevated cardiac biomarkers and 87.5% of those with elevated cardiac biomarkers had abnormal ECG suggestive of ACS.
Conclusion: This study showed that cardiac biomarker is an important point-of-care test in the evaluation of chest pain. Cardiac biomarkers should therefore be a routine test in the emergency room.

Keywords: Cardiac biomarkers; troponins; CK MB; myoglobin; acute coronary syndrome; ischemic heart disease; chest pain.

1. INTRODUCTION

Cardiovascular diseases are the major cause of disability and premature death worldwide with hypertension and Coronary artery disease (CAD) being the leading cause [1-3]. CAD was previously thought to be rare in sub - Saharan Africa [4] but its prevalence is now reported to have increased. [1,2,5-9] At present Ischemic heart disease (IHD) is becoming a modern epidemic in developing countries partly as a consequence of urbanization, poor lifestyle and increasing longevity [3,10]. The risk factors of Ischemic heart disease are also on an increase in Nigeria especially in the last decades [5,11-14]. Acute coronary syndrome (ACS) is a leading cause of death in the United States and accounts for 625,000 hospital discharges annually [15]. The morbidities and mortality associated with ACS in Nigeria is also increasing [6] and the most common presentation is still chest pain [1,7,9]. Etiology of chest pain is however diverse and some patients presenting with ACS may not have the typical chest pain expected of ACS [15].

Chest pain is a common presentation in the emergency room which needs to be evaluated [16]. Non cardiac causes of chest pain may mimic ACS and subject the patients to needless invasive procedures [17]. Cardiac enzymes evaluation could therefore be a way of making rapid diagnosis in order to make prompt decision on further intervention when a patient presents with chest pain and clinical suspicion of ACS [18,19]. As at now, cardiac biomarker testing is not yet routinely recommended in all patients presenting to the emergency room on account of chest pain probably for fear of false-positive test results and consequent needless intervention, however, patients with high probability risk of ACS should have cardiac biomarker assay done as further evaluation following history, physical examination and 12-lead electrocardiogram (ECG) evaluation [18,19].

In a review of over 430,000 patients with confirmed acute myocardial infarction, from the National Registry of Myocardial Infarction 2, one-third had no chest pain on presentation to the hospital [15]. Cardiac markers troponin T, creatine kinase MB fraction (CK-MB mass) and myoglobin were helpful in the differential diagnosis of chest pain, even when the ECG was unremarkable or nonspecific. [15] Also, a rise and fall of cardiac markers have been shown to correlate positively with electrocardiographic changes peculiar to ACS [20,21]. Cardiac biomarkers are therefore valuable and sensitive tools to rapidly detect myocardial necrosis, which is a hallmark of acute coronary syndromes (ACS), and their use in the evaluation of chest pain in the emergency room for early diagnosis of ACS and timely intervention cannot be overemphasized [19,21-24].

Inadvertent undiagnosed ACS may be catastrophic [17,25]. The 2% to 5% of Acute MI patients who were inadvertently discharged home from the emergency room in the United States had poor outcomes and resulted in malpractice suits [17]. A combination of different protocols involving the use of prompt and oriented history taking, physical examination, resting ECG and rapid bedside cardiac marker

testing will help in triaging ischemic chest pain and help prevent missed diagnosis [3].

The clinical utility of cardiac biomarkers is yet to be well explored in emergency room in the Nigerian setting, so also is the comparison of the patients with positive cardiac biomarkers with their ECG features. Therefore, there is a need to fill this knowledge gap. This study set out to determine the indications and clinical utility of cardiac biomarkers in an emergency room as well as to evaluate the electrocardiographic (ECG) changes of patients with positive cardiac biomarkers.

2. METHODOLOGY

This is a retrospective study conducted at Lagos State University Teaching Hospital, Ikeja, Lagos, the only State owned tertiary health Institution. The Medical emergency department of the hospital attends to over 35,000 patients per annum with about 15,000 admissions. The Medical emergency unit is equipped with a standard side Laboratory where rapid cardiac biomarker assay and other biochemical and hematology tests were done round the clock.

