Diabetes & Metabolic Syndrome: Clinical Research & Reviews xxx (2017) xxx–xxx

Contents lists available at ScienceDirect

Diabetes & Metabolic Syndrome: Clinical Research & Reviews

journal homepage: www.elsevier.com/locate/dsx

Original article

Elevated cardiac troponin I, creatine kinase and myoglobin and their relationship with cardiovascular risk factors in patients with type 2 diabetes

Ehimen Phyllis Odum[a], Ekenechukwu Esther Young[b,*]

[a] Department of Chemical Pathology, University of Port Harcourt Teaching Hospital Port Harcourt, Rivers State, Nigeria
[b] Department of Medicine, University of Nigeria, Ituku/Ozalla, Enugu State, Nigeria

ARTICLE INFO

Article history:
Available online xxx

Keywords:
Diabetes
Cardiac markers
Cardiovascular risk

ABSTRACT

Background: Elevated cardiac troponin I, Creatine kinase (CK-MB) and Myoglobin levels are observed in the setting of acute myocardial damage. However sub-clinical elevations occur in patients with diabetes mellitus. This study was carried out to determine the relationship between the presence of multiple cardiovascular risk factors and the metabolic syndrome and elevations in cardiac markers in patients with type2 diabetes mellitus.
Subjects and methods: Consecutive stable out-patients with type2 diabetes mellitus at the University of Port Harcourt Teaching Hospital, Nigeria were recruited. Non-diabetic individuals such as hospital staff and the general public acted as controls. Baseline demographic data collection was done and waist circumference, weight, height and blood pressure were measured. Venous samples were assayed for CTnI, CK-MB and Myoglobin levels using ELISA. Data was analysed using SPSS v 20.
Results: There were 188 DM patients, who were older than the 200 control subjects (56.1 ± 13.1 years and 42.7 ± 5.7 years, $p < 0.001$). Mean duration of diabetes was 7.1(5.7) years. Hypertension was present in 59%, 84.6% had dyslipidaemia, while 76.1% had metabolic syndrome. All the cardiac markers were significantly higher in DM patients than controls. The presence of hypertension or dyslipidaemia was not significantly associated with the cardiac markers ($p > 0.05$ for all), however the DM patients with metabolic syndrome had higher levels of CK-MB and myoglobin but not CTnI than those without.
Conclusion: Diabetes mellitus is associated with chronic sub-clinical elevation of cardiac markers and this is more in those with multiple cardiovascular risk factors and/or the metabolic syndrome.

1. Introduction

Diabetes mellitus (DM) is a metabolic disorder principally characterized by elevated blood glucose levels and by microvascular and macrovascular complications that considerably increase the morbidity and mortality related to the disease [1]. The cardiovascular complications that are well recognized in patients with longstanding diabetes include coronary artery disease (CAD), myocardial infarction (MI), stroke, congestive heart failure (CHF), and peripheral vascular disease (PVD) [2].

Diabetes increases the risk for acute myocardial infarction (AMI) as much as a previous myocardial infarction in a non-diabetic person[3]. Atherosclerotic coronary artery disease (ASCAD) is the leading cause of morbidity and mortality among patients with diabetes mellitus, accounting for up to 80% of mortality in type 2 diabetes (T2D) patients [1,4,5]. DM patients have a risk of cardiovascular mortality two to four times that of people without diabetes and life expectancy is reduced by five to ten years [1,4,5]. Furthermore, long-term prognosis after a coronary event is significantly worse among people with DM than those without [1].

Diabetes has been classified as a CAD "risk equivalent". However, hyperglycemia, which is the core metabolic defect in DM, does not by itself confer this level of cardiovascular risk, but a constellation of metabolic risk factors combines with hyperglycemia to impart a high risk [1]. Diabetes interacts with these other cardiovascular risk factors to accelerate atherogenesis [4]. The most notable of these abnormalities include insulin resistance, hypertension, obesity and dyslipidemia which often occur concomitantly. This constellation of abnormalities is referred to as the insulin resistance syndrome or the metabolic syndrome, which has been shown consistently to have a higher prevalence in diabetic patients than in healthy control populations [1,3,6]. These

* Corresponding author.
E-mail address: ekenechukwu.young@unn.edu.ng (E.E. Young).

https://doi.org/10.1016/j.dsx.2017.12.001
1871-4021/

abnormalities promote cardiovascular disease (CVD) by inducing atherosclerosis, endothelial cell dysfunction, oxidative stress, inflammation and vascular remodelling [6]. Although each component of the metabolic syndrome brings an individual increased CVD risk, the effect is enhanced when in combination [1].

Identification of patients at high risk for future cardiovascular events, ideally with a simple test or biomarker, can help to reduce their long-term risk of adverse events, as they may benefit from closer monitoring and treatment, or even from prevention strategies [7–9]. Elevated cardiac biomarkers viz cardiac troponins I and T, creatine kinase MB (CK-MB) and myoglobin levels are associated with myocardial damage [7,10,11]. Although these biomarkers are usually measured in the setting of a suspected cardiac ischaemic event, there have been several studies which have shown chronic subclinical elevation of these biomarkers in DM patients, suggesting on-going myocardial damage [12–14]. This is significant because it is known that patients with diabetes mellitus who have no reported symptoms of myocardial ischaemia may have repeated episodes of silent myocardial ischaemia, and thus present late with arrhythmias, heart failure or sudden death [1,4,12].

