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Full Length Research Paper

Comparison of the phenotypic patterns of the diagnostic criteria for cardiometabolic syndrome amongst type 2 diabetics and non-diabetic subjects

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Abstract

Background and objective: Cardiometabolic syndrome is an important risk factor for a number of clinical conditions especially type 2 diabetes mellitus and cardiovascular disease (CVD). This study was conducted to determine the patterns of occurrence of diagnostic parameters of cardiometabolic syndrome amongst type 2 diabetes mellitus (T2DM) subjects and non-diabetic controls, and to compare , if any, unique phenotypic findings or differences between these two subject groups. Materials and methods: We undertook a case-control study involving two hundred and sixty-two (262) adult Nigerians comprising 137 T2DM and 125 non-diabetic controls respectively, matched for age and sex. The subject groups were assessed for cardiometabolic syndrome using the National Cholesterol Education Program Third Adult Treatment Panel (NCEP-ATP III) criteria and comparisons were made between these groups on patterns of occurrence of the diagnostic parameters. Results: Findings showed that cardiometabolic syndrome had prevalence rates of 57.6% and 16.8% amongst the T2DM and healthy subject groups respectively. Analysis of the frequency of occurrence of the parameters showed that hypertension, obesity, decreased high density lipoprotein (HDL) cholesterol and hypertriglyceridaemia in decreasing order, and was the pattern in both the diabetic and healthy subject groups respectively. Multiple linear regression analysis showed a fair fit (R^2_{adj} =27.7%) for all subjects with cardiometabolic syndrome using triglycerides (TG), HDL-c and WC as regressors. Low HDL-c and increased WC were better predictor variables for cardiometabolic syndrome among non-diabetics (HDL-c: Beta=0.337, WC: Beta=0.341), than diabetics (HDL-c: Beta=0.207, WC: Beta=0.225). Hypertriglyceridemia however had a stronger level of association to cardiometabolic syndrome among diabetics (TG: Beta=0.272) than non-diabetics (TG: Beta= 0.191). Conclusion: The findings from this study show similar patterns in the occurrence of the individual components of cardiometabolic syndrome among the type 2 diabetics and non-diabetic subjects though with different prevalent rates.

Keywords: Cardiometabolic, Diabetes mellitus, Triglycerides, Lipoprotein, Phenotype.

INTRODUCTION

Cardiometabolic syndrome is a constellation of metabolic dysfunction characterized by impaired glucose tolerance consequent upon insulin resistance, hypertension, dyslipidemia, and truncal obesity (Srivastava, 2012). These metabolic derangements can singly and/or in an interdependent manner lead to increased predisposition to cardiovascular disease (CVD) morbidity and mortality (Castro et al., 2003). The likelihood of death from stroke and myocardial infarction in patients with this syndrome is put at three times that in unaffected individuals (Ford, 2005). Studies posit that about a fourth of the world's adults is afflicted by this syndrome (International Diabetes Federation, 2014) and this makes cardiometabolic syndrome a major public health problem, with increasing prevalence (Kelli et al., 2015),(Ford et al., 2004),(Okafor, 2012). This rising prevalence has largely

been attributed to lifestyle changes in diet and physical activity leading to higher obesity rates (Vorster, 2002). In parallel to the increasing prevalence of cardiometabolic syndrome is that of type 2 diabetes mellitus and there is an interplay of factors driving both (Uusitupa, 2002). The aetiological basis of cardiometabolic syndrome is taken as the culmination of genetic and environmental factors with the latter having a dominant contribution (Reilly and Raider 2003), (Deedwania, 2004).

Although central to the pathophysiological fulcrum for this disorder is insulin resistance, (Tenerez and Norhammer, 2003), (Ferrannini et al., 1999) it needs to be stated that insulin resistance is not synonymous with cardiometabolic syndrome (American College of Endocrinology (ACE), 2003), Reaven, 2002) and epidemiological data do not support the idea that this can account for all of the cluster abnormalities. (American College of Endocrinology (ACE) 2003), Zimmet et al.,1999). Though there is some data from Nigeria concerning cardiometabolic syndrome especially involving prevalence studies in both the general population and amongst diabetics, there is virtually no study that looked at the patterns of expression of the component diagnostic parameters comparatively between diabetic and non-diabetic subjects.

In this study we evaluated the patterns of expression of component diagnostic parameters of the cardiometabolic syndrome using the National Cholesterol Education Programme (NCEP)-Adult Treatment Panel (ATP) III criteria (Third Report of the National Cholesterol Education Programme (NCEP), 2002), in diabetic subjects comparatively to those of non-diabetic controls.