We analyzed the records of all the patients who were admitted, over a 3 year period, in the Medical emergency department of the Hospital from January 2017 to December 2019. We extracted the data of all the patients who had point of care cardiac biomarkers (Serum Troponin-I, Creatine kinase MB isoenzyme and myoglobin) done during this study period. Their demographic data, indication for testing and electrocardiographic parameters were recorded. Patients with incomplete or lost data were excluded. Also excluded were individuals who had presented previously with similar complaints within the study duration, patients who discharged against medical advice or died before investigations were concluded.

Rapid cardiac biomarkers tests were done with FIA8000 quantitative immunoassay analyzer of Getein biotechnology co. ltd with cut off value for CK-MB, Troponin I and Myoglobin set at <5.0ng/ml, <0.5ng/ml and <70ng/ml respectively.

Resting 12 lead Electrocardiogram (ECG) was performed on all patients using a 3- channel electrocardiograph (cardiofax YD-907D) machine with a paper speed of 25mm/s and amplitude of 10mm/mv using the recommendation of the American Heart Association (AHA) concerning standardization of leads [26]. The electrocardiographs were interpreted by two cardiologists

Data was analyzed using statistical product and service solutions (SPSS) version 20.0 software (SPSS Inc, Chicago, IL). The mean age of the study population was expressed as mean $\pm$ standard deviation while Pie chart, bar chart and frequency tables (percentages) were generated for categorical variables.

3. RESULTS

593 tests were done in the 3 years period of study. However, only the complete records of 397 patients were analyzed having excluded the incomplete records. 48.6% were male. The mean age of the study population was 55.02 $\pm$ 16.64 years (range 13-94 years).

Fig. 1 showed the indication for test. The commonest indication for testing was chest pain (91% of patients). Other indications included Loss of consciousness, palpitations, seizures and unexplained dyspnea. The mean duration of chest pain prior to presentation was 9 days.

Fig. 2 showed the frequency and percentage distribution of the positive cardiac biomarkers of the study population. Troponin I was elevated in 93.8% (60) of the 64 positive results. CK-MB was positive in 32 patients (50%) while myoglobin was elevated in only 4 patients (6.25%).

Table 1 showed that 64 tests were positive for elevated cardiac biomarkers out of a total of 397 tests done. The male to female distribution was 34:30. None of the patients under the age of 20 years had a positive test. Majority of the positive tests were seen in the 40-59 year age group.

Table 2 showed the electrocardiographic abnormalities seen in the patients with elevated cardiac biomarkers. ECG abnormality was seen in 87.5% of the patients with elevated biomarkers while ECG was normal in 12.5% of the patient population. The commonest ECG abnormality was ST segment depression followed by T wave inversion.

4. DISCUSSION

This study evaluated the indications for request and the clinical utility of cardiac biomarkers as well as the electrocardiographic abnormalities seen in the patients with positive biomarkers in an emergency room of a Teaching hospital.

