

Serum Troponin I levels among Hypertensive Military Service Personnel at a Military Health Facility in Abuja, Nigeria

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Summary: Hypertension constitutes one of the major metabolic disease in Nigeria especially among military personnel and their families. Myocardial infarction and other cardiovascular diseases may occur in this group of patient due to uncontrolled or poorly controlled hypertension. The objective of this study was to determine serum cardiac Troponin I (cTnI), levels in hypertensive Nigerian Military service personnel attending clinic in a military Health facility. We measured the serum levels of cTnI in 126 hypertensive subjects [76 males (19-73 years) and 50 females (26-77years)] and 82 normotensive controls [41 males (19-60years) and 41 females (18-53years)] using Latex Enhanced Immunoturbidimetry technique. The data were compared between test and control group using Students't-test. Serum cTnI was detected in the sample of 95(75.4%) subjects and was not detected in 31 (24.6%) subjects. Nine subjects (2.38%) had cTnI levels within the normal range(0.00-0.01ng/mL), 85 (67.5%) subjects had significantly higher ($p < 0.001$) cTnI levels (0.100 ± 0.091 ng/ml; CL: 0.02 – 0.47ng/mL), while one (0.8%) subject had a cTnI value of 1.09 ng/mL. Nine (10.98%) control subjects had detectable cTnI levels (0.01ng/mL) while 73(89.02%) controls had a 0.00 ng/mL cTnI level. There was no significance difference in cTnI levels when subjects on chemotherapy were compared with newly diagnosed subjects ($P = 0.0694$). This study revealed that cTnI was detectable in the serum of majority of the study participants which may suggest sub-clinical cardiac necrosis. There may be risk of developing adverse cardiovascular disorders and the need for appropriate intensive management is emphasized.

Keywords: Cardiac Troponin I, Hypertension, Military service personnel.

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INTRODUCTION

Hypertension (High blood pressure) is a major health risk factor for heart attack and stroke with attendant biochemical consequences (Boyles and Salynn, 2011). It is a common condition, but little is known about its prevalence among military service personnel and their families. Rigorous-stress activities such as combat deployment of military service personnel might pose a potential risk factor for hypertension. There are paucity of published reports on the levels of cardiac biomarkers in the serum of hypertensive Nigerian military personnel and their families. Uncontrolled hypertension leads to heart attacks, stroke and cardiovascular diseases (CVDs) and kills more than infectious diseases (Kearney et al., 2005; Ogah et al., 2012). Early prediction of cardiovascular disease risk among subjects with hypertension provides an opportunity for appropriate intensive management, reduces morbidity and mortality. Assay of serum cardiac troponins are considered as standard biochemical markers in the diagnosis of myocardial infarction (MI) (Karar et al., 2015) but these markers are rarely assayed for in this health facility.

Troponin which is a trimeric regulatory protein complex consisting of troponin C, troponin I, and troponin T, is very necessary for muscle contraction in skeletal and cardiac muscles, but not smooth muscle (Takeda et al., 2003). They are released into circulation about 3-4 hours after myocardial infarction and are still detectable for 10 days afterwards. The long half-life allows for late diagnosis of MI, but makes it difficult to detect re-infarction. These three Troponin subunits form a complex that checks the interaction of actin and myosin, and thus regulate heart contraction. Troponin is localized primarily in the myofibrils (94-97%) with smaller cytoplasmic fraction (3-6%) (Heresi et al., 2012). Cardiac troponin (cTn) subunits I and T have different amino acid residue on the amino sequences encoded by different genes, and are different from skeletal muscle. Troponin I in humans is presented in three isoforms, two isoforms are expressed in skeletal muscle tissue and one isoform is expressed in cardiac muscle tissue (Scheitz et al., 2015). Cardiac troponin has absolute myocardial tissue specificity and reflect even microscopic zones of myocardial necrosis but

cTn elevations are not always attributable to acute Coronary syndromes (Jeremias and Gibson, 2005; Barry et al., 2008), as individuals belonging to stressful occupations could have increased cTn levels. Stress-induced Cardiomyopathy however, is a reversible cardiac syndrome characterized by acute chest pain and wall motion abnormalities. It is usually triggered by physical and emotional stress and the subjects will usually recover within a few weeks (Ramaraj et al., 2009).

