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Serum Cardiac Troponin I Levels in Adults with Sickle Cell Disease Visiting the University College Hospital, Ibadan, Nigeria

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Abstract
Recurrent vaso-occlusive crisis and haemolysis normally affect the lifestyle of patients with sickle cell disease. This may occur for a few hours or some weeks, making many of them to require hospital admission and blood transfusion, with inevitable financial implications on care givers. Due to its tissue specificity, cardiac troponin I and T have been claimed to be important in detecting cardiac damage even in the presence of elevated total creatine kinase (CK) and CK-MB that can likely occur in exercise-induced skeletal muscle damage. The significance of cardiac assessment in sickle cell patients was emphasized in a previous report which showed that evidence of mortality related to cardiovascular causes was often encountered during autopsy. This study aimed at accessing serum cardiac Troponin I (cTnI) in adult patients with sickle cell disease at University College Hospital, Ibadan. After written consents were obtained, 131 individuals above 18 years were recruited, 95 of which were sickle cell disease subjects and 36 were non-sickle cell disease controls. Mean age was 35.4years ±SD=7.54years with age range of 19 to 56years for the sickle celled subjects and 36.8years ±SD=9.11years with age range of 19 to 58 years for controls. Male to female ratio was approximately 2:1 for control and 2.4 :1 for sickle cell subjects. A total of 4(4.2%) sickle cell patients had abnormal troponin I level. There was a significant difference in mean troponin I level between sickle cell subjects and control, but there was no significant association between troponin I and haematological parameters of the sickle cell patients. The likelihood of the sickle cell subjects developing crisis is low, but there was no significant association between troponin I level in sickle cell subjects and their haematological parameters, while there was a significant difference in mean troponin I between Sickle cell subjects and non-Sickle cell controls.

Keywords: Sickle Cell, Serum Cardiac Troponin I (cTnI), Cardiovascular Risk Biomarkers, Haematology, Haemoglobin Electrophoresis

Introduction

Sickle Cell Disease is a genetic problem that has been critically examined globally. Yet, the pathophysiology is still not fully understood. It is a major public health issue in Nigeria as about 25% of Nigerians carried the gene for sickle haemoglobin (Akinyanju *et al.,* 2005). This gene has a global distribution, but the main incidence and prevalence is prominent in the sub-Sahara Africa with the majority in Nigeria where the prevalence of sickle cell trait is between 20% to 30%, but the prevalence rate of Sickle Cell Anaemia is 6-8% (Akinyanju *et al.,* 2005).

Recurrent vaso-occlusive crisis and haemolysis normally affect the lifestyle of patients with sickle cell disease. This may occur for a few hours or some weeks, making many of them to require hospital admission and blood transfusion, with inevitable financial implications on care givers. The economic importance of this disease is so enormous that there is need for immediate source for alternative ways to combat it.

One of the components of the cardiac regulatory proteins that control the calcium-mediated association between actin and myosin is cardiac

troponin 1 (cTnI) (Sharma *et al.,* 2006). This protein is found concentrated in the heart, and the standard biochemical marker for the diagnosis of myocardial damage as seen in conditions such as myocardial infarction (MI) and acute coronary syndrome is concluded to be elevated serum levels. Cardiac troponin I and cardiac troponin T (cTnT) have been found very relevant in detecting cardiac damage even in the presence of raised total creatine kinase (CK) and CK-MB that may be found in exercise-induced skeletal muscle damage due to its tissue specificity. The importance of assessing sickle cell patients' cardiac was stressed in a previous report which showed that evidence mortality associated with cardiovascular causes was often found during autopsy (Sharma *et al.,* 2006).

This study therefore aimed to access serum cardiac Troponin I in adults with sickle cell disease visiting the University College Hospital, Ibadan, Nigeria, with a view to improving knowledge on the role of Troponin I as an indicator for a possible cardiac attack on sickle cell patients who are on routine visit to the Haematology Day care Unit of the University College Hospital.

Materials and Methods

Study Area

The study was carried out in the Haematology Day Care Unit, University College Hospital, Ibadan, Ibadan North Local Government area longitude 7.3569°N and latitude 3.8743°E. It is bordered to the East by Ibadan North East Local Government and to the West by Ibadan North West Local Government.

