A Comparison of Cardiovascular Disease Risk Factor Biomarkers in African Americans and Yoruba Nigerians

M. Deeg, MD, PhD; O. Baiyewu, MD; S. Gao, PhD; A. Ogunniyi, MBChB; J. Shen, MS; O. Gureje, MBBS, MSc, PhD; S. Taylor, MA; J. Murrell, PhD; F. Unverzagt, PhD; V. Smith-Gamble, MD; R. Evans, MD; J. Dickens, MD; H. Hendrie, MBChB, DSc; K. Hall, PhD

Objective: Classical risk factors for coronary artery disease are changing in the developing world while rates of cardiovascular disease are increasing in these populations. Newer risk factors have been identified for cardiovascular disease, but these have been rarely examined in elderly populations and not those of developing countries.

Methods: This study was a cross-sectional comparison from a longitudinal, observational, epidemiologic study in which participants are interviewed at three-year intervals. The sample included 1510 African Americans from Indianapolis, Indiana, and 1254 Yoruba from Ibadan, Nigeria. We compared anthropomorphic measurements; biomarkers of endothelial dysfunction (plasminogen activator inhibitor type 1 [PAI-1] and E-selectin), inflammation (C-reactive protein), and lipid oxidation (8-isoprostane); and levels of lipids, homocysteine, folate, and vitamin B12.

Results: Cholesterol, triglycerides, and low-density lipoprotein cholesterol levels were higher in African Americans. For markers of endothelial dysfunction, E-selectin and homocysteine differed between men, and PAI-1 was higher in the Yoruba. C-reactive protein differed only in women, but 8-isoprostane was higher in the Yoruba.

Conclusion: Higher lipid levels in African Americans are consistent with their Western diet and lifestyle. Oxidative stress appears to be higher in the Yoruba than in African Americans, which may be secondary to dietary differences. Whether these differences in classical and emerging risk factors account for the different rates of cardiovascular disease, dementia, or other morbidities in these two populations remains to be determined. (*Ethn Dis*. 2008;18:427–433)

Key Words: Cardiovascular Risk, Biomarkers, African Americans, Nigerians

From the Departments of Medicine (MD, SG, JS, ST), Biochemistry and Molecular Biology (MD), Pathology (JM), Psychiatry (FU, VSG, JD, HH, KH), Neurology (RE), Regenstrief Institute (HH), Indiana University School of Medicine; Department of Veterans Affairs, Roudebush VAMC (MD, VSG), Indianapolis, Indiana; Department of Neurology (AO), Department of Psychiatry (OB, OG), University of Ibadan, Ibadan, Nigeria; Eli Lilly and Company (MD), Indianapolis, Indiana.

Address correspondence and reprint requests to: Kathleen S. Hall, PhD; Department of Psychiatry; Indiana University School of Medicine; 1111 West Tenth St, PB A319; Indianapolis, IN 46202; 317-274-1249; khall@iupui.edu

Introduction

Various studies have documented that the classical risk factors for coronary artery disease, including type 2 diabetes, hypertension, cholesterol, and obesity, are increasing in the developing world.[1–3] These changes in risk factors are also reflected in the increasing rates of cardiovascular disease in these same populations.[1,4,5] Recently, newer, emerging risk factors for cardiovascular disease have been reported. Epidemiologic studies measuring these newer risk factors have been conducted primarily in middle-aged populations in developed societies. In contrast to the measurement of classical cardiovascular risk factors, few studies have examined these risk factors in elderly African Americans and none in the elderly populations of developing countries. These newer biomarkers can provide additional information on the risk for cardiovascular disease. In addition, more evidence shows that cardiovascular risk factors also increase the risk for cognitive decline, dementia and Alzheimer disease.[6–8]

The Indianapolis-Ibadan Dementia Project is a longitudinal comparative study of dementia and Alzheimer disease in two elderly communities, African Americans living in Indianapolis, Indiana, and Yoruba living in Ibadan, Nigeria. This study provides a unique opportunity to compare these biomarkers in these two populations. In 2001, biomarker measurements were added to this study; these include lipid measurements; markers of endothelial dysfunction (plasminogen activator inhibitor type 1 [PAI-1] and E-selectin), inflammation (C-reactive protein), and lipid oxidation (8-isoprostane); and levels of homocysteine, folate, and vitamin B12. In this article, we compare biomarkers between the two populations.