Cardiac Troponin-I (cTnI) is derived from genes specifically expressed within the myocardial tissue. It is one of the sarcometric protein apparatus of the myocardium and controls myocardial contraction together with cTnT and cTnC in response to calcium increment. About 3.5% of cTnI and 7% of cTnT exist freely in cardiac myocyte cytoplasm. The rest is bound within the sarcomere and is released as a result of proteolytic degradation. Myocardial Injury results to a disruption of the intracellular contractile proteins leading to an increase in the cytoplasmic pool content of cTnI and cTnT. Calcium and troponin controls the production of cardiac muscular force. Increased cardiac muscle calcium concentration leads to muscle contraction (Adams et al., 1993). Calcium is bound to troponin-C triggering activation of tropomyosin which in turn binds troponin-T to form troponin-tropomyosin complex. Cardiac troponin I now binds actin to link and sustain the troponin-tropomyosin complex in place thereby maintaining normal cardiac muscle contraction and normal heart physiology. Troponin-I is cardiac specific (Adams et al., 1993), while Troponin-T is derived from both the myocardium and skeletal muscles. The release of cardiac troponin I into the circulation is a manifestation of reversible or irreversible myocyte injury (Reichlin et al., 2009; Quarck et al., 2009). The World Health Organization (WHO) had suggested that elevated cTI ≥ 2 $\mu\text{g/L}$ (2ng/mL) is diagnostic of myocardial infarction (Amsterdam et al., 2014). In this study we evaluate the levels of serum cTI in hypertensive Nigerian military personnel and their families.

MATERIALS AND METHODS

Subjects and Study Protocol. The study was approved by Ministry of Defence Health Research Ethics Committee, Abuja- Nigeria (code MODHREC APP/045 dated 3rd July 2015). One hundred and twenty-six (126) hypertensive individuals (76 males and 50 females aged 19-77years) were randomly selected for the study, while 82 normotensive individuals (41 males and 41 females aged 18-60 years) were used as controls.

Sampling. Fasting serum samples were collected from patients above 18years that were diagnosed of hypertension at the DHQ MC Abuja, and referred to

DRL for laboratory analysis. The routine requests were done while some portion of the serum was separated and stored for not more than 24-48 hours prior to analysis. Serum samples were collected from non-hypertensive apparently healthy adult military personnel which were used as controls. Subjects diagnosed with other metabolic disorders such as Diabetes Mellitus in addition to hypertension were excluded from the study.

Assay Technique. Serum Troponin I was assayed by latex Enhanced Immunoturbidimetry technique using reagent kit supplied by Diazyme Chemicals (USA). The detectable range of reagent was 0.005 – 10.0ng/mL.

Statistical Analysis:

Statistical analysis was done using the Statistical package for social sciences (SPSS) version 16.0 (Chicago, IL USA). All values were expressed as Mean $\pm$ Standard error of the mean. The students't-test was used to compare the mean values of the observed measured parameters between the groups. A p-value of 0.05 was considered as statistically significant.

RESULTS

The results obtained from this study are as presented in tables 1,2 and 3. Table 1 shows the demographic characteristics of studied participants and serum cTnI levels. The mean serum cTnI in hypertensive subjects was significantly higher ($P<0.001$) when compared with controls. The differences in the means of serum cTnI between newly diagnosed hypertensive subjects not yet on treatment and those already on treatment was not statistically significant (table 2). Table 3 shows that of the 126 hypertensive subjects, serum cTnI above the manufacturer's recommended reference range ($<0.01\text{ng/mL}$) was detected in 86 (68.3%) participants, while cTnI was not detected in 31 (24.6%) hypertensive subjects. Among the control subjects, serum cTnI was detected in 9 (10.98%) subjects but values were within normal reference range and 73 (89.02%) control subjects had undetectable levels.

Table 1: Serum Troponin I in hypertensive subjects and controls (means $\pm$ SEM).

Measured variables	Hypertensive (n=126)	Control (n=82)
Sex: Males	76	41
Females	50	41
Age (Years)	47.4 $\pm$ 0.91	46.0 $\pm$ 1.2
Weight (Kg)	84.51 $\pm$ 1.5	80.52 $\pm$ 1.8*
Height (Cm ²)	163.16 $\pm$ 4.2	164.67 $\pm$ 3.6
BMI (Kg/m ²)	31.5 $\pm$ 1.3	29.8 $\pm$ 1.2
BP (mmHg): Systolic	135.6 $\pm$ 2.5	120 $\pm$ 1.6*
Diastolic	80.2 $\pm$ 2.3	70.0 $\pm$ 0.8*
Troponin I (ng/mL)	0.077 $\pm$ 0.011	0.001 $\pm$ 0.00*

BMI, Body Mass Index; BP, Blood Pressure; * $P\leq 0.01$

Table 2: Comparison of the measured parameter in newly diagnosed hypertensive subjects not yet on treatment and those on treatment.