Study Time Frame

A period of four months was used for the study

Study Subjects/Population

Following informed consent, One hundred and thirty-one (131) individuals above 18 years were grouped into 2 as follows:

1. Known sickle cell disease group: Ninety-Five (95) sickle cell disease patients who had previously been diagnosed to have Haemoglobin S (HbS) by haemoglobin electrophoresis. They were enrolled consecutively at presentation during their routine visit to Haematology Day care (emergency) unit of University College Hospital, Ibadan.
2. Control group: This group comprised of Thirty-Six (36) Haemoglobin A individuals. Their HbA status was confirmed with the aid of haemoglobin electrophoresis. They were students and workers in the study hospital.

Inclusion and Exclusion Criteria

Only individuals who consented to participating in the study, were within the age bracket 18-60, confirmed Sickle Cell Disease patients, and HbA controls with no previous history of any chronic ill health *were enrolled for the study, while* Patients with infection, chronic inflammatory condition other than Sickle Cell Disease, renal disease unrelated to Sickle cell Disease, symptomatic heart disease, rheumatoid arthritis or other autoimmune diseases, hypothyroidism, diabetes mellitus, or steroid therapy were excluded. Also, non-consenting individuals, pregnant sickle cell disease patients, and others who do not meet up with the selection criteria were excluded from the study.

Sample Collection and Storage

Sample was collected into Lithium Heparin bottle (3ml) and was subsequently centrifuged. Plasma was separated from the blood, aliquoted in 2 vials and stored at -80°C at the Blood bank, University College Hospital Ibadan.

Haemoglobin Electrophoresis

Haemoglobin electrophoresis at pH 8.4–8.6 was done using the cellulose acetate method.

Principle

At alkaline pH, haemoglobin is a negatively charged protein, and when subjected to electrophoresis will migrate toward the anode (+). Structural variants that have a change in the charge on the surface of the molecule at alkaline pH will separate from haemoglobin A. Haemoglobin variants that have an amino acid substitution that is internally sited may not separate, and those that have an amino acid substitution that has no effect on overall charge will not separate by electrophoresis.

Statistical Analysis
Data analysis was done using the Statistical Package for Social Sciences (SPSS) version 21.0. Data was summarized into Tables and Graphs as appropriate. Discreet variables were expressed as numbers and percentages, while continuous variables were also expressed as mean and standard deviation. Normally distributed continuous variables were compared using the student's t-test. The Wilcoxon rank sum test was used for non-normally distributed continuous variables. Proportions were compared using the Chi-square (X2) test.

Ethical Consideration
A letter for ethical approval was sought and obtained from the ethical committee of the Oyo state Hospital Management Board, Ministry of Health, Ibadan. Also, consent from all the participants was obtained prior to their inclusion into the study.

Results
Table 1 showed socio demographic characteristics of subjects and controls. The mean age was 35.4years ±SD=7.54 years with age range from 19 to 56years for sickle celled subjects and 36.8years ±SD=9.11 years which ranges from 19 to 58years for control. The male to female ratio was approximately 2:1 in control and 2.4 :1 in subjects which there were 67(70.0%) male and 28(29.5%) female in subjects and there were 24(66.7%) male and 12(33.3%) female in control.

Table 2 showed that there were 4(4.2%) sickle cell patients with abnormal troponin I level. This implied that there was likelihood of 4(4.2%) Sickle cell patients to develop crises secondary to Myocardial Infarction.

There was a significant difference in mean Troponin I between Sickle cell subjects and non-Sickle cell controls (p=0.001). Table 3

Table 4 showed that there was no significant relationship between Troponin I in HBSS and haematological parameters like white blood cell (p=0.618) and platelets(p=0.382).

Table 1: Socio-demographic characteristics of respondents

Variables	Subject (N=95) N(%)	Control(N=36) N (%)
Age (years)		
≤20	2(2.1)	1(2.8)
21-30	22(23.2)	8(22.2)
31-40	50(52.6)	13(36.1)
41-50	19(20.0)	12(33.3)
51-60	2(2.1)	2(5.6)
Mean (SD) range	35.4(7.54) 19-56	36.8(9.11) 19-58
Gender		
Male	67(70.0)	24(66.7)
Female	28(29.5)	12(33.3)

Table 2: Effect of Troponin I level in relation to Sickle cell patients in crises secondary to Myocardial Infarction.

