THE CENTRAL AFRICAN JOURNAL OF MEDICINE

ORIGINAL ARTICLES

Metabolic syndrome disorders in urban black Zimbabweans with type 2 *Diabetes mellitus*

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Abstract

Objective: The main aim of the study was to determine the prevalence of metabolic syndrome disorders and their interrelations in black Zimbabwean type 2 diabetic patients.
Study Design: Prospective cross sectional study.
Setting: Outpatient diabetic clinics at Harare and Parirenyatwa tertiary hospitals.
Main Outcome Measures: We recruited 109 adult diabetic subjects attending a tertiary hospital Diabetic Clinic. Anthropometric and metabolic parameters were measured by standard methods. Eighty percent of the patients were hypertensive, 32% dyslipidaemic, 32% obese, 50% hyperinsulinaemic, 61% had poor glycaemic control and 43% of the participants had the metabolic syndrome. The means of BMI and triglycerides were significantly different in hyperinsulinaemic versus non-hyperinsulinaemic patients ($p<0.001$ and 0.041 respectively), and diastolic blood pressure was significantly raised in the obese group ($p=0.043$).
The following significant associations were observed, hyperinsulinaemia with the metabolic syndrome (odds ratio=3.9, $p<0.001$) as well with obesity (odds ratio=4.8, $p<0.001$), however, only a weak association was observed between hypertension and hyperinsulinaemia (odds ratio=2.5, $p=0.064$). Patients exhibiting three metabolic disorders (dyslipidaemia, hypertension and obesity) were five times more likely to be hyperinsulinaemic ($p=0.025$) and hypertensive patients were almost three times more likely to be hyperinsulinaemic.
Conclusion: In comparison to their counterparts from certain ethnic groups, this urban diabetic population is also burdened with a variety of metabolic disorders which are risk factors for coronary artery disease. In this population, hyperinsulinaemia has a relatively weak association with hypertension and the relationship between obesity versus diastolic blood pressure as well as hypertriglyceridaemia versus serum insulin levels requires further investigation.

Cent Afr J Med 2004;50(3/4):24-9

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Introduction

Several studies have suggested a possible link between hyperinsulinaemia, dyslipidaemia, obesity, hypertension, and abnormal glucose metabolism.[1,2] These disorders are common in the metabolic syndrome also known as the insulin resistance syndrome (IRS). According to the WHO definition of the metabolic syndrome, patients with type 2 *Diabetes mellitus* and are insulin resistant, have the syndrome if they fulfill two or more of the following criteria: are hypertensive, have dyslipidaemia, have obesity/ abdominal obesity and have microalbuminuria.[3] However, there is limited information available about the prevalence of the metabolic syndrome in various ethnic populations, and considerable controversy exists about the exact abnormalities that are part of the syndrome.[4,5]

Some epidemiological studies confirm that the metabolic disorders occur commonly in certain ethnic groups with type 2 *Diabetes mellitus* including Afro-Americans, Mexican-Americans, Australian-Aborigines, Asians and Europids[6,7] Zimbabwe has a population that is in transition from a phase of parasitic and infectious diseases to that of cardiovascular and degenerative diseases, due to urbanisation, development and change in dietary habits. It follows that the prevalence of *Diabetes mellitus*, especially type 2 *Diabetes mellitus* is on the increase and will afflict a significant percentage of our population. It is, therefore, imperative to know the patterns of metabolic aberrations inherent in our type 2 diabetic population.

Insulin resistance is characterised by impaired insulin-mediated glucose uptake, which provokes a compensatory increase in pancreatic beta-cell secretory activity, resulting in hyperinsulinaemia and hyperglycaemia. Thus insulin resistance may be a fundamental aspect of the aetiology of type 2 *Diabetes mellitus,* and fasting insulin levels can be used as a reasonable surrogate for insulin resistance in type 2 diabetic subjects. There is some evidence that the combination of insulin resistance and compensatory hyperinsulinaemia predisposes the development of the cluster of abnormalities which include glucose intolerance, dyslipidaemia and high blood pressure.[8,9] However, there is little information from the literature to predict if endogenous insulin concentrations are responsible for the development of these metabolic disorders. A number of studies have confirmed that hyperinsulinaemia is associated with hypertension, although this remains a controversial area.[10,11] Blood insulin levels are a relatively weak predictor of the development of hypertension in black Americans and a high proportion of black type 2 diabetic patients have been found to be insulin sensitive.[12,13] Also a large number of Pima Indians are afflicted with hyperinsulinaemia, but exhibit low rates of hypertension.[14] It is possible that blood insulin expresses itself differently in diverse ethnic groups and this could indicate genetic as well as environmental variation.[15,16]

