The TG/HDL-C Ratio Does Not Predict Insulin Resistance in Overweight Women of African Descent: A Study of South African, African American and West African Women

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Women of African descent have a high prevalence of diseases caused by insulin resistance. To positively impact cardiometabolic health in Black women, effective screening tests for insulin resistance must be identified. Recently, the TG/HDL-C ratio has been recommended as a tool to predict insulin resistance in overweight people. While the ratio predicts insulin resistance in White women, it is ineffective in African American women. As there are no data for African women, we tested the ability of the TG/HDL-C ratio to predict insulin resistance in Black women from South Africa, West Africa and the United States. For comparison, the ratio was also tested in White women from South Africa. Participants were 801 women (157 Black South African, 382 African American, 119 West African, 143 White South African, age 36±9y [mean±SD]). Standardized scores were created from log-transformed homeostasis model assessment-insulin resistance values from each population. Participants in the upper third of their population distribution were classified as insulin-resistant. To predict insulin resistance by the TG/HDL-C ratio, area under the receiver operating characteristic (AUC-ROC) curve was used and criteria were: 0.50 for no discrimination and ≥0.70 for acceptable. Seventy-one percent of the Black women were overweight vs 51% of White women ($P<.01$). In overweight White women, AUC-ROC curve for prediction of insulin resistance by TG/HDL-C was 0.76±0.06, but below the 0.70 threshold in each group of overweight Black women (Black South African: 0.64±0.06, African American: 0.66±0.03, and West African: 0.63±0.07). Therefore, TG/HDL-C does not predict insulin resistance in overweight African American women and this investigation extends that finding to overweight Black South African and West African women. Resources to identify effective markers of insulin resistance are needed to improve cardiometabolic health in women of African descent. (*Ethn Dis*. 2011;21(4):490–494)

Key Words: Triglyceride, TG/HDL-C Ratio, Insulin Resistance, Africans, African Americans

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Introduction

The prevalence of type 2 diabetes and cardiovascular disease (CVD) is significantly higher in African American and African women than White women.[1–3] Screening tests are designed to detect risk for disease when intervention could improve outcome. As insulin resistance promotes the development of type 2 diabetes and CVD, identifying a screening test that identifies insulin resistance in women of African descent could be beneficial. Hundreds of research articles have discussed the efficacy of the triglyceride/high density lipoprotein-cholesterol (TG/HDL-C) ratio as a marker of insulin resistance for many population groups.[4–5] But, it is unknown if the TG/HDL-C ratio is able to predict insulin resistance in African women.

Studies in overweight Whites suggest that the TG/HDL-C ratio effectively identifies insulin resistance.[4–5] Yet, the pattern of the dyslipidemia of insulin resistance differs in African Americans and Whites,[6] and therefore the ability of the TG/HDL-C to predict insulin resistance may vary by race. In Whites, the dyslipidemia of insulin resistance follows the classic pattern of elevated TG and low HDL-C. However, in African Americans, West Africans and Black South Africans, normal TG with low HDL-C is the characteristic lipid profile of insulin resistance.[6–9] In addition, there are sex differences in the lipid profile. Women have lower TG and higher HDL-C levels than men[6]. Unless sex-specific differences in the lipid profile are recognized, misleading results may occur. For example, in a cohort of 90 overweight African Americans in which men and women were evaluated together, the TG/HDL-C ratio was found to be of no value in predicting insulin resistance.[10] However, when 2000 African Americans from the Jackson Heart Study were stratified by sex, it became apparent that the TG/HDL-C ratio was able to predict insulin resistance in men but not women.[11] Unanswered by the Jackson Heart Study was whether the TG/HDL-C ratio could predict insulin resistance in African women. Therefore, we tested the ability of TG/HDL-C to predict insulin resistance in Black women from South Africa, West Africa and the United States. For comparison, the ratio

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METHODS

Subjects

Eight hundred one non-diabetic, premenopausal women from four studies[12] were enrolled. Criteria were: age 18–50y, BMI 18.5–55.0 kg/m^2, HDL-C 20–100 mg/dL, TG 20–500 mg/dL, fasting insulin <50 μU/mL, fasting glucose 55–125 mg/dL. The women were not taking any medications that affected either insulin resistance or the lipid profile. Pregnant women and women receiving hormonal contraception were excluded. All women denied a history of HIV infection. Studies were approved by institutional review boards at the National Institute of Diabetes, Digestive and Kidney Disease and each participating university (South Africa: University of Cape Town. United States: Howard University; Ghana: University of Ghana Medical School, Accra, and University of Science and Technology, Kumasi; Nigeria: University of Nigeria Teaching Hospital, Enugu, University of Lagos, Lagos, University College Hospital, Ibadan. Participants gave informed consent.