Variables	Frequency	Percentage (%)
Troponin I		
Normal	91	95.8
Abnormal	4	4.2

Table 3: Comparing difference in mean of Troponin I level in HBSS patients and non- HBSS patients

Variables	Group	N	Mean	Std. Deviation	95%CI	Range	p-value
Troponin I	Subject	95	.097	.084	.079-0.11	.00-.40	.001
	Control	36	.047	.051	.0301-0.064	.00-.12	
	Total	131	.083	.079	.0695-0.097	.00-.40	

Table 4: Troponin I level and haematological parameters of HBSS patients

Parameters	Status	Troponin I		Total	p-value
		Normal N(%)	Abnormal N(%)		
White blood cell	Normal	19(95.0)	1(5.0)	20	0.618
	abnormal	72(96.0)	3(4.0)	75	
Platelets	Normal	71(94.7)	4(5.3)	75	0.382
	Abnormal	20(100.0)	0	20	

Discussion

This was a descriptive cross-sectional study of patients with sickle cell disease visiting the Haematology Day Care Unit, University College Hospital, Ibadan, Nigeria. A sample size of 131 participants made up of 95 were HbSS subjects and 36 Haemoglobin A controls. The sickle cell status of participants was confirmed with the aid of haemoglobin electrophoresis. The control group were students and workers in the study area.

The mean age of sickle cell patients was 35.4 ± SD=7.54 years with a range 19 to 56 years, while the control group had a mean age of 36.8years ± SD=9.11 years with a range of 19 to 58 years. This is similar to the age variation among HBSS patients at University College Hospital, Ibadan (Haematology Day care clinic record of UCH, 2016) and healthy workers at University College Hospital (Human resource, UCH record 2016). Lubeck *et al* (2019) estimated 54 years to be the life expectancy of adults with sickle cell disease. Although, still shorter than the life expectancy for normal adult without sickle cell disease, some of the sickle cell participants in this study were aged 59 years. This might be due to recent improvements in interventions which made it possible to treat complications more effectively and have decreased death rate. The male to female ratio was approximately 2:1 in control and 2.4:1 in HbSS subjects. This implied that more males accepted to participate among the control group, and there were more male HBSS patients than females. This is similar to the result of a previous study (Nagose, 2018) on haematological profile of sickle cell anemia

subjects in central India. However, Udezue and Girshab (2004) recorded different result in a similar study where the number of males was almost the same with that of female.

The results revealed that there were 4(4.2%) sickle cell patients with abnormal troponin I level. This implied that there was likelihood of 4(4.2%) sickle cell patients to develop crisis secondary to Myocardial Infarction. *Tanindi et al (2016) stated* that a person who recently had a myocardial infarction would have an area of damaged heart muscle and elevated cardiac Troponin I levels in the blood. The percentage of sickle cell patients with abnormal cTnI level in this study is relatively low compared to that of Desai *et al.* (2021) who recorded that 18% of the sickle cell patients had elevated troponin. Aslam *et al* (2009) however found 6.3% of sickle cell disease participants to have abnormal cTnI level. He also related abnormal or elevated cTnI with likelihood of sickle cell crisis or myocardial ischemia. It should however be noted that this study did not focus on patients in crisis condition.

The finding of this study showed that there was a significant difference in mean cardiac serum Troponin I between Sickle cell subjects and non-Sickle cell controls (p =0.001). This disagreed with Aneke *et al.* (2017) who reported that there were no significant differences in the mean serum levels of cTnI between sickle cell participants in steady state and HbAS and HbAA participants.

There was no significant relationship between Troponin I in HBSS and haematological parameters like white blood cell (p=0.618) and platelets (p=0.382). The implication of these is that haematological parameters act independently of troponin I and therefore will not influence predisposition to crisis in adults with sickle cell disease. This agreed with Roaa *et al.* (2023) that no significant association exists between cardiac markers such as troponin and the need for blood transfusion either simple or exchange, the use of hydroxyurea, ECG and the use of anticoagulation. He stated further that those who required blood transfusion among the patients had normal troponin level. According to Akkus et al. (2021), elevated troponins were significantly associated with GFR <60 mL/mi/1.73m2, lower Hgb, lower haematocrit, lower platelets, higher mean platelet volume, higher LDH, higher AST, and higher bilirubin.

Conclusions and Recommendations

The likelihood of sickle cell disease resulting into crisis in the subjects is low as only 4.2% of them had abnormal troponin I. There was no significant association between troponin I level in sickle cell subjects and their haematological parameters, but there was a significant difference in mean troponin I between Sickle cell subjects and non-Sickle cell controls. It should be a matter of urgency that appropriate interventional programmes backed by an effective national policy be instituted on conditions to use Cardiac Troponin I as one of the indicators to check sickle cell disease patients from going into cardiac arrest.

Conflict of Interest Declaration

All authors declared no conflict of interest.

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