The main lipid disorder in the metabolic syndrome is thought to arise from abnormalities in triglycerides metabolism. Hypertriglyceridaemia and hypo-HDL-cholesterolaemia are the most common lipid abnormalities in type 2 diabetes subjects. The levels of tissue triglycerides determine the degree of insulin resistance and insulin production.[17,18] Despite the fact that African-Americans are at a higher risk of developing cardiovascular complications than whites or Hispanics in the presence of type 2 diabetes, they have lower blood triglycerides levels and low HDL-cholesterol is less common.[19] The low levels of triglycerides may have considerable effect on insulin sensitivity in this ethnic population and this suggests that other adverse effects contribute to the heightened cardiovascular risk in African-Americans.

Obesity has been found to be associated with reduced insulin sensitivity and high fasting levels and post prandial blood insulin concentrations. Weight is the only factor with a consistent positive association with insulin levels.[20]

Over the last few years, there have been suggestions that metabolic syndrome disorders are aetiological factors for cardiovascular disease.[20,22] However, it is not clear, which of the components are primary despite the fact that in subjects exposed to a Western lifestyle, insulin resistance is thought to be the common denominator. Before strategies of prevention and/or management of the cardiovascular complications are explored, it is crucial to know the extent of the metabolic disorders in our urban diabetic population, that has undergone a substantial socio-economic transition. Thus the main objective of this study was to establish the prevalence of the disorders (components) of the metabolic syndrome and their interrelations in urban black Zimbabwean type 2 diabetic patients.

Materials and Methods

Subjects.

Adult diabetics at a tertiary hospital Diabetic Clinic were eligible to participate in the study. Young diabetics were not eligible in order to avoid patients with MODY (maturity-onset diabetes of the young), a subphenotype of type 2 *Diabetes mellitus.* Type 2 diabetes was defined according to the World Health Organization (WHO) criteria in terms of resistance to insulin action and inadequate compensatory insulin secretory response.[23] All patients who were undergoing a combination of diet and/or oral hypoglycaemic treatment for type 2 *Diabetes mellitus* and gave their informed consent were recruited into the study. The study was approved by the local Ethics Committee.

Anthropometric, Blood Pressure Measurements and Laboratory Analyses.

The history of each participant was obtained at enrolment using a standardised data form. Fasting venous blood was withdrawn from the participants and each sample was delivered into a potassium oxalate/sodium fluoride vial for fasting glucose analysis, an EDTA vial for HbA1c and a plain tube for other assays. The samples were sent to the laboratory for separation of plasma or serum.

Plasma glucose concentration was determined on the Beckman CX5 Synchron analyzer by the hexosekinase

method. Fasting levels of plasma insulin were carried out in an Abbott Laboratories IMX analyzer using the Abbott insulin microparticle enzyme immunoassay (MEIA), which has no cross-reactivity with proinsulin. GLYCO-Tek Affinity Chromatography kits from Helena laboratories (Beaumont, Texas) were used to measure the blood levels of HbA1c The method quantitates all glycated haemoglobin including the A1c fraction and has a between run precision of 6.8%. Serum triglycerides, cholesterol and HDL-C (direct HDL-C method) assays were carried out on the Cobas Mira Plus autoanalyzer using Boehringer Mannheim kits by enzymatic determination. The above assays except for HbA1c were carried out at 37°C.

Height was measured to the nearest 0.1 cm using a stadiometer with a right angle and weight measurements up to the nearest 0.1 kg were done on a calibrated scale. The BMI was calculated from these parameters (weight in kg divided by height in metres squared). Blood pressure was measured in the sitting position using a mercury sphygmomanometer after a five minute rest. Disappearance of Korotkoff sounds (phase V) was taken as the diastolic blood pressure. Two readings were taken at one and a half minute intervals and the second reading used in the statistical analyses.

Patient Classification.

The participants were classified as;

i) Obese if their BMI was equal or greater than 30 Kg/m^2.
ii) Hypertensive if the SBP was greater than 140 mm Hg and/or the DBP was greater. than 90 mm Hg or if they were on treatment for hypertension.
iii) Hyperinsulinaemic if the plasma insulin levels were above 9.2 μU/ml
iv) Dyslipidaemic if the serum triglyceride levels were above 2.3 mmol/L or serum HDL-cholesterol was below 0.9 mmol/L or both.

Statistics.