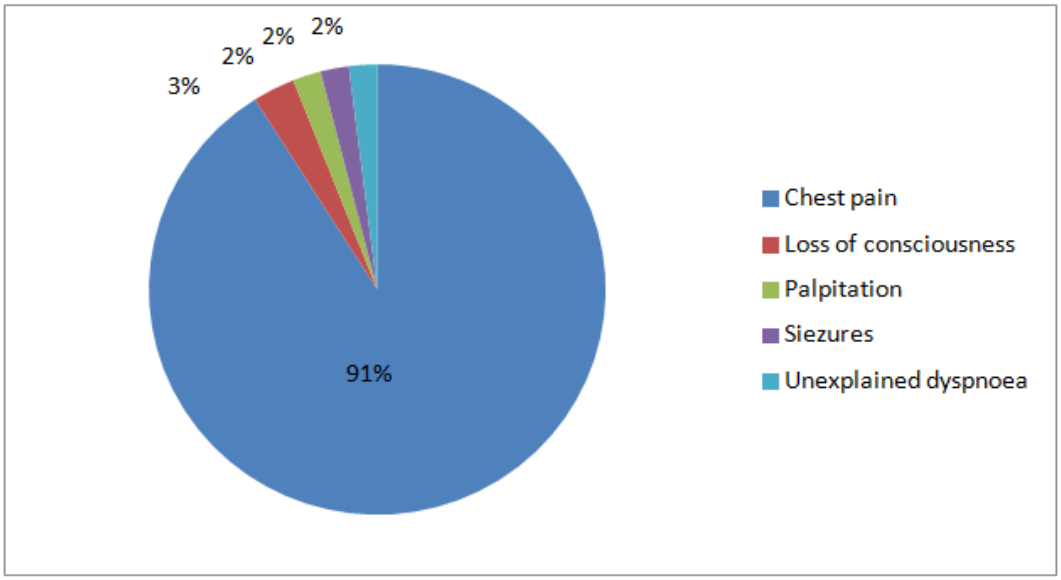

Fig. 1. Indications for Test

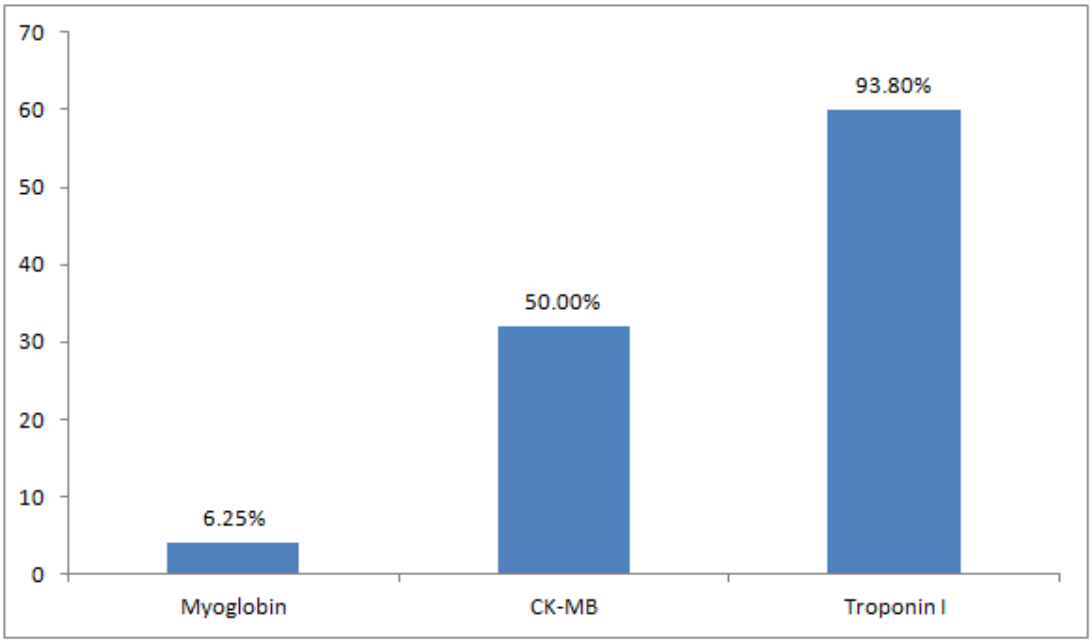

Fig. 2. Frequency and percentage distribution of the patients with positive cardiac biomarkers

Table 1. Age and gender distribution of tests

Age (Years)	Male N (Positive tests)	Female N (Positive tests)	Total N (Positive tests)
≤20	**3 (0)**	**4 (0)**	**7 (0)**
20-39	**23 (3)**	**27 (1)**	**50 (4)**
40-59	**101 (21)**	**99 (19)**	**200 (40)**
60-79	**57 (9)**	**58 (7)**	**115 (16)**
≥80	**9 (1)**	**16 (3)**	**25 (4)**
Total	**193 (34)**	**204 (30)**	**397 (64)**

Table 2. ECG abnormalities in the patients with elevated cardiac biomarkers

ECG Interpretation	Male N	Female N	Total (%)
Normal ECG	**4**	**4**	**8 (12.5)**
T wave Inversion	**5**	**6**	**11 (17.2)**
ST Segment Elevation	**6**	**3**	**9 (14.1)**
ST segment Depression	**10**	**9**	**19 (29.7)**
Pathological Q waves	**7**	**2**	**9 (14.1)**
Non Specific	**2**	**6**	**8 (12.5)**
Total	**34**	**30**	**64 (100)**

We found that the commonest indication for requesting cardiac biomarkers test was chest pain just as was noted in previous works [1,8,16,27-29]. Similarly, typical chest pain in patients with a high probability risk of ACS was the major indication for testing the majority of patients analyzed by Makam et al [18] in the report of the National Hospital Ambulatory Medical Care Survey. While biomarker tests were done in 8.2% of visits in the absence of ACS-related symptoms by Makam et al, [18] our study similarly showed that biomarker test was done in 9% of patients without chest pain. Other indications for testing in this index study were loss of consciousness, palpitations, seizures and unexplained dyspnea.

