ORIGINAL ARTICLE

Insulin resistance, metabolic syndrome, and lipids in African women

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Abstract

Background: The metabolic syndrome is closely related to insulin resistance (IR) and cardiovascular disease. This study examined the prevalence of IR and metabolic syndrome as well as factors associated with IR among Nigerian women.
Materials and Methods: Eighty-six women living in an urban area in Enugu, South-East Nigeria, were assessed. Demographic information included age, residence, physical activity, alcohol and tobacco intake and were collected with questionnaires. Blood pressure and anthropometric parameters were measured using standard methods. Fasting lipids, blood glucose, and insulin were measured. IR was calculated with homeostasis model assessment of IR formula. The ratios; triglyceride/high-density lipoprotein (TG/HDL), total cholesterol (TC)/HDL, and atherogenic index of plasma; log (TG/HDL) were calculated and compared with IR. Metabolic syndrome was sought for using both the WHO and the harmonized joint criteria.
Results: The mean age was 44.4 (13.1) years. Hypertension, obesity/overweight, and abdominal obesity were present in 31.5%, 81.1%, and 92.2%, respectively. There was elevated TC (62.2%), elevated low-density lipoprotein (45.6%), low HDL (40%), and elevated TG (14.4%) levels. IR was present in 39 (45.3%). Metabolic syndrome was present in 25 (29.1%) and 17 (19.8%) using the joint criteria and the WHO criteria, respectively. The sensitivity and specificity of the joint revised criteria in identifying IR individuals were 48.7% and 87.2%, respectively, and for the WHO criteria, were 38.5% and 95.7%, respectively. The only significant predictor of IR was the presence of diabetes; $P = 0.03$, odds ratio = 7.2 (95% confidence interval = 1.19–41.88).
Conclusion: IR and metabolic syndrome were common. They were not related to any of the lipoprotein ratios. Metabolic syndrome had a low sensitivity in detecting IR.

Key words: Insulin resistance, metabolic syndrome, triglycerides, women

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Introduction

The relationship between insulin resistance (IR) and cardiovascular disease (CVD) is well established by meta-analyses, which showed that elevated insulin and glucose levels in persons without diabetes were associated with an increased risk of CVD.[1-3] IR promotes the development of atherosclerosis through elevated levels of glucose and insulin, dyslipidemia, hypertension, and inflammation.[4] IR is the central abnormality in the metabolic syndrome and is identified by central obesity, abnormal lipoprotein levels; particularly triglycerides (TGs) and high-density lipoproteins (HDLs) and glucose

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intolerance.[5] In addition, obesity and diabetes mellitus are closely linked with IR.[6] The concept of the metabolic syndrome has been widely used as a way of identifying persons with increased risk of developing CVD.

Representatives from the World Heart Federation, International Atherosclerosis Society, and International Association for the Study of Obesity recently developed a revised set of criteria. These included the usual five components which are dysglycemia, hypertension, abdominal obesity, elevated TG levels, and low levels of HDL.[7] However, none of the components was designated to be mandatory for a diagnosis. It also recommended the use of ethnic or country-specific cut-off points for central obesity, similar to the International Diabetes Federation (IDF) criteria.[8]

The metabolic syndrome has not been as well studied in African populations as in Caucasians. Although ethnic-specific cutoffs are recommended for waist circumference as a marker of central obesity, such data are not available for the African population. Recently, some researchers have demonstrated that in Africans, the criteria for the metabolic syndrome may need to be revisited. They have argued that these criteria do not have the same significance in the black population as in their white counterparts.[9]

Elevated TG levels are usually accompanied by low HDL cholesterol. This is because HDL particles participate in the clearance of TG-rich lipid particles.[10] Hence, when TG levels are high, HDL levels are expected to be low and vice-versa. The pattern of high TG and low HDL is highly atherogenic and is usually referred to as "the dyslipidemia of IR."[10]

Population studies have consistently shown lower TG levels in African Americans than whites or Hispanics.[11] Indeed, a TG paradox has been well documented in blacks.[12] This TG paradox has been described as the combined presence of normal TG levels and low HDL.[9,11,12] It is thus likely that isolated low HDL and not elevated TG could be a major contributor to high rates of CVD in blacks. It has been reported that a TG/HDL ratio of >3.0 is predictive of IR in Caucasians while a value of 2.0 is more predictive in African Americans.[13,14] However, some studies have shown that this ratio does not predict IR in African American women.[15,16]

The aim of this study was to determine the frequency of IR and metabolic syndrome in a cohort of women in a semi-urban area of South-Eastern Nigeria. It also attempts to determine the relationships between the TG/HDL ratio, other common lipoprotein ratios and the metabolic syndrome and IR in the subjects.