The White (n=143) and Black South Africans (n=157) were participants in protocols at the University of Cape Town.[12] Black South Africans were from the Xhosa tribe. The African Americans were enrolled in the Triglyceride and Cardiovascular Risk in African American (TARA) cohort at the NIH Clinical Center (n=85) or the Howard University Family Study (HUFS) (n= 297).[12] The West Africans (n=119) were Nigerian from the Ibo or Yoruba tribes or Ghanaian from the Akan or Gaa tribes, and participated in the Africa America Diabetes Mellitus (AADM) study.[12]

Analytic Methods

Laboratory analyses were performed at three sites: University of Cape Town in South Africa (White and Black South Africans), NIH Clinical Center in Bethesda, Maryland (TARA) and Howard University in Washington, DC (HUFS and AADM).

For South Africans, glucose was determined by the glucose oxidase method (YSI 2300 STAT Plus; YSI, Yellow Springs, Ohio). Insulin concentrations were measured by immunochemiluminometric assays using ADVIA Centaur (Bayer Diagnostics, Tarrytown, NY). TG and HDL-C were analyzed with the Roche Modular autoanalyzer.

For African Americans from TARA, glucose was determined by the glucose oxidase method (YSI 2700 Select, Yellow Springs, Ohio). Insulin was measured with double-antibody chemiluminescent sandwich assays (Diagnostic Products, Los Angeles, Calif). TG and HDL-C were analyzed on automated analyzers (Hitachi 917, Boehringer Mannheim, Mannheim, Germany; and LX20, Beckman Coulter, Brea, CA, respectively).

Samples from HUFS and AADM were analyzed at Howard University. Assays for glucose, TG and HDL-C were performed using the Auto-analyzer – COBAS INTEGRA 400 plus (Roche Diagnostics, Indianapolis, Indiana). Insulin was measured on an Elecsys1010 immunoassay analyzer (Roche Diagnostics).

Insulin Resistance

Insulin resistance was determined by homeostasis model assessment-insulin resistance (HOMA-IR). To allow for differences in insulin and glucose assays among the three sites, standardized HOMA-IR values for each group of participants were created from log transformed HOMA-IR values. Participants in the upper third of their population distribution, corresponding to a Z-score of 0.42 or higher, were classified as insulin-resistant. HOMA-IR values corresponding to a Z-score of 0.42 were 2.11 for White and Black South Africans, 2.0 for the African Americans from TARA, and 2.18 for the Blacks from the HUFS and AADM. These analyses were repeated with the participants divided by quartiles of HOMA-IR, and the results did not change. The data presented are based on tertiles of HOMA-IR.

Statistics

Data are presented as geometric means with 95% CI. The Student's t-test was used to determine differences in age and BMI between Black and White women. Then one-way ANOVA with Bonferroni correction was used to examine differences in age and BMI among the three groups of Black women (Black South Africans vs African Americans vs West Africans). For TG, HDL, TG/HDL-C and HOMA-IR, regression was used to generate age- and BMI-adjusted values. An indicator term for racial group was used to examine racial differences between groups. Area under the receiver operating characteristic (AUC-ROC) curve was used to determine the ability of the TG/HDL-C ratio to identify insulin resistance. Values for AUC-ROC curve are presented as mean±SE and categorized as: 0.5 for no discrimination, 0.7–0.8 for acceptable, 0.8–0.9 for excellent, >0.9 for outstanding[13–16] Analyses were performed with STATA v.11 (STATA, College Station, Texas).

RESULTS

All the participants were pre-menopausal, but both the Black and White South Africans were younger than the African Americans and West Africans (Table). Among the Blacks, West Africans were the oldest and South Africans the youngest. BMI was higher in the Black women than the White women. Among the Black women, African Americans had the highest BMI and West Africans the lowest (Table).

Due to differences in age and BMI among groups, lipids and HOMA-IR

Table. Participant Characteristics[a]