The results for continuous data are given as mean ± standard deviation. The students' two tailed t-test was used for continuous variables, Chi-square test and analysis for categorical variables. To investigate the association of the metabolic disorders and other variables, we used binary logistic regression. The statistical packages were WHO Epi-Info version 6 and SPSS version 10. The level of statistical significance was set at a p value less than 0.05.

Results

The characteristics of the study population are presented in Table I. The study population comprised 109 urban black type 2 female (n=77) and male (n=32) diabetics aged between 36 and 78 years. There were no significant gender differences in age, duration of diabetes, SBP, DBP, fasting plasma glucose, HbA1c, plasma insulin, HDL-C, cholesterol and triglyceride levels. The only significant gender difference was a higher BMI of 25.7 versus 28.2 (p=0.044) for men and women respectively. The main effects of gender, age and duration of diabetes on obesity (represented by BMI) were not significant using binary logistic regression, p>0.05. The prevalence of various metabolic syndrome components in the 109 type 2 *Diabetes mellitus* patients are given in Table II.

Table I: Baseline characteristics of 109 type 2 ***Diabetes mellitus*** *patients.*

Characteristic	Men mean±SD(n=32)	Women mean±SD(n=77)	p -value
Age (years)	55±9	55±9	0.902
Duration# (years)	4.2±4.0	5.3±4.5	0.224
BMI* (Kg/m2)	25.7±4.6	28.2±6.2	0.044
SBP* (mmHg)	151±24	153±25	0.758
DBP* (mmHg)	94±14	93±11	0.769
Plasma glucose (mmol/L)	9.7±5.6	11.2±5.9	0.234
HbA_{1c} *(%)	10.2±3.6	10.0±2.9	0.794
Plasma insulin (FU/ml)	11.3±8.9	13.4±12.0	0.663
HDL-C* (mmol/L)	1.25±0.49	1.35±0.48	0.649
Triglyceride (mmol/L)	1.68±1.10	1.61±0.86	0.748
Cholesterol (mmol/L)	5.3±1.4	5.6±1.4	0.658

 # Duration of diabetes.
**** BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; HbA1c haemoglobin A1c; HDL-C, high density lipoprotein cholesterol.***

The significant relationships between the various components of the metabolic syndrome in our study population are shown in Table III. The means of insulin were significantly different in those patients who were obese (p<0.001), hypertriglyceridaemic (p=0.049), and who had the metabolic syndrome (p=0.018). Those patients that were hyperinsulinaemic and hypertensive had significantly elevated BMI (p<0001 and 0.015 respectively). The means of DBP were significantly different in the obese diabetics compared to the non-obese (p=0.043).

Table II: Prevalence of metabolic syndrome components in type 2 ***Diabetes mellitus*** *patients (n=109).*

Metabolic Component	Prevalence (%)
Hypertension (n=87)	80
Dyslipidaemia* (n=35)	32
Hypo-HDL-C** (n=26)	24
Hypertriglyceridaemia (n=20)	20
Obesity (n=35)	32
Hyperinsulinaemia (n=54)	50
Metabolic syndrome (n=47)	43
3 risk factors*** (n=11)	10
2 risk factors** (n=37)	34
1 risk factor** (n=52)	48

**** Serum triglyceride levels above 2.3 mmol/L or serum HDL-cholesterol was below 0.9***
***** Hypo—HDL-C, hypo-high density lipoprotein cholestrol.***
****** The risk factors are obesity, hypertension and dysilpidaemia.***

Table IV shows the associations between various metabolic syndrome components. The metabolic syndrome was associated with hyperinsulinaemia (p<0.001).

Hypertension was weakly associated with hyperinsulinaemia, p=0.064 and obesity was associated with hyperinsulinaemia, p<0.0001. A patient who had three risk factors was associated with high plasma levels of insulin (p=0.025).

Table III: Means of measured variables compared to metabolic disorders in type 2 diabetic patients (n=109).