Materials and Methods

A cohort of 90 women residing in Trans-Ekulu, an urban community in Enugu-East Local Government Area (LGA) in South-East Nigeria participated in the study. Enugu-East LGA has an estimated population of 280,000 people.[17] It is populated mainly by middle to high-income earners. The women were attending an annual women's religious conference during which free health screenings are usually rendered. Christianity is the predominant religion in Enugu. Women who met the study criteria were recruited consecutively as they enrolled for the conference and written informed consent obtained.

Only women who were 18 years or more were considered eligible. Women who were pregnant or breastfeeding and also those with known chronic medical conditions such as chronic kidney disease, liver disease, goiter, or severe arthritis requiring steroid therapy were excluded. Ethical approval for the study was obtained from the University of Nigeria Teaching Hospital Ethics Committee. In addition, approval was obtained from the resident chaplain of the church to conduct the study during the women's meeting.

Study protocol

The women had been earlier informed to fast overnight for at least 8 h prior to the study day. On the day of the study, structured self-administered questionnaires were distributed to obtain demographic data, menopausal history, alcohol, and tobacco history as well as the history of physical activity.

Their weight was measured with a weighing scale to the nearest kg and height was measured with a stadiometer. Waist circumference was measured to the nearest 0.5 cm using a flexible tape at a landmark halfway between the iliac crest and the lower rib cage. The blood pressure (BP) was measured using a mercury sphygmomanometer and the average of two readings taken at least 5 min apart was recorded.

Venous blood was collected for insulin and lipid assay and blood glucose estimation. Insulin assay was performed using an enzyme-linked immunosorbent assay technique with a commercially available kit obtained from Diagnostic Automation, Inc., USA®. The sensitivity of the assay was <1.5 μU/l with inter- and intra-assay coefficient of variation of 8.3% and 8.4%, respectively. A Hitachi 902® (Mannheim, Germany) blood chemistry autoanalyzer was used to measure blood glucose, serum TG, total cholesterol (TC), low-density lipoprotein (LDL), and HDL. TG was assayed using the Wahlefeld enzymatic method. Glucose estimation was done using the automated enzymatic oxidation method. TC was measured by the Roeschlau and Allain photometric assay while LDL and HDL were assayed using automated direct methods. The homeostasis

model assessment of IR (HOMA-IR) was calculated with the formula:[18] HOMA-IR = ([Insulin [μU/mL] × blood glucose [mmol/L])/22.5.

Definition of terms

Body mass index (BMI) was calculated using the formula weight (kg)/height^2 (m^2). BMI was classified as 20–24.9 kg/m^2; normal, 25–29.9 kg/m^2; overweight, ≥30 kg/m^2; Obese.

Hypertension was defined as systolic BP >140 mmHg and/or diastolic BP >90 mmHg or use of antihypertensive medication.

Abdominal obesity was defined using IDF ethnic-specific criteria of waist circumference >80 cm in women.[12]

Dyslipidemia was defined using the WHO criteria of TC >5.2 mmol/l, LDL >3.6 mmol/l, TG >1.5 mmol/l and HDL <1.0 mmol/l.[19]

Atherogenic index of plasma (AIP) was calculated using the formula; AIP = Log (TG/HDL).[20]

IR was defined as HOMA-IR values >2.[21]

Metabolic syndrome was defined using both the WHO[22] and the Joint revised criteria.[23] For the WHO criteria, metabolic syndrome was said to be present in subjects who had either IR or FBG >5.6 mmol/l plus any two of the following; waist: Hip ratio >0.85 or BMI >30 kg/m^2, BP >140/90 mmHg, TG >1.7 mmol/l, and/or HDL <1.0 mmol/l.[22]

Using the joint criteria, metabolic syndrome was defined as the presence of any three of; waist circumference >80 cm, systolic BP >130 and/or diastolic BP >85 mmHg, TG >1.7 mmol/l, HDL <1.3 mmol/l, FBG >5.6 mmol/l including DM.[7]

Data analysis

Statistical analysis was carried out using SPSS version 17 for windows (IBM Corporation Armonk, NY, USA). Comparisons between continuous data were made using the Student's *t*-test and Chi-square test for categorical variables. Sensitivity and specificity of the different metabolic syndrome criteria to identify IR individuals were calculated using the following formula:

Sensitivity = true positives/(true positives + false negatives) and specificity = true negative/(true negative + false positive) whereas kappa coefficient of concordance (κ) was used to evaluate the agreement between both metabolic syndrome criteria. Binary logistic regression was carried out to identify factors, which could predict IR. A $P < 0.05$ was considered to be statistically significant.