Measured variable	Hypertensive subjects not yet on treatment (n= 40)	Hypertensive subjects on treatment (n = 86)
Age (years)	41.73 ±1.77	50.05 ±0.92*
Serum Troponin I (ng/mL)	0.062 ±0.02	0.08 ±0.01

* $P \leq 0.01$ **Table 3:** Stratification and Categorization of hypertensive and control subjects with detectable serum troponin levels based on values > 0.01ng/mL as a benchmark marker of cardiac risk

S/N	Serum Troponin I Levels	Number of hypertensive subjects (%)	Number of Control subjects (%)
1	0.00 ng/mL (Undetected)	31(24.6%)	73(89.02%)
2	≤0.01 ng/mL	9 (7.1%)	9 (10.98%)
3	0.02-1.00 ng/mL	85(67.5%)	0 (0%)
4	1.01-1.99ng/mL	1 (0.8%)	0 (0%)
5	2ng/mL & above	0 (0%)	0 (0%)
	Total	126 (100%)	82 (100%)

DISCUSSION

This study was aimed at determining the level of cTnI, among hypertensive Nigerian military service personnel and comparing the results obtained with normotensive Nigerians. Serum cTnI was detected in the sample of 95 (75.4%) hypertensive subjects while 31 (24.6%) hypertensive subjects had an undetectable level (0.0ng/mL). Nine of the subjects had normal values of ≤0.01ng/mL while 86 had significantly diagnostic values of 0.02 – 1.09ng/mL. None of the subjects had up to 2ng/mL which is the WHO diagnostic criteria that indicates myocardial infarction. Nine normotensive (control) samples (10.98%) had detectable value of ≤0.01ng/mL in their serum while 73 control subjects (89.02%) gave an undetectable (0.00 ng/mL) result for cTnI. There was significantly higher ($p < 0.001$) levels of cTnI in hypertensives when compared with controls. Subjects within categories 3-4 were at risk of cardiovascular diseases according to WHO stratification. Majority of the subjects constituting 67.5% had cTnI values ranging from 0.02-1.0ng/mL while only one HTN subject (0.8%) had a cTnI value above 1.0ng/mL. Findings also showed that there was no significant difference in the mean value of serum cTnI in hypertensives on chemotherapy when compared with newly diagnosed hypertensives ($P = 0.59$).

Death of cardiac muscles due to cardiac myopathies such as hypertension leads to spillage of cTnI into the blood stream. Thus, this cardiac specific biomarker is

very important in the diagnosis and management of hypertension and heart diseases.

The detection of significant levels of cTnI in samples of hypertensive Nigerians is in agreement with earlier studies elsewhere (Platek et al., 2014; Aeschbacher et al., 2015). It was reported that detectable cTnI and other biomarkers like brain natriuretic peptide (BNP) are found in the serum of patients with pulmonary hypertension (Velez-Martinez et al., 2013). The complications of hypertension include Aneurysm (abnormal bulge in the wall of an artery), chronic kidney disease, cognitive changes, eye damage, heart attack and failure as well as peripheral artery disease and stroke (National Heart, Lung and Blood Institute, 2015). In most cases, hypertension is undetected for years because symptoms may not appear until damages occur in the body. Such damages take place due to sustained elevation of blood pressure over time. If untreated, circulatory failure from severe left ventricular dysfunction or any of the mechanical complications of MI frequently account for most fatalities (Batal et al., 2016). The results of this study may indicate sub-clinical myocardial injury since hypertension is commonly associated with microvascular and macrovascular complications (Whiteley et al., 2009; Sata et al., 2016). Even though circulating cTnI may reflect myocardial necrosis and diagnostic of MI in the presence of signs and symptoms (Morrow et al., 2007), elevated cTnI may be detected in other conditions such as coronary artery disease (Eggers et al., 2017), left ventricular failure (Horwich et al., 2003), Chronic kidney disease (Apple et al., 2002), sepsis (Ammann et al., 2001), Demand Ischaemia (Barry et al., 2008) and mixed critical care population (Quenot et al., 2005). It was suggested that underlying mechanism other than myocardial necrosis may be responsible for the high cTnI levels. Irrespective of the aforementioned observations, detectable cTnI is specific for ongoing myocardial damage and may be associated with worse prognosis. Elevated cTnI has been associated with left ventricular hypertrophy (LVH) among hypertensive subjects (Siliciano et al., 2000). These authors observed higher serum cTnI levels in 12 out of 23 hypertensive subjects with LVH. It was concluded that a significant proportion of hypertensive subjects with LVH had slightly higher cTnI levels (Siliciano et al., 2000).