Characteristic	White South Africans (WSA) *n*=143	All Blacks *n*=658	*P* value	Black South Africans (BSA) *n*=157	African Americans (AA) *n*=382	West Africans (WA) *n*=119	*P* value[e]
Age (y)[b]	32 (30,33)	35 (34,36)	<.001	26 (25,27)	37 (36,38)	44 (43,44)	1[g], 2[g], 3[g]
BMI (kg/m^2)[b]	27.6 (26.4,28.8)	29.7 (29.2,30.3)	.001	29.1 (27.9,30.3)	30.5 (29.8,31.3)	28.0 (27.0,29.0)	3[g]
Overweight, *n* (%)[c]	79 (55)	469 (71)	<.001	96 (61)	289 (76)	84 (71)	1[f]
TG (mg/dL)[d]	78 (72,84)	71 (69,73)	.02	69 (64,74)	70 (67,73)	79 (73,86)	2[f], 3[g]
HDL-C (mg/dL)[d]	58 (56,61)	51 (50,52)	<.001	53 (51,56)	52 (50,53)	43 (41,46)	2[g], 3[g]
TG/HDL-C[d]	1.34 (1.22,1.47)	1.40 (1.34,1.47)	.48	1.29 (1.17,1.42)	1.34 (1.27,1.42)	1.83 (1.64,2.04)	2[g], 3[g]
HOMA-IR[d]	1.60 (1.44,1.78)	1.55 (1.47,1.63)	.52	1.49 (1.33,1.66)	1.57 (1.47,1.67)	1.57 (1.39,1.78)	

a Data presented as geometric mean (95% CI).
b *P* values were obtained by Student's *t*-test for WSA vs all Blacks. For the 3 groups of Blacks, one-way ANOVA with Bonferroni correction was used.
c Percent overweight (BMI ≥25kg/m^2), *P*-values by chi-square.
d Data adjusted for age and BMI with comparison by logistic regression.
e 1: If *P* value for difference between BSA and AA was significant.
2: If *P* value for difference between BSA and WA was significant.
3: If *P* value for difference b3: If *P* value for difference between AA and WA was significant.
f $P \leq .05$.
g $P \leq .01$.

were adjusted accordingly. As presented in the Table, TG and HDL-C levels were higher in the White South African women than the Black women. Among the Blacks, the West Africans had the highest TG and lowest HDL-C, and highest TG/HDL-C ratio.

The proportion of overweight women in each group is provided in the Table. The AUC-ROC curve for the ability of the TG/HDL-C ratio to predict insulin resistance in overweight women was: 0.76±0.06 for White South Africans and 0.63±0.03 for all Blacks combined (Figure 1A). Presented by ethnic group, the AUC-ROC curve for overweight Blacks was: 0.64±0.06, 0.66±0.03, 0.63±0.07 for Black South Africans, African Americans and West Africans, respectively (Figure 1B).

DISCUSSION

We extend the finding that the TG/HDL-C ratio does not identify overweight insulin-resistant African American women to other Black women, specifically West African women from four tribal groups and South Africans from one tribal group. Despite differences in TG and HDL-C levels among the groups, we found that the ratio was unable to identify insulin resistance in overweight women of African descent. For each group of Black women, the AUC-ROC curve was below 0.70. In contrast, the AUC-ROC curve was 0.76 for White women, which is in accordance with the generally accepted concept that the TG/HDL-C ratio is an effective predictor of insulin resistance in Whites.[4,5,14]

One other study has tested the ability of the TG/HDL-C ratio to predict insulin resistance in Africans, specifically East Africans from Seychelles.[17] In accordance with our methods, insulin resistance was defined by the upper third of HOMA-IR in their population distribution. They found that the AUC-ROC curve for the ability of TG/HDL-C ratio to predict insulin resistance was 0.65. Therefore the authors reported that the ratio was able to predict insulin resistance in East Africans. Yet, with our *a priori* criterion of AUC-ROC ≥0.70 as "acceptable,"[11,13–16] an AUC-ROC of 0.65 for the TG/HDL-C ratio in East Africans would have led to the conclusion that the ratio was not a satisfactory predictor of insulin resistance. In addition, East African men and women were combined into a single group. As described earlier, results from the Jackson Heart Study cohort have shown that the effectiveness of the ratio to predict insulin resistance is sex-specific.[11] If East Africans are similar to African Americans, then separate analyses of men and women may reveal that the TG/HDL-C ratio predicts insulin resistance in East African men, but not women. However, this remains to be confirmed.

We recognize that there is some controversy about the usefulness of the TG/HDL-C ratio as a predictor of insulin resistance, even in Whites.[18] We report that the AUC-ROC curve was 0.76 for the White women. Therefore, the TG/HDL-C ratio would be considered only "acceptable" and not an "excellent" predictor of insulin resistance. In addition, from a prospective analysis of the Framingham Offspring study, a cohort of White individuals, the ratio was found to be an imperfect surrogate of both insulin resistance and future cardiac events.[18] One limitation of our study is that we