Results

A total of 90 women participated in the study though only 86 had complete results. They had a mean age of 44.4 (13.1) years. Alcohol intake was documented in 15 (17.4%) women. There was no history of cigarette or tobacco use in any of the women. Physical activity in the women consisted mostly of informal exercise such as trekking, farming, and vigorous house chores. Formal exercise was uncommon; however, 21 (24.4%) were completely sedentary. The mean BMI was 29.7 (5.7) kg/m^2; 39 (43.3%) of them were overweight whereas 34 (37.8%) were obese. They had a mean waist circumference of 94.3 (11.7) cm with abdominal obesity being present in 83 (92.2%) women. There was a significant correlation between BMI and waist circumference ($r = 0.7$, $P < 0.001$). Hypertension was present in 31 (36.0%) women, nine of whom did not have a previous history of hypertension. Dysglycemia (FBS >5.6 mmol/l) was present in 36 (41.9%) women whereas 19 (22.1%) had diabetes mellitus of which 10 (11.6%) were self-reported diabetes. Further details are shown in Table 1.

The most common abnormal lipid parameters in the entire population were elevated total cholesterol in 54 (62.8%) and elevated LDL in 34 (39.5%) of the participants. Low HDL was present in 5 (5.8%), and only 15 (17.4%) had high TG. The TG/HDL ratio ranged from 0.24 to 4.10 with a median (interquartile range [IQR]) of 0.72 (0.56–1.10). Table 2 shows the various lipoprotein parameters in the women.

Metabolic syndrome criteria and insulin resistance

The median (IQR) HOMA was 1.45 (0.82–4.06) and 39 (45.3%) women had IR. Metabolic syndrome was present in 25 (29.1%) women using the joint criteria while it was present in 17 (19.8%) using the WHO criteria [Table 3].

IR was present in 15 (88.2%) of the women who had metabolic syndrome according to the WHO criteria while 19 (76%) of those with metabolic syndrome according to the joint criteria had IR [Table 3].

The sensitivity and specificity of the joint revised criteria in identifying IR individuals were 48.7% and 87.2%, respectively. Using the WHO criteria, the sensitivity and specificity were 38.5% and 95.7%, respectively [Table 3]. The concordance between both metabolic syndrome definitions was moderate; k = 0.63, standard error = 0.09, $P < 0.001$.

HOMA-IR did not correlate with TG/HDL ratio ($P = 0.73$), waist circumference ($P = 0.60$), or waist/hip ratio ($P = 0.32$). However, there was a positive correlation with BMI ($r = 0.34$, $P = 0.001$).

Table 1: Age distribution, sociodemographic and clinical characteristics of the study population

Parameter	Age group in years				*P*
	18–39 (*n*=26)	40–64 (*n*=37)	>65 (*n*=23)	Total (*n*=86)	
Sedentary (%)	7 (26.9)	9 (24.3)	5 (21.7)	21 (24.4)	0.62
Alcohol use (%)	5 (19.2)	8 (21.6)	2 (8.7)	15 (17.4)	0.36
BMI (kg/m^2)†	29.2 (4.5)	29.6 (5.3)	30.5 (7.4)	29.7 (5.7)	0.72
BMI categories					
Normal BMI (%)	4 (15.4)	6 (16.2)	6 (26.1)	19 (18.6)	0.62
Overweight (%)	11 (42.3)	16 (43.2)	6 (26.1)	36 (41.9)	0.96
Obese (%)	9 (34.6)	14 (37.8)	11 (47.8)	34 (39.5)	0.73
Waist circumference†	92.4 (9.9)	93.8 (12.6)	97.2 (11.8)	94.3 (11.7)	0.34
Waist-hip ratio†	0.86 (0.05)	0.87 (0.06)	0.89 (0.06)	0.88 (0.06)	0.05
Systolic BP† (mmHg)	122.6 (15.8)	140.0 (30.9)	137.5 (24.7)	134.1 (26.4)	0.03*
Diastolic BP† (mmHg)	76.8 (11.9)	83.4 (16.1)	81.7 (14.9)	81.0 (14.8)	0.24
Hypertensive (%)	4 (15.4)	15 (40.5)	12 (52.2)	31 (36.0)	0.02*
Dysglycemia					
FBG>5.6 (%)	11 (42.3)	12 (32.4)	13 (56.5)	36 (41.9)	0.08
DM present (%)	4 (15.4)	9 (24.3)	6 (26.1)	19 (22.1)	0.23