It is needful to note that there are potential causes of cTnI elevations without underlying acute or chronic cardiovascular disease. The cytosolic-bound cTnI may be released by altered cellular wall permeability due to myocardial stretch or mild ischaemia (deFillippi et al., 2010).

This study revealed that cTnI was detected in the serum of majority of Nigerian military service personnel diagnosed with hypertension. The levels of

cTnI detected may indicate sub-clinical cardiac necrosis which could predict the possibility of developing adverse cardiovascular disorders such as stroke and myocardial infarction in hypertensive individuals. The data presented may indicate cardiac involvement in hypertensive Nigerian Military personnel and an appropriate intensive management is suggested.

This study had the following limitations: (a) The level of compliance to drug therapy and other medications are not known to the researcher; (b) The exact duration of hypertension in the subjects was not stated; (c) Other cardiac biomarkers such as lactate dehydrogenase (LDH), B-type Natriuretic Peptide (BNP), Total CK, Myoglobin and others were not measured, and; (d) The interferences by other metabolic disorders such as Diabetes mellitus, Obesity, Cancers and even infectious diseases in the study population were not ruled out.

REFERENCES

- Adams JE, Bodor GS, Dávila-Román VG, Delmez JA, Apple FS, Ladenson JH et al (1993). Cardiac troponin I. A marker with high specificity for cardiac injury. *Circulation*, 88(1):101-106.
- Aeschbacher S, Schoen T, Bossard M, van der Lely S, Glättli K, Todd J et al (2015). Relationship Between High-Sensitivity Cardiac Troponin I and Blood Pressure Among Young and Healthy Adults. *Am J Hyperten*, 28 (6): 789-796.
- Ammann P, Fehr T, Minder EI, Gunter C, Bertel O (2001). Elevation of troponin I in sepsis and septic shock. *Intensive Care Med*, 27:965–969.
- Amsterdam, E. A., Wenger, N. K., Brindis, R. G., Casey, D. E., Ganiats, T. G., Holmes et al (2014). 2014 AHA/ACC Guideline for the Management of Patients with Non-ST-Elevation Acute Coronary Syndromes: A Report of the American College of Cardiology/ American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol*, 64(24):2654-2687.
- Apple FS, Murakami MM, Pearce LA, Herzog CA (2002). Predictive value of cardiac troponin I and T for subsequent death in end-stage renal disease. *Circulation*, 106:2941–2945.
- Barry JAW, Barth JH, Howell SJ (2008). Cardiac troponins: their use and relevance in anaesthesia and critical care medicine. *Continuing Education in Anaesthesia*. *Crit Care Pain*, 8(2):62-66.
- Batal O, Jentzer J, Balaney B, Kolia N, Hickey G, Dardari Z et al (2016). The prognostic significance of troponin I elevation in acute Ischemic Stroke. *J Crit Care*, 31(1):41-47.
- Boyles M, Salynn B (2011). Heart attacks in the mornings are more severe. WebMD News Archive. Reviewed by: Martin, LJ Suarez-Barrientos, A. and Borijia I, National center for cardiovascular Research, Madrid, Spain. News release by BMJ Specialist Journals.
- deFilippi CR, de Lemos JA, Christenson RH, Gottdiener JS, Kop WJ, Zhan M (2010). Association of serial measures of cardiac troponin T using a sensitive assay with incident heart failure and cardiovascular mortality in older adults. *JAMA*, 304: 2494–2502.
- Eggers KM, Lagerqvist B, Venge P, Wallentin L, Lindahl B (2017). Persistent cardiac troponin I elevation in stabilized patients after an episode of acute coronary syndrome predicts long-term mortality. *Circulation*, 116:1907–1914.
- Heresi GA, Tane WHW, Aytekin M, Hammel J, Hazen SL, Dweik RA (2012). Sensitive Cardiac troponin I predicts poor outcomes in Pulmonary arterial hypertension. *Eur Respir J*, 39:939-944.
- Horwich TB, Patel J, MacLellan WR, Fonarow GC (2003). Cardiac troponin I is associated with impaired hemodynamics, progressive left ventricular dysfunction, and increased mortality rates in advanced heart failure. *Circulation*, 108:833–838.
- Jeremias A, Gibson CM (2005). Narrative review: alternative causes for elevated cardiac troponin levels when ACSs are excluded, *Ann Intern Med*, 142: 786-791.
- Karar T, Elfakir EM, Qureshi S (2015). Determination of the serum levels of Troponin I and creatinine among Sudanese type 2 Diabetes mellitus patients. *J Natl Sci Biol Med*, 6: S80-S84
- Kearney PM., Whelton M, Reynolds K, Muntner, P, Whelton, PK, He J (2005). Global burden of hypertension: analysis of worldwide data. *Lancet*, 365(9455): 217-223.
- Morrow DA, Cannon CP, Jesse RL, Newby LK, Ravkilde J, Storrow AB et al (2007). National Academy of Clinical Biochemistry Laboratory Medicine Practice Guidelines: clinical characteristics and utilization of biochemical markers in acute coronary syndromes. *Circulation*, 115: e356–e375.
- National Heart, Lung and Blood Institute (2015). What is the signs, symptoms and complications of High blood pressure? US Department of Health and Human Services. <https://nhlbi.nih.gov> accessed on 02/01/2017.
- Ogah OS, Okpechi I, Chukwunonye II, Akinyemi JO, Onwubere BJ C, Falase AO et al (2012). Blood pressure, prevalence of hypertension and hypertension related complications in Nigerian Africans: a review. *World J Cardiol*, 4(12): 327-340
- Platek AE, Szymanski FM, Filipiak KJ, Karpinski G, Hryniewicz-Szymanska A, Kotkowski M et al (2014). Prognostic value of troponin I and NT-proBNP concentrations in patients after in-hospital