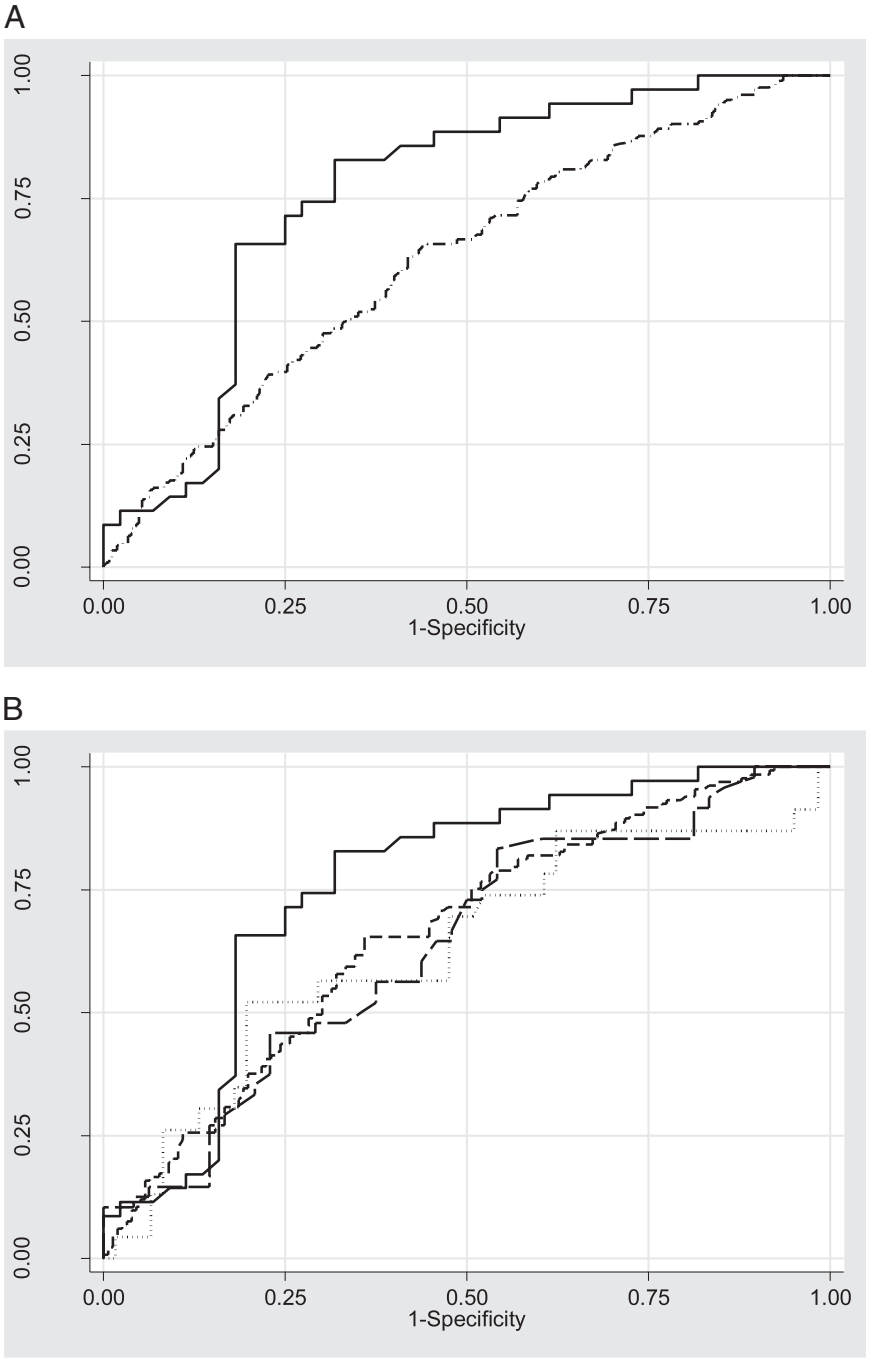

Figure 1A, 1B. The AUC-ROC curve to identify insulin resistance by the TG/HDL-C ratio

A. White South Africans vs all Blacks combined
– White South African: AUC-ROC curve is 0.76±0.06
⋯ All Blacks (Combined): AUC-ROC curve is 0.63±0.03
B. White South Africans vs each group of Black women
– White South African: AUC-ROC curve is 0.76±0.06
—— Black South African: AUC-ROC curve is 0.64±0.06
--- African American: AUC-ROC curve is 0.66±0.03
⋯ West African: AUC-ROC curve is 0.63±0.07

For overweight Black women in Africa and the United States, current evidence does not support the use of the TG/HDL-C ratio as a screening tool to identify insulin resistance.

do not have prospective data relating the TG/HDL-C ratio to outcomes such as type 2 diabetes and CVD in White or Black women.

Overall, we conclude that research demonstrating the lack of efficacy of the TG/HDL-C ratio as a predictor of insulin resistance in overweight African American women provided an important signal that the ratio may not work in Black African women.[10–11,14] For overweight Black women in Africa and the United States, current evidence does not support the use of the TG/HDL-C ratio as a screening tool to identify insulin resistance.

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