

Original Article

Cardiac Troponin T and Creatine Kinase MB Fraction Levels Among Patients with Acute Ischemic Stroke in Nigeria

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ABSTRACT

Background: Stroke has been a global burden, with increasing morbidity and mortality. Serum cardiac troponin t (cTnT) and creatine kinase (CK-MB) fraction are reported to be elevated in patients admitted with acute ischaemic stroke and high level of these biomarkers indicated more severe stroke and neurologic deficit in some of the patients. **Objective:** To evaluate the serum levels cardiac troponin t (cTnT) and creatine kinase MB fraction (CK-MB) in patients with acute ischaemic stroke and relate the analytes to severity of stroke. **Method:** Patients with clinical diagnosis of ischaemic stroke diagnosed, confirmed by brain Computerized Tomography scan and equal number of apparently healthy age and sex-matched were recruited. Serum cardiac troponin t (cTnT) and creatine kinase MB fraction (CK-MB) were analysed using ELISA method and Stroke severity was determined using National Institute of Health Stroke Score (NIHSS). **Results:** Mean serum cardiac troponin t (cTnT) and creatine kinase MB fraction (CK-MB) in stroke patients were found to be higher than age sex matched control ($p < 0.05$). NIHSS Score of 12.2 ± 5.43 and 9.78 ± 3.97 were observed in Patients with elevated and normal cTnT respectively ($p = 0.009$) while NIHSS Score were similar in patients with elevated and normal CK-MB ($p = 0.772$). **Conclusion:** The mean values of serum cTnT and CK-MB were higher in acute ischaemic stroke patients compared to controls. Serum cardiac Troponin t level may be a significant biomarker of the severity of stroke.

KEYWORDS: Creatine kinase MB, Nigeria, serum cardiac troponin T, stroke

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INTRODUCTION

Stroke is defined as a clinical syndrome of sudden onset of rapidly developing symptoms or signs of focal and at times global loss of cerebral function, with symptoms lasting more than 24 h or leading to death, with no apparent cause other than that of vascular origin. Stroke constitutes one of the main causes of morbidity and mortality worldwide.^[1] The World Health Organization estimates stroke to be one of the likely leading cause of death and disability worldwide by 2020.^[2] The current prevalence of stroke in Nigeria is 1.14/1000 while the 30-day case fatality rate is as high as 40%.^[3]

The identification of predictors of morbidity and mortality of stroke may contribute to reducing mortality

and increasing functional outcome by allowing adaptation of prompt therapeutic management strategies to patients at risk.^[4] Heart-brain connections were described early in the 20th century and showed that changes in central nervous system metabolism influence cardiac function.^[5] There is considerable clinical and experimental evidence that cardiac changes in ischemic stroke result from excessive sympathetic nervous activity secondary to insular cortical damage.^[6] Cardiac troponin T (cTnT) is a new biochemical marker of myocardial


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damage with high specificity and sensitivity.^[4] Creatine kinase MB (CK-MB) which is also a cardiac enzyme increases in some patients with stroke, with no clear evidence of an acute coronary syndrome.^[7]

Several conditions could result in elevated concentrations of these analytes during the acute phase of ischemic stroke; these include primary myocardial damage with secondary cardioembolic, cerebral damage or primary cerebral ischemia with secondary myocardial injury. The mechanism is unknown; however, some attributed it to central activation of the sympathoadrenal system resulting in cardiac sequelae including myocytolysis, serum enzyme elevation, and arrhythmia are known to develop in some ischemic stroke patients.^[8] It is also possible that the secondary rise in CK-MB seen might represent brain damage since the B subunit also exists in the brain as CK-BB.^[9] CTnT and CK-MB are not routinely requested in patients with ischemic stroke in our environment, and thus, there is paucity of data in the pattern of this analytes among stroke patients in our center.

This study is therefore aimed at determining the levels of cTnT and CK-MB in patients admitted with acute ischemic stroke in our environment.

SUBJECTS AND METHODS

Subjects

This study was carried out over 13 months. One hundred ischemic stroke patients confirmed by brain computerized tomography scan admitted in Ahmadu Bello University Teaching Hospital (ABUTH), Zaria, within 72 h of onset of stroke and 100 apparently healthy age- and sex-matched controls from the community population were studied. However, patients with recent history (within 3 weeks) of myocardial infarction, long-standing hypertension, myopathies or muscular dystrophy, renal disease, previous stroke, recent surgery, or trauma were excluded from the study. Informed consent was obtained from the patient or their relation and the controls group. Approval was obtained from Ethical and Scientific committee of ABUTH, Zaria, before embarking on the study.