- cardiac arrest. *Portuguese J Cardiol*, 34(4): 255-261.
- outcome in pulmonary arterial hypertension. *J Am Coll Cardiol*, 53: 1211–1218.
- Quenot JP, Le Teuff G, Quantin C, Doise JM, Abrahamowicz M, Masson D et al (2005). Myocardial injury in critically ill patients: relation to increased cardiac troponin I and hospital mortality. *Chest*, 128: 2758–2764.
- Ramaraj R, Sorrell VL, Movahed MR (2009). Levels of troponin release can aid in the early exclusion of stress-induced (takotsubo) cardiomyopathy. *Exp Clin Cardiol*, 14(1):6-8.
- Reichlin T, Hochholzer W, Bassetti S, Steuer S, Stelzig C, Hartwiger S et al (2009). Early diagnosis of myocardial infarction with sensitive cardiac troponin assays. *N Engl J Med*, 361: 858–867.
- Sata Y, Yamamoto E, Sawa T, Toda K, Hara T, Iwasaki T et al (2011). High sensitive cardiac troponin T in essential hypertension. *J Cardiol*, 58:226-231.
- Scheitz JF, Nolte CH, Laufs U, Endres M (2015). Application and Interpretation of High-sensitive
- Quarck R, Nawrot T, Meyns B, Delcroix M (2009). C-reactive protein: a new predictor of adverse Cardiac Troponin assays in patients with Acute Ischemic stroke. *Stroke*, 46:1132-1140.
- Siliciano M, Mettimano M, Dondolini-Poli A, Ballarin S, Migneco A, Annese R et al (2000). Troponin I serum concentration: a new marker of left ventricular hypertrophy in patients with essential hypertension. *Ita Heart J*, 1(8):532-535.
- Takeda S, Yamashita A, Maeda K, Maeda Y (2003). Structure of the core domain of human cardiac troponin in the Ca^{2+} -saturated form. *Nature*, 424 (6944): 35–41.
- Vélez-Martínez M, Ayers C, Mishkin JD, Bartolome SB, García CK., Torres F et al (2013). Association of cardiac troponin I with disease severity and outcomes in patients with pulmonary hypertension. *Am J Cardiol*, 111(12): 1812-1817.
- Whiteley W, Chong WL, Sengupta A, Sandercock P (2009). Blood markers for the prognosis of Ischemic stroke: A systemic Review. *Stroke*, 40:e380-e389.