MATERIALS AND METHODS

Type 2 diabetic patients and non-diabetic subjects attending the metabolic research unit of a tertiary hospital (University College Hospital Ibadan) were used for the study. These subjects comprised type 2 diabetics screened and diagnosed at the unit, and apparently healthy individuals who came for routine medical assessment/check-up, which the unit traditionally conducts. A total of 262 subjects consisting of 125 non-diabetic (apparently healthy) controls and 137 type 2 diabetics were recruited for the study over a 9-month period. The study subjects were aged 40-70years. Ethical clearance was obtained from the Joint Ethical Committee serving both the hospital and its parent university. Written informed consent was given by each participant prior to the commencement of the study. These subjects were assessed for cardiometabolic syndrome based on the National Cholesterol Education Program-Adult treatment Plan III (NCEP-ATP III) criteria. (Third Report of the National Cholesterol Education Programme 2002).The subset of subjects consisting of both diabetics and non-diabetics who had cardiometabolic syndrome and their cardiovascular risk factors, being components of the diagnostic criteria, were subsequently compared for patterns of similarities and dissimilarities of expression.

Statistical analysis involved descriptive characteristics, regression analysis and correlations of the various variables using the statistical software- SPPS (version 10).

RESULTS

The prevalence rates of cardiometabolic syndrome was 57.6% amongst the diabetics while 16.8% in the non-diabetic subject subset. The mean age for diabetics with cardiometabolic syndrome which was 55.5years, was lower than the mean age (61.2years) of the healthy subjects with cardiometabolic syndrome. The gender defined prevalence rates among the diabetic group of subjects were 40% and 73.8% for males and females respectively. This was in contrast to a higher male to female prevalence rate in the non-diabetic group (18.8% vs 14.8%). (Table 1)

Out of the 78 diabetics with metabolic syndrome, 31(39.7%) had 4 components of the ATP III diagnostic criteria, and 13(16.7%) had all the 5 components (“full blown metabolic syndrome” (Isezuo and Ezunu, 2005). A similar percentage (38%) of the healthy subject group with metabolic syndrome had greater than 3 components of the ATP III criteria, but none had ‘full blown metabolic syndrome’. (Table 1)

Hypertension was the commonest component of cardiometabolic syndrome, in both the diabetic and non-diabetic groups though of higher prevalence in the diabetics (93.1%) than non-diabetics (61.9%). All the diabetics with hypertriglyceridemia were noted to have metabolic syndrome and 69% of these 29 individuals had increased waist circumference; the so called ‘hypertriglyceridaemic waist phenotype’. It was also observed that 86% of these 29 subjects had both dyslipidaemic components i.e. low HDL and hypertriglyceridemia. HDL hypocholesterolemia was observed in 25.6% of the 125 healthy subjects studied, while hypertriglyceridemia was seen in only 8.8% of these subjects. Unlike in the diabetic group wherein all who had hypertriglyceridemia were positive for cardiometabolic syndrome, only 63.6% of these non-diabetic subjects with hypertriglyceridemia had cardiometabolic syndrome. 76.2% of the non-diabetics with cardiometabolic syndrome in contrast to 51.4% of the diabetics with cardiometabolic syndrome had HDL hypocholesterolaemia. Multiple linear regression analysis of the data, using triglycerides (TG), HDL-c and waist circumference (WC) as regressors, was done. Amongst all subjects with cardiometabolic syndrome, the regression was a fair fit (R^2_{adj}=27.7%), but the overall relationship was significant

Table 1: Prevalence of Cardiometabolic syndrome by NCEP-ATP III diagnostic criteria

Status	Diabetics	Non-diabetics
	Percentage (%)	
Cardiometabolic syndrome positive (total)	57.6	16.8
Male	40	18.8
Female	73.8	14.8
4 components of NCEP-ATP III criteria	39.7	38
"Full blown" cardiometabolic syndrome (5components of NCEP-ATP III)	16.7	0

Table 2: Summary of multiple regression analysis

NON-DIABETICS

Model	Standardized Coefficient		
	Std Error	Beta	p
WC	.003	.341	.000
TG	.001	.191	.013
HDL	.002	-.337	.000

DIABETICS

Model	Standardized Coefficient		
	Std Error	Beta	p
WC	.003	.225	.007
TG	.001	.272	.001
HDL	.003	-.207	.004

Dependant variable: Metabolic Syndrome.
p (level of significance) < 0.05
Units for parameters WC: cm
TG, HDL-c,: mg/dl

($F_{3.24}$=32.8,p < 0.01). Data analysis showed similar measures of contribution, in the form of standardized coefficients(Beta), between the variables ,in decreasing order as follows; WC,TG and HDL-c (Beta= 0.279,0.275 and 0.243 respectively). (Table 2). Amongst diabetics with cardiometabolic syndrome, the regression analysis showed a poor fit (R^2_{adj}= 19.9%). Standardized coefficients showed the effects of the predictor variables; TG (Beta=0.272), WC (Beta=0.225) and HDL-c (Beta=0.207). (Table 2).