…more evidence shows that cardiovascular risk factors also increase the risk for cognitive decline, dementia and Alzheimer disease.[6–8]

Methods

Since 1992, we have been conducting a comparative, community-based epidemiologic study of prevalence, incidence, and risk factors for Alzheimer disease in populations of African origin: elderly African Americans in Indianapolis, Indiana, and Yoruba in Ibadan, Nigeria. In 2001, we conducted a two-stage study in which survivors of the 1992 cohort were interviewed, and new participants were enrolled. A detailed description of the construction of the original cohorts has been previously reported.[9] The enrollment of the new

study participants in Indianapolis in 2001 used a list of African American Medicare participants, age >70 years, living in Marion County. After a notification letter was sent, potential participants were contacted by telephone or home visit. Of 4433 persons who were contacted, 1893 (43%) were enrolled, 2020 (46%) refused, 369 (8%) were too ill, 100 (2%) were dead, 54 (1%) were in a nursing home, and 14 (.3%) were not African American. In Ibadan, after we obtained approval from community leaders, the catchment area for the study was expanded to contiguous, politically defined geographic districts, a census was conducted, and 1940 participants were enrolled. The study is well regarded in the community, and no one refused. A blood sample was drawn from participants who consented. Before each interview and blood draw, informed consent was obtained from participants and their informants. The institutional review boards at Indiana University School of Medicine and University of Ibadan approved the study.

During the interview, study participants and a family member were asked whether the participant had a medical history of diabetes. Alcohol use was obtained by self-report or report by a family member to the question "Was there ever a period when you (he or she) drank alcoholic beverages regularly?" Smoking status was obtained by self-report or report by a family member to the question "Has there ever been a period when you (he or she) smoked cigarettes, cigars, a pipe, chewing tobacco, or snuff nearly every day?" Body mass index (BMI) was derived from height and weight measurements.

Omron digital units (Omron Healthcare, Inc, Bannockburn, Ill) were used to measure blood pressure in both study sites. Blood pressure was taken three times, and the average of the three readings was used.

Blood samples were drawn in 10-mL EDTA Vacutainer tubes. The specimens were transported on ice from the field to the laboratory at Ibadan University College Hospital. In the laboratory, erythrocytes, buffy coat, and plasma were separated. After labeling the plasma and buffy coat tubes with a unique bar code for each participant, the samples were stored in a -70°C freezer. Samples were shipped to Indiana University in approved blood shipping containers with dry ice and arrived usually within three days. Samples from Indianapolis were directly processed at Indiana University. Biochemical analyses were carried out on the plasma.

Cholesterol, triglyceride, and high-density lipoprotein (HDL) cholesterol levels were determined by using commercial kits from Roche Diagnostics (Indianapolis, Ind). Low-density lipoprotein (LDL) cholesterol levels were calculated by using the Friedewald equation. PAI-1, E-selectin, 8-isoprostane, homocysteine, folate, vitamin B12, and C-reactive protein were determined by using commercial kits from BioRad, Hercules, Calif; Cayman, Ann Arbor, Mich; and Diasorin, Stillwater, Minn.

Statistical Analysis

For categorical demographic variables, frequency tables were produced and compared between sites with χ^2 tests. For continuous demographic measures, the means and standard deviations were generated and compared between sites or fasting status by using two sample t tests. For each individual biomarker, the means, stratified by sex, were compared between sites after adjusting for age, BMI, alcohol use, and smoking. Partial correlation coefficients were calculated stratified by sex to determine the relationship of PAI-1, E-selectin, C-reactive protein, and 8-isoprostane with other biomarkers, adjusting for age, BMI, alcohol use, and smoking.

RESULTS

Serum samples were available from 1510 participants from Indianapolis, of which 503 (33.3%) were fasting, and 1254 from Ibadan, all of which were fasting. No significant differences in demographic characteristics were seen between the fasting and nonfasting groups in Indianapolis, with the exception that those who had a fasting sample had significantly more education. Looking at the biomarkers in the Indianapolis group, only the triglyceride, LDL cholesterol, and PAI-1 were statistically different between the fasting and nonfasting cohort. Comparing the fasting samples from the two cohorts, the sex distribution was similar between populations. Very few of the Ibadan participants had formal education, while most of the African Americans had some schooling. The Indianapolis population had a higher BMI and prevalence of diabetes and current or former smokers. The participants were younger and the blood pressures were higher in Ibadan than in Indianapolis. To ensure comparable results, all subsequent biomarker comparisons were conducted with fasting samples only.

The results of all biomarker comparisons are summarized in Table 2. After adjusting for covariates, cholesterol was higher in both men and women in Indianapolis. Additionally, HDL cholesterol was higher in Indianapolis women, and LDL cholesterol and triglycerides were higher in Indianapolis men. This is consistent with the higher BMI and prevalence of diabetes in the Indianapolis cohort. Overall, the lipid values were normal for triglycerides (<150 mg/dL) and HDL for an elderly population (>45 mg/dL) but slightly elevated for LDL (>100 mg/dL) for persons at high risk for cardiovascular disease events as recommended by the National Cholesterol Education Program.

The E-selectin level was significantly higher in men in Indianapolis, but not different for women. PAI-1 was, unexpectedly, twice as high or more among both men and women from Ibadan. Homocysteine, which is detrimental to

Table 1. Comparison of demographic characteristics and biomarkers among elderly African Americans in Indianapolis, Indiana, and Yoruba people in Ibadan, Nigeria

	Indianapolis			Ibadan	
	Fasting (*n*=503)	Nonfasting (*n*=1007)	*P* value*	Fasting (*n*=1254)	*P* value†
Mean years of age (SD)	77.09 (5.53)	77.49 (5.48)	.182	76.07(5.37)	<.001
Mean BMI (SD) (kg/m^2)	30.43 (6.58)	30.52 (6.95)	.818	21.78 (4.62)	<.001
Mean SBP (SD) (mm Hg)	146.58 (22.23)	144.74 (21.78)	.141	152.09 (30.95)	<.001
Mean DBP (SD) (mm Hg)	79.16 (12.00)	78.48 (11.77)	.318	85.08 (15.34)	<.001
Mean years of education (SD)	11.22 (2.68)	10.92 (2.81)	.045	NA	NA
No. attended school (%)	NA	NA	NA	186 (14.84)	NA
No. women (%)	344 (68.39)	666 (66.14)	.381	842 (67.15)	.615
No. use alcohol (%)	178 (38.95)	362 (40.45)	.595	504 (40.22)	.634
No. smokers (%)	278 (55.60)	555 (55.33)	.922	477 (38.07)	<.001
No. diabetes (%)	133 (26.65)	302 (30.11)	.164	23 (1.84)	<.001
Mean cholesterol (SD) (mg/dL)	188.35 (38.63)	185.95 (40.83)	.272	174.661 (40.88)	<.001
Mean triglycerides (SD) (mg/dL)	104.71 (46.99)	117.74 (59.09)	<.000	89.47 (36.44)	<.001
Mean HDL cholesterol (SD) (mg/dL)	51.48 (15.39)	51.18 (15.65)	.724	50.02 (13.79)	.064
Mean LDL cholesterol (SD) (mg/dL)	115.93 (34.50)	111.22 (34.41)	.012	106.70 (33.30)	<.001
Mean 8-isoprostane (SD) (pg/mL)	586.25 (1282.8)	569.52 (1138.2)	.821	1270.30 (1585.50)	<.001
Mean CRP (SD) (mg/L)	14.81 (26.56)	13.83 (27.44)	.520	8.10 (18.94)	<.001
Mean PAI-1 (SD) (ng/mL)	21.93 (27.50)	26.27 (28.64)	.006	39.51 (31.94)	<.001
Mean E-selectin (SD) (μg/L)	44.49 (23.61)	43.98 (24.32)	.699	37.87 (34.07)	<.001
Mean homocysteine (SD) (μmol/L)	17.37 (7.35)	16.91 (7.21)	.241	17.42 (6.85)	.900
Mean folate (SD) (ng/mL)	9.81 (8.38)	10.96 (14.55)	.053	5.87 (6.72)	<.001
Mean vitamin B12 (SD) (pg/mL)	612.63 (352.74)	621.77 (347.73)	.633	785.49 (310.19)	<.001

SD, standard deviation; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; NA, not applicable; HDL, high-density lipoprotein; LDL, low-density lipoprotein; CRP, C-reactive protein; PAI-1, plasminogen activator inhibitor type 1.

* Comparing fasting and non-fasting samples.

† Comparing fasting samples between Indianapolis and Ibadan cohorts.

endothelial function, was also higher in Ibadan men. Folate and vitamin B12 could affect homocysteine levels. Folate levels were consistently lower and B12 was higher in the Ibadan cohort.

A nonspecific marker of inflammation, C-reactive protein, was not statistically different for men but was higher in women in Indianapolis than in women in Ibadan. We measured lipid oxidation and oxidative stress using 8-isoprostane as a marker. In the Ibadan cohort, 8-isoprostane was nearly twice as high as in men and women from Indianapolis.

To further examine the relationship between these biomarkers, we calculated the partial correlation coefficients for PAI-1, E-selectin, C-reactive protein, and 8-isoprostane with the other biomarkers for each cohort stratified by sex (Table 3). We observed no consistent correlation between biomarkers between sexes and cohorts.

In women from Ibadan, PAI-1 correlated with 8-isoprostane; E-selectin negatively correlated with 8-isoprostane and homocysteine; C-reactive protein negatively correlated with cholesterol, LDL cholesterol, and HDL cholesterol; and, 8-isoprostane correlated with triglycerides and negatively with folate. In the male Ibadan cohort, E-selectin negatively correlated with 8-isoprostane; C-reactive protein negatively correlated with HDL cholesterol and positively with folate; 8-isoprostane correlated negatively with LDL cholesterol. In the Indianapolis cohorts, only PAI-1 was positively correlated with triglycerides in men but not women.

DISCUSSION

Numerous studies have demonstrated that as developing countries adopt more of a Western lifestyle, risk factors for cardiovascular disease and type 2 diabetes worsen. Not unexpectedly, the Indianapolis cohort had a higher BMI and higher prevalence of diabetes and smoking. In contrast, blood pressure was higher in the Ibadan cohort.

Lipids

Consistent with differences in obesity and diabetes between the cohorts is

Not unexpectedly, the Indianapolis cohort had a higher BMI and higher prevalence of diabetes and smoking. In contrast, blood pressure was higher in the Ibadan cohort.

Table 2. Adjusted means and SEs for biomarkers among elderly African Americans in Indianapolis, Indiana, and Yoruba people in Ibadan, Nigeria

Biomarker	Indianapolis Mean (SE)*	Ibadan Mean (SE)*	*P* value
	Women		
Cholesterol (mg/dL)	194.72 (2.90)	182.88 (1.75)	.001
Triglycerides (mg/dL)	99.77 (2.82)	94.72 (1.70)	.147
HDL cholesterol (mg/dL)	56.49 (1.01)	51.50 (.61)	<.001
LDL cholesterol (mg/dL)	118.27 (2.45)	112.43 (1.48)	.055
8-isoprostane (pg/mL)	566.35 (118.74)	1165.3 (66.34)	<.001
CRP (mg/L)	12.54 (1.50)	7.28 (.89)	.005
PAI-1 (ng/mL)	20.45 (2.28)	40.25 (1.36)	<.001
E-selectin (μg/L)	40.64 (2.65)	39.46 (1.60)	.720
Homocysteine (μmol/L)	16.38 (.45)	16.74 (.27)	.516
Folate (ng/mL)	10.02 (.55)	5.87 (.33)	<.001
Vitamin B12 (pg/mL)	649.67 (24.10)	794.27 (14.53)	<.001
	Men		
Cholesterol (mg/dL)	178.83 (3.85)	162.30 (2.14)	<.001
Triglycerides (mg/dL)	96.72 (4.25)	86.15 (2.36)	.038
HDL cholesterol (mg/dL)	49.75 (1.43)	46.39 (.80)	.050
LDL cholesterol (mg/dL)	109.73 (3.18)	98.67 (1.77)	.004
8-isoprostane (pg/mL)	784.75 (189.16)	1271.7 (100.32)	.029
CRP (mg/L)	9.88 (2.20)	9.50 (1.19)	.882
PAI-1 (ng/mL)	15.48 (3.45)	41.93 (1.83)	<.001
E-selectin (μg/L)	43.44 (2.07)	37.96 (1.15)	.028
Homocysteine (μmol/L)	17.93 (.81)	19.84 (.44)	.047
Folate (ng/mL)	10.32 (.67)	5.28 (.37)	<.001
Vitamin B12 (pg/ml)	597.21 (31.06)	735.92 (17.28)	<.001

SE, standard error; HDL, high-density lipoprotein; LDL, low-density lipoprotein; CRP, C-reactive protein; PAI-1, plasminogen activator inhibitor type 1.

* Means were compared by sites after adjusting for age, BMI, alcohol drinking, and smoking and stratified by sex.

the observation that the Indianapolis sample had higher cholesterol levels in both men and women, and higher triglyceride and LDL cholesterol levels in men, even though 25.7% of the fasting Indianapolis cohort—and none of the Ibadan cohort—were taking statins. Statin use was associated with lower cholesterol, LDL cholesterol, and HDL cholesterol levels compared with those who did not use statins in the Indianapolis cohort, but no difference was seen in 8-isoprostane, E selectin, C-reactive protein, and triglycerides between statin users and those who did not use statins.[10] Additionally, in the fasting Indianapolis cohort, 10% of participants were taking antidiabetes medications, and 74.3% were taking antihypertensive medications. Medication usage in Ibadan is, in most cases, sporadic because of chronic shortages.

The higher lipid levels in African Americans are consistent with the differences in rates of cardiovascular disease in developed vs developing countries. These differences may reflect differences in the constituents of the diets in these two very different environments. Our preliminary study using standardized 24-hour recall methods [11,12] demonstrated that the diet in Yoruba (n=20) is very low in fat (78% carbohydrates, 10% fat, and 12% protein) compared with the African American (n=50) diet (52% carbohydrate, 34% fat, and 15% protein). The diet of the Yoruba consists primarily of tubers, vegetables, and fish.[13] Diet can have a substantial effect on the biomarker parameters we measured. Lipid levels and their interaction with apolipoprotein E can affect risk for Alzheimer disease in these two populations.[14,15] Although both populations demonstrate an interaction between cholesterol and *ApoE* genotype, the rates of dementia are higher in the Indianapolis cohort.

Endothelial Dysfunction