Methods

Blood samples were obtained from the antecubital fossa of each individual after disinfecting it with methylated spirit and allowed to dry. A tourniquet was applied 10 cm above the cubital fossa using 5 ml syringe, and a 21G needle was used to draw blood from anterior cubital vein. The blood was transferred into a plain bottle and allowed to stand for about 30 min for it to clot and retract. This was then centrifuged for 5 min at

10,000 rpm. The serum was separated from the cells and transferred into plain (sample) bottles and then frozen at -20°C until the time for analysis. Serum cTnT and CK-MB fraction concentrations were measured using commercial enzyme-linked immunosorbent assay kits and were procured from Wkea medical supplies corporation, Changchun, China, manufactured in November 2013 to expire in November 2017.

The chemicals and kits used for measurements of serum cTnT and CK-MB were procured from Wkea medical supplies corporation, Changchun China, and labkit, chemlex s.a. Barcelona Spain respectively. Data from the proforma were recorded and analysed using Statistical Program for Social Sciences 20.0 (SPSS 20.0) for windows (SPSS Inc. Chicago 20). Student's *t*-test was used to analyze continuous normally distributed variables. $P < 0.05$ was considered statistically significant.

RESULTS

A total of 200 individuals were recruited, 100 cases and 100 age- and sex-matched controls between the age of 18–96 years with average of 59 years. The mean age of the patients and controls were 59 ± 14.08 and 59 ± 13.91 years, respectively ($P = 0.9888$). The majority were males (62%) in both patients and control

Table 1: Age and sex distribution of the patients and controls (n=100)

Characteristics	Patients	Controls	P
Age			
Mean±SD	59±14.08	59±13.91	0.988
Sex (%)			
Male	62	62	
Female	38	38	
Risk factor profile			
Hypertension	91	0	
Diabetes mellitus	8	0	
Sickle cell anemia	1	0	
Blood pressure			
Systolic±SD	156±32	120±12	<0.0001*
Diastolic±SD	94±20	76±7	<0.0001*

*Statistically significant ($P \leq 0.05$); SD=Standard deviation

Table 2: Pattern of serum troponin T and creatine kinase MB fraction mean±standard deviation in stroke patients and controls

Subjects	n	Mean±SD	
		cTnT (ng/L)	CK-MB (ng/ml)
Patients	100	90.40±19.84	25.41±1.48
Control	100	61.16±19.60	17.33±1.14
P		0.0000	0.0000

Statistically significant ($P < 0.05$). cTnT=Cardiac troponin T; CK-MB=Creatine kinase MB fraction; n=Frequency; SD=Standard deviation

Table 3: Relationship between the levels of cardiac markers (cardiac troponin T and creatine kinase MB fraction) and National Institute of Health Stroke Score (mean±standard deviation) in stroke patients

Levels of cardiac markers	Number of patients	NIHS score, mean±SD	P
Normal cTnT	59	9.78±3.97	
Elevated cTnT	41	12.29±5.43	0.009
Normal CK-MB	35	11.00±5.01	
Elevated CK-MB	65	10.71±4.67	0.772

$P < 0.05$ statistically significant. NIHSS=National Institute of Health Stroke Score; cTnT=Cardiac troponin T; CK-MB=Creatine kinase MB fraction

groups. Ninety-one percent of the patients ($n = 91$) had hypertension while 8% ($n = 8$) had diabetes mellitus and 1% ($n = 1$) had sickle cell anemia. Both systolic and diastolic blood pressures were significantly higher among the cases (156 ± 32 mmHg vs 120 ± 20 mmHg) and controls (94 ± 20 vs. 76 ± 7 mmHg), respectively ($P < 0.0001$) as shown in Table 1.

Table 2 shows pattern of serum cTnT and CK-MB fraction of the acute ischemic stroke patients and controls. Stroke patients had significantly higher serum cTnT 90.40 ± 19.84 ng/L than the controls 61.16 ± 19.60 ng/L ($P = 0.0000$), while the CK-MB fraction was 25.41 ± 1.48 ng/mL and 17.33 ± 1.14 ng/ml among the patients and controls, respectively ($P = 0.0000$).