Variable vs Metabolic Disorder (n*)	Variable mean (±SD)**		p value
BMI*** levels vs hyperinsulinaemia (n=54)	30 (6)	vs 25 (5)	<0.001
BMI levels vs hypertension (n=87)	28 (6)	vs 25 (5)	0.015
DBP vs obesity (n=35)	97 (10)	vs 92 (13)	0.043
Triglyceride levels vs hyperinsulinaemia (n=54)	1.81 (0.95)	vs 1.46 (0.90)	0.049
Insulin levels vs obesity (n=35)	15.7 (9.2)	vs 11.4 (11.8)	<0.001
Insulin levels vs hypertriglyceridaemia (n=20)	17.7 (14.4)	vs 11.7 (10.1)	0.041
Insulin levels vs metabolic syndrome (n=47)	15.6 (11.0)	vs 10.6 (10.9)	0.018

**** n, is the number of patients afflicted by a metabolic disorder.***
***** Means and SD of variables in those patients that have the metabolic disorder versus those where it's absent.***
****** BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; lipoprotein cholesterol.***

Table IV: Associations of metabolic disorders in type 2 ***Diabetes mellitus.***

Metabolic components	Odds Ratio	95% Confidence Limits	p-value
Obesity vs hyperinsulinaemia	4.8	1.78-12.94	<0.0001
Hypertension vs hyperinsulinaemia	2.5	0.84-7.72	0.064
Obesity vs DBP	2.2	0.90-5.33	0.061
Hyperinsulinaemia vs metabolic syndrome	3.9	1.60-9.51	<0.001
HypertrighypoHDL-C* vs 3 risk factors	7.4	1.39-40.00	0.013
3 risk factors vs hyperinsulinaemia	5.3	0.98-38.12	0.025

**** hypertrighypo-HDL-C, hypertriglyceridaemia and hypo-high density lipoprotein cholesterol.***

Discussion

Our results clearly demonstrate that the metabolic syndrome, characterised by obesity, hypertension and dyslipidaemia is common in urban black type 2 diabetic patients, just as in their Caucasian counterparts. The most prevalent disorder was hypertension which was found in 80% of the patients. The high prevalence of hypertension in these type 2 diabetic patients is bound to increase the risk of the development of diabetic nephropathy. Although a strong association between insulin resistance and hypertension in lean rather than obese subjects has been reported,[24,25] this relationship remains the most controversial part of the metabolic syndrome.[16,26,27] Our study demonstrated a weak association between hyperinsulinaemia and hypertension. Since a sizeable number of the study population was obese, this could explain the weaker association between blood pressure and insulin levels compared to other metabolic disorders. Alternatively, the weak relationship could be explained by ethnic differences.

A clustering of metabolic disorders is a characteristic finding in individuals with insulin resistance, as reported in several studies.[28-30] In our study 50% of the diabetic patients were hyperinsulinaemic and a strong significant association was demonstrated between hyperinsulinaemia and the metabolic syndrome. A subject who had high levels of fasting plasma insulin was three times more likely to be hypertensive, almost four times more likely to have the metabolic syndrome, and five times more likely to be obese or to have three metabolic disorders.

It must be pointed out that there is little information from the literature to predict if endogenous insulin concentrations are responsible for the development of these metabolic disorders.

In this study, as in some studies, we confirmed that hypertriglyceridaemic patients have elevated fasting insulin levels.[31,32] The blending of hypertriglyceridaemia and hypoHDL-cholesterolaemia has been found to be a particularly potent risk factor for coronary heart disease.[31,33,34] Our study demonstrated that a subject who has hypertriglyceridaemia combined with low levels of HDL-C is about seven times more likely to have three metabolic risk factors. The three independent risk factors, obesity, hypertension or dyslipidaemia are related to atherosclerosis and the widespread hyperinsulinaemia and poor glycaemic control present in this population could result in accelerated atherogenesis.

Hyperinsulinaemia had a consistent positive relation with all the weight indices and obesity was a strong predictor of fasting hyperinsulinaemia. The hyperinsulinaemia in these patients could be explained by an increase in android fat. Weight indices were associated with dyslipidaemia, hypertension, hyperglycaemia, and hyperinsulinaemia, suggesting that obesity is a heterogeneous condition. Thus anthropometric measures can be used as indicators of the probability of dyslipidaemia, high blood pressure and hyperinsulinaemia in type 2 *Diabetes mellitus*.

Hypertension, poor glycaemic control, hyperinsulinaemia, obesity and dyslipidaemia seem to be a major health burden in type 2 *Diabetes mellitus* patients in this population. In our study, the clustering of obesity, hypertension and dyslipidaemia was associated with hyperinsulinaemia and it appears that hyperinsulinaemia has the potential to explain at least two of these metabolic disorders, i.e. obesity and hypertriglyceridaemia. Although the association between hyperinsulinaemia and hypertension remains somewhat controversial, it is possible that it is weaker in blacks.

In conclusion, the metabolic syndrome is common in this diabetic population and the constellation of the metabolic disorders may expose them to coronary artery disease as well as to the severe microvascular complications of

diabetes. A longitudinal study to investigate the effects of the multitudinous metabolic disorders in these patients is warranted.

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