This is in contrast to the cardiometabolic syndrome-positive non-diabetics who showed a low measure of association of TG to the syndrome (Beta=0.191), compared to the other two predictor variables with higher and similar values. (HDL-c; Beta=0.337, WC; Beta=0.341). For this latter group of subjects the fit was relatively better than in the diabetics, (R^2_{adj} =34.4%) with a significant relationship maintained ($F_{3.12}$=22.6, p<0.01). This finding on TG was further highlighted on logistic regression where hypertriglyceridaemia showed an insignificant association with metabolic syndrome in both diabetics (p=0.38) and non-diabetics (p=0.75).

DISCUSSION

In our study we sought primarily to examine, if any, patterns of cardiovascular risk phenotypes, in terms of diagnostic parameters peculiar to cardiometabolic syndrome, existing in diabetic in contradistinction to non-diabetic subjects. Expectedly the prevalence of cardiometabolic syndrome was higher amongst the diabetics given that diabetes mellitus is a composite part of diagnostic criteria for cardiometabolic syndrome. The effect of gender on the prevalence of the syndrome is uncertain; while some reports show higher rate among females than males, others show no such relationship (Isezuo and Ezunu, 2005). The higher percentage of female diabetics with cardiometabolic syndrome in this study, corroborates the findings of Isezuo and Ezunu in

the northern part of the country (Isezuo and Ezunu, 2005) and (Martinez-Larrad et al., 2003). This however contrasts from the observations in the study by (Alebiosu and Odusan 2004). Contrastingly, amongst non-diabetics, more males had cardiometabolic syndrome than females. This is finding will be difficult to explain but may be a function of the diagnostic criteria whereby certain parameters of the NCEP-ATP III criteria might be skewed in favour of a particular gender. For example WC, which in this study was second in terms of frequency of occurrence amongst the parameters, has been a subject of debate regarding ethic-based cut-points. Whereas the Asians have been able to generate their own ethno-specific cut-offs (International Diabetes Federation, 2005) (Tan et al., 2004) (McGill, 1986), Africans are still assessed using European values. (International Diabetes Federation, 2005). And it is known by anthropology that African women tend to have smaller waist circumference in comparison to hip circumference and studies have buttressed this (Conway et al., 1995).

Hypertension was the commonest diagnostic criterion both study groups. This tallies with other studies which have shown hypertension as a very common component of cardiometabolic syndrome in people of African descent (Hanley et al., 2003),(Makuyana and Gomo 2004). However there was significant difference between elevated blood pressure in cardiometabolic syndrome-positive diabetics and the non-diabetics (p=0.001). This could be due to the well documented association between hypertension and diabetes which has been traced to hyperinsulinaemia (Sowers and Frohlich, 2004), (Robyn 1999).

In both the diabetic and non-diabetics with cardiometabolic syndrome, the prevalence of decreased HDL cholesterol (HDL-c) was low and is supported by previous studies (Alebiosu and Odusan 2004), (Isezuo 2005). This once again calls to question the usefulness of HDL-c in the diagnosis of metabolic syndrome in native type 2 diabetic Africans. The higher levels of HDL-c noted in diabetics with metabolic syndrome as compared to the non-diabetics is supported, though only partially, by the study by (Isezuo 2005). Unfortunately there are no data to assess for the apparently healthy (non-diabetic) population. The least frequent parameter seen in both study groups was elevated triglyceride levels. It is also instructive to note that hypertriglyceridaemia was strongly correlated with low HDL-c levels in both diabetic and non-diabetics with cardiometabolic syndrome in contrast to subjects without the syndrome in both groups.

Generally the strength of association was higher in the non-diabetic than in the diabetic group, between cardiometabolic syndrome and the predictor variables with the exception of hypertriglyceridaemia.

In summary, hypertension, obesity as defined by waist circumference, and dyslipidaemia, in decreasing order of prevalence was noted among metabolic syndrome cases. This trend of features was similar in both diabetics and non-diabetics though expectedly, higher in frequency in the former. However by regression analysis, HDL-c levels and waist circumference were seen to be better predictors of metabolic syndrome in non-diabetics, whereas triglyceride levels was a better predictor in diabetics. Given our findings it is imperative that advocacy be made for the inclusion of WC as part and parcel of clinical assessments as it is less clinically applied than BMI.

An apt conclusion can best be drawn using the findings from a study by Oghagbon et al at UITH which showed inadequate awareness of lipid disorders as a risk factor for atherosclerosis, and consequently the need for greater enlightenment of the population as a whole in this regard.

Limitation

A larger population of subjects would have further strengthened this study.

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