In the large multicenter National Hospital Ambulatory Medical Care Survey done in the United States, [18] only adults > 18years were recruited. The age distribution of the population in our study was 13-94 years, however none of the subjects below the age of 20 years had elevated cardiac biomarkers. Our study also corroborated previous works that have shown rarity of acute coronary syndromes in adolescence [2,8,9,27,28]. However, epidemiological shift has being noted and ischemic heart disease had been reported in younger people [5,10].

In this study, elevated Troponin I was seen in 93.8% of the patients with elevated cardiac biomarkers while CK-MB and Myoglobin were seen in 50% and 6.25% of the patients respectively. This may not be unrelated to the fact that most of our patients presented late with a mean time of chest pain prior to presentation of 9 days. It is thus understandable that there would have been a rise and fall in the myoglobin and CK-MB levels and so elevated level may not be detected. While myoglobin provides the earliest identification of myocardial injury, [18,19,22] Troponin-I may still be detectable up till about 14 days post ACS [30]. Walter et al [29] in a study of 233 patients reported that troponin was elevated in 16% and CK-MB mass in 24% probably due to early presentation of their patients to the emergency room. Late presentation of diseases had previously been reported among Nigerians [31].

In our study, the cardiac biomarker elevation cut across all the age groups but majority of the positive tests were seen in the 40-59 year age group. This is in keeping with the mean age of acute coronary syndromes earlier reported [2,8,15,28]. The findings in our study tallied with that of Walter et al that reported elevated cardiac biomarkers in similar age group and in male subjects [29]. Our study also had male preponderance. Male gender and advancing age are known risk factors for ischemic heart diseases [1,27,28].

Troponins, CK-MB mass and myoglobin have previously been shown to be helpful in the evaluation of chest pain in patients with normal or nonspecific ECG changes [19,21]. Elevated cardiac biomarkers had previously been reported in patients with unremarkable ECG changes for ACS [19,21]. Walter et al reported elevated cardiac biomarkers in 16 to 24% of patients with chest pain and normal ECG [29]. Similarly, this index study found normal ECG in 12.5% of the patient population that had elevated cardiac biomarkers.

In this study, abnormal ECG was seen in 87.5% of the patients with elevated cardiac biomarkers. ECG findings usually evolve in ACS and may change with the evolution, extent and severity of the coronary occlusion [20]. ST segment elevation and pathological Q waves still remains the commonest ECG manifestation of ST segment elevation ACS while ST segment depression and T wave inversion are seen in unstable angina/ Non-ST segment elevation ACS [3,20]. Birnbaum et al reported ST segment depression with inverted T waves and ST-

segment elevation in lead aVR as evidence of sub-endocardial ischemia in their cohorts [20]. Similarly, the commonest ECG abnormality noted in our study was also ST segment depression followed by T wave inversion while ST segment elevation and pathological Q waves were seen in 14.1% each in our cohort. Though, 12.5% of our patient population had non-specific ECG changes, subtle and unrecognizable ECG changes have been reported in patients with severe acute coronary stenosis with severe symptoms [3].

From the foregoing, cardiac marker elevation and detection greatly complemented the evaluation of patient with suspected ACS and thus will help patient seek early revascularization and limit morbidities and mortality [18,19,21]. The fact that cardiac biomarkers assay is relatively cheap and test result could be ready within 10 minutes of request, as a rapid point-of-care test, will make it a good adjunct in the evaluation of patients with chest pain [22].

5. CONCLUSION

This study concluded that rapid point of care cardiac biomarker tests complemented electrocardiography in the evaluation of patients with chest pain in emergency unit.

Cardiac biomarkers assay should therefore be made available as a routine test in the emergency units of hospitals for early evaluation of chest pain and early diagnosis of acute coronary syndrome. This will go a long way in making rapid diagnosis and instituting early life saving interventions.

DISCLAIMER

The products used for this research are commonly and predominantly used products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

CONSENT

It is not applicable.

ETHICAL APPROVAL

Ethical approval was sought and obtained from the Lagos State University Teaching Hospital ethics and research committee.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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