Table 3 shows the relationship between the levels of cardiac markers (cTnT and CK-MB) and National Institute of Health Stroke Score (NIHS) score. NIHS score of 12.2 ± 5.43 and 9.78 ± 3.97 was observed in patients with elevated and normal cTnT, respectively ($P = 0.009$), while NIHS score was similar in patients with elevated and normal CK-MB ($P = 0.772$).

DISCUSSION

This shows that certain age groups are more at risk of ischemic stroke than others and therefore requires more medical attention for the prevention of stroke. Patients with ischemic stroke present around their fifth to sixth decade of life in this environment. The mean ages of the patients and controls were similar and comparable with those patients and controls of University of Benin and University of Lagos Teaching Hospitals.^[10] Stroke was more common in males than females in this study; however, the male to female ratio in this study was slightly higher than the findings in the united states^[11] but similar to the report from Sokoto.^[12] It has been reported that male sex is a risk factor, especially for thrombotic stroke, until the eighth and ninth decades when the risk becomes equal for both sexes. It may be due to protective

effect of female sex hormones before menopause.^[13] The other possibilities include the influence of cultural factors such as the easy accessibility of males to health care and the greater life expectancy in women. However, a report from South Western Nigeria in 2005 reported higher females than males and suggested that this is due to the changing pattern in sub-Saharan Africa.^[14] Awareness of oral contraceptives use and obesity which is more common in southern Nigeria may be another explanation as it is one of the modifiable risk factors of stroke worldwide. Other risk factors that are more common in males than females are hypertension, heart diseases such as atrial fibrillation and heart failure, hyperlipidemia, cigarette smoking, excess alcohol consumption, and polycythemia.^[15]

In the present study, the serum levels of cTnT and CK-MB of ischemic stroke patients were significantly higher than those in the apparently healthy controls. This is similar to the findings of other studies.^[16-18]

In a study in Turkey, serum CK-MB was elevated above the normal cutoff value in patients with acute ischemic stroke.^[17] It has been suggested that the elevated levels of cardiac markers in acute ischemic stroke patients could be related to cardiac myocytolysis that occurred as a result of activation of the sympathetic nervous system.^[19] The presumed cause for this elevation in acute neurologic disease is related to an increase in systemic catecholamines.^[6] It is also possible that the secondary rise in CK-MB seen might represent brain damage since the B subunit also exists in the brain as CKBB.^[9] Several studies have also suggested that cTnT could be a valuable marker for evidence of myocardial injury in ischemic stroke patients.^[17] Another study demonstrated elevation of noradrenaline and adrenaline, followed by elevation of troponin T and CK-MB, associated with decrease in cardiac output and new left ventricular wall motion abnormalities in stroke. Several other studies have confirmed the presence of troponin elevation in high catecholamine states such as in ischemic stroke. The high concentration of catecholamines in the myocardium would bring about a calcium overload of myocardial cells which can cause a reduction of myocardial contractility and can lead to an impairment of cardiac function due to the perfusion disturbance at the level of capillaries caused by an enhanced platelet aggregation.^[20]

The current study demonstrated relationship between cTnT, CK-MB, and severity of stroke using NIHS score. Severity of stroke relates positively with cTnT but not with CK-MB. This is in agreement with the findings of other studies were Severity of stroke relates positively with cTnT but not with CK-MB.^[21,22] The mean values of NIHS score was significantly higher in patients with

elevated cTnT, while the mean NIHSS score was similar in those with elevated and normal CK-MB values. This implies that stroke patients with elevated cTnT presented with more severe neurologic deficits than patients with normal cTnT values. However, CK-MB could not assess the severity of acute ischemic stroke in patients as shown above. A similar study in 2013 demonstrated that patients with elevated cTnT presented with more severe neurologic deficits (mean NIHSS score 10.1) than patients with normal cTnT values (mean NIHSS score 7.4)^[23] Similarly, research conducted in Berlin,^[22] Korea,^[4] and Iraq all found that elevated serum cTnT in patients with acute ischemic stroke was associated with severe neurological deficits.^[16] On the other hand, the level of CK-MB activity did not show significant association with stroke severity. This is probably because CK-MB is less specific than cTnT and/or signifies the noncardiac source of CK-MB.

CONCLUSION

The mean values of serum cTnT and CK-MB were higher in acute ischemic stroke patients than in the apparently healthy controls. cTnT levels increase with severity of stroke using NIHSS score; thus, cTnT may be a good marker of severity of stroke.

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Conflicts of interest

There are no conflicts of interest.

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