The cardiac troponins (cTns) T and I are extremely sensitive and considered as specific biomarkers of myocardial necrosis and crucial biomarkers for the diagnosis, prognosis and risk stratification of patients with suspected acute coronary syndrome (ACS) and myocardial infarction (MI) [8,12]. Elevated cTns are associated with reduced left ventricular ejection and poor prognosis in patients with CHF and are related to the severity of heart failure[12]. Troponin elevations have also been documented in multiple clinical settings in the absence of ACS.9. Serum troponin elevations in stable, asymptomatic patients may reflect subclinical microinfarctions, identify high risk patients and predict worse long-term cardiovascular outcomes and all-cause mortality [10,11]. The specificity and sensitivity of CK-MB is much lower than that of the cTns and the interpretation of an elevation of CK-MB alone is not reliable [7,10,11]. However serum CK-MB may be useful in ruling out myocardial necrosis and to monitor for additional myocardial injury over time [7,10,11].

Myoglobin is highly sensitive but not cardio-specific. It is released from the cell following injury more rapidly than CK-MB or the cardiac troponins [10]. It derives its usefulness as a cardiac marker because serum levels rise within 1–3 h of onset of myocardial damage and thus it can be used in early detection of myocardial necrosis [7,10]. It also has a high negative predictive value which allows expeditous rule out of myocardial necrosis [10].

This study was undertaken to determine the relationship between multiple cardiovascular risk factors and the levels of cardiac troponin I, CK-MB and myoglobin in patients with type 2 diabetes.

2. Subjects and methods

2.1. Subjects

This was a cross-sectional case - control study. The target population included diagnosed stable type 2 diabetic patients of the medical outpatient clinics of the University of Port Harcourt Teaching Hospital (UPTH). Patients with other acute conditions, other chronic illnesses and pregnant women were excluded. Those with past history of diagnosed Coronary artery disease were also excluded. Control subjects were drawn from members of staff of UPTH and University of Port Harcourt and the general public who had no history of cardiovascular disease, diabetes, hypertension, lipid disorders or other acute or chronic conditions. Approval was obtained from the Ethical Committee of UPTH and informed consent was obtained from all participants. Demographic, social and medical data of participants were assessed with the use of questionnaires.

2.2. Physical examination

Blood pressure (BP) of each participant was measured with a mercury sphygmomanometer after five minutes of rest and hypertension was taken as a BP equal to or greater than 140/90 mmHg or the use of anti-hypertensive medication. Waist circumference (WC) was measured and abdominal obesity was defined as WC > 102 cm in men and >88 cm in women.

2.3. Specimen collection

Participants were asked to come in the morning after 10–12 h overnight fast. Observing aseptic procedure, 10 mL of venous blood were taken from the antecubital fossa of participants for the analysis of fasting plasma glucose, lipid profile and cardiac markers. Plasma/serum was separated from blood cells after centrifugation at 2500 g for 10 min, harvested with a clean Pasteur pipette and stored at −20 °C.

2.4. Laboratory analysis

Estimation of fasting plasma glucose was done using the colorimetric glucose oxidase method, HDL-cholesterol by precipitation technique, total cholesterol and triglyceride by enzymatic method [15] while LDL-cholesterol was calculated using the Friedewald's formula [16]. The cardiac markers were determined using Calbiotech ELISA kit. Reference ranges provided by the manufacturer for cardiac troponin I, CK-MB and myoglobin were ≤0.5 ng/mL, 0–9.0 ng/mL and ≤100 ng/mL respectively.

2.5. Statistical analysis

Data obtained from this study was analysed using the Statistical Package for Social Sciences (SPSS) version 20.0 (SPSS Inc. Chicago, Illinois, U.S.A.). Frequencies and percentages were obtained for categorical variables. Differences in proportions were analyzed using the chi-squared test. The means of continuous variables were compared using unpaired students *t*-test and one way analysis of variance (ANOVA) and expressed as mean ± standard deviation (SD). P-values less than or equal to 0.05 were taken to be significant in all analyses.

2.6. Definition of variables

2.6.1. Dyslipidaemia

Any one or more of hypercholesterolaemia (plasma total cholesterol ≥5.2 mmol/L), hypertriglyceridaemia (plasma triglyceride ≥1.7 mmol/L), high LDL (plasma LDL-cholesterol ≥2.6 mmol/L) and low HDL (HDL-cholesterol <1.0 mmol/L in men and < 1.3 mmol/L in women) [17].

2.6.2. Metabolic syndrome

Based on the NCEP-ATP III (2005) definition, any three or more of the following criteria: hyperglycaemia (FPG ≥ 5.6 mmol/L), abdominal obesity (WC >102 cm in men and >88 cm in women), BP ≥130/85 mmHg, triglyceride (TG) ≥1.7 mmol/L, HDL <1.0 mmol/L (men) and <1.3 mmol/L (women) [18].

3. Results

DM patients were 188 in number, made up of 67 (35.6%) males and 121 (64.4%) females and control subjects were 200, consisting

Please cite this article in press as: E.P. Odum, E.E. Young, Elevated cardiac troponin I, creatine kinase and myoglobin and their relationship with cardiovascular risk factors in patients with type 2 diabetes, Diab Met Syndr: Clin Res Rev (2017), https://doi.org/10.1016/j.dsx.2017.12.001