†Mean (SD); *Significant values. BMI=Body mass index; BP=Blood pressure; FBG=Fasting blood glucose; SD=Standard deviation; DM=Diabetes mellitus

Table 2: Lipoprotein parameters and ratios of the study population

Lipids	Age group (years)				
	18-39, *n* (%) (*n*=26)	40-59, *n* (%) (*n*=37)	≥60, *n* (%) (*n*=23)	Total, *n* (%) (*n*=86)	*P*
High TC	16 (61.5)	22 (59.5)	16 (69.6)	54 (62.8)	0.58
High LDL	9 (34.6)	16 (43.2)	9 (39.1)	34 (39.5)	0.73
High TG	2 (7.7)	6 (16.2)	7 (30.4)	15 (17.4)	0.04*
Low HDL	1 (3.8)	3 (8.1)	1 (4.3)	5 (5.8)	0.92
AIP†	−0.14 (0.18)	−0.11 (0.23)	−0.04 (0.28)	−0.10 (0.23)	0.26
TG/HDL‡	0.80 (0.50)	0.69 (0.61)	0.90 (0.96)	4.0 (1.54)	0.54
TC/HDL‡	3.86 (0.96)	3.93 (1.62)	4.58 (2.91)	0.72 (0.55)	0.17

†Mean (SD); ‡Median (IQR); *Significant values. TC=Total cholesterol; LDL=Low-density lipoprotein; HDL=High-density lipoprotein; TG=Triglycerides; AIP=Atherogenic index of plasma; SD=Standard deviation; IQR=Interquartile range

Table 3: Sensitivity and specificity of the metabolic syndrome criteria to identify insulin resistance

	WHO criteria		
	MS present	MS absent	Total
IR present	15	24	39
IR absent	2	45	47
Total	17	69	86
	Joint criteria		
	MS present A	MS absent B	Total
IR present C	19	20	39
IR absent D	6	41	47
Total	25	61	86

$\text{Sensitivity} = \frac{AC}{AC+BC}$; $\text{Sensitivity} = \frac{BD}{BD+AD}$. MS=Metabolic syndrome; IR=Insulin resistance; WHO=World Health Organization

Binary logistic regression was carried out to determine predictors of IR. Variables entered into the model were BMI, waist circumference, waist/hip ratio, TC/HDL ratio, AIP, being hypertensive, and being diabetic. Overall, the model was significant, $P = 0.04$, Nagelkerke $R^2 = 0.208$. The only significant predictor of IR was the presence of diabetes; $P = 0.03$, odds ratio = 7.2 (95% confidence interval = 1.19–41.88).

Discussion

This study was carried out in a cohort of urban women in the South-Eastern part of Nigeria to determine the relationships between the TG/HDL ratio, other lipid ratios, the WHO and the joint revised metabolic syndrome criteria and IR. The women had high rates of hypertension, obesity, and dysglycemia including diabetes mellitus, but low rates of elevated TG. Almost half of them had IR. Metabolic syndrome was more prevalent using the joint revised criteria than the WHO criteria. The two definitions of the syndrome had a low sensitivity for detection of IR, with the WHO definition having a higher specificity.

Majority of the women were either obese or overweight. Abdominal obesity was also common, and its prevalence (92.2%) was higher than that reported by a study done in a rural population in Enugu (42.6%).[23] However,

the cut-off for abdominal obesity in our study (80 cm) was lower than that used in that study (88 cm). Women have been found to have higher rates of obesity than men in some studies on cardiovascular risk factors in Nigeria.[24,25] The women in the study were resident in an urban area, and this could likely result in the consumption of highly processed foods rich in sugar in addition to consumption of meals high in carbohydrate and low in protein, which is common in African communities. The prevalence of hypertension increased significantly with increasing age in the women [Table 1], which is as expected based on the fact that the risk of hypertension is known to increase with older age.

Lipid abnormalities were common in the study subjects, the most common being elevated TC and elevated LDL while low HDL and elevated TG were uncommon. This is similar to other studies on dyslipidemia in Nigerians, which have reported low prevalence of hypertriglyceridemia, with elevated LDL and low HDL being the more common pattern in apparently healthy Nigerians.[26-28] Elevated TG was more common than low HDL in our study. This is possible because we used a different cut-off point of <1.0 mmol/l for low HDL, based on the WHO guidelines while most of the other studies that reported a higher prevalence of low HDL used a cut-off point of <1.3 mmol/l based on NCEP-ATP III guidelines. Elevated TG was significantly associated with increasing age [Table 1], similar to other studies.[29] This may be due to hormonal changes.

In studies on the metabolic syndrome in Nigerians it has been observed that elevated TGs are one of the least contributors to the syndrome, while central obesity and hypertension are major contributors.[30] Sumner *et al*. demonstrated that in West Africans and African Americans with the metabolic syndrome, the most likely abnormalities were central obesity, low HDL, and hypertension.[31] Low-TGs and dysglycemia were least contributory. This pattern was also observed in our study; as generalized and central obesity were also significant findings, with elevated TG being uncommon. It has thus been suggested that blacks may require a separate definition of the metabolic syndrome due to these differences.[9] Indeed low HDL and normal TG levels in blacks suggest that the criteria for the metabolic syndrome in blacks need to be revisited. This pattern of normal or low TG and low HDL in blacks has been referred to as a "triglyceride paradox" and is attributed to increased TG clearance.[32]

It is possible that the threshold of TG required to make a diagnosis of metabolic syndrome in them may need to be lowered, or that elevated TG levels need to be removed entirely as a criterion for metabolic syndrome from the definition. Higher prevalence of hypertriglyceridemia (34.1%) was reported in a study in women in another state in South-East Nigeria.[33] These women were older (mean age 54.9 ± 10.7 years) and this may have accounted for higher TG levels in them. However, they were less obese (overweight 38.5%, obesity 20.7%) than in our own study.

There was a high prevalence of IR in the study subjects (45.3%). This is similar to the prevalence obtained in a study on IR in a healthy population in Nigeria, which demonstrated a prevalence rate of about 35% and women were observed to have a higher rate of IR (44.9%) than their male counterparts (27.5%).[34]

The ratio TG/HDL was not correlated with IR in this population of African women. Studies have suggested that AIP is a more useful ratio for determining the presence of cardiovascular risk. It correlates well with the size of HDL and LDL particles and with the fractional esterification rate of cholesterol by lecithin: Cholesterol acyltransferase in plasma.[20] This ratio accurately reflects the presence of atherogenic small LDL and HDL particles, is a sensitive predictor of coronary atherosclerosis and cardiovascular risk[20] and a useful surrogate for IR.[13] However, this was not apparent in our study as AIP did not predict IR; however this may have been due to the small sample size in the study.

The TC/HDL ratio was also not predictive of IR in our study. This suggests that in blacks, other mechanisms such as hypertension and obesity may be more important in the development of IR, metabolic syndrome, and CVD than lipid abnormalities, possibly due to genetic differences in lipid metabolism in comparison with Caucasians.

There was a significantly higher prevalence of IR in the women who had metabolic syndrome using the WHO criteria than with the joint criteria. This is expected because the WHO definition requires the presence of either IR or dysglycemia for diagnosis unlike in the joint metabolic syndrome criteria where it is not a prerequisite. The two criteria had similar degree of sensitivity, but the WHO criteria had a higher specificity. This suggests that they may not be very sensitive screening tools for IR in our study population. It therefore appears that the metabolic syndrome may not be a useful tool to detect the presence of IR in women in this study. This is because some of its components such as the TG level, HDL level, and waist circumference appear not to be significantly related to IR in the subjects using present cut-off values. This however may have been due to the small sample size in the study and possibly insufficient power to detect the associations. Hence, it is recommended that large-scale studies need to be done to determine ethnic-specific cut-off values that reliably predict IR, and therefore the risk of CVD in our population.

The strength of this study lies in the fact that this is probably the first community-based study, with all age groups represented, to examine the relationships between

IR, lipids and the metabolic syndrome using different criteria in women in this part of Nigeria. However, the main limitations of the study are small sample size, and the fact that the women were of one ethnic group hence may not be truly representative of Nigerian women. A larger study population involving several ethnic groups would have been more representative, but this was not possible due to financial constraints. Further studies on larger populations are advocated.

Conclusion

This study has shown that IR is a common finding in this group of African women, and is not predictable by commonly used lipoprotein ratios such as the TG/HDL ratio and the AIP or by the metabolic syndrome. However, larger epidemiological studies will be needed to further confirm these findings.

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Conflicts of interest
There are no conflicts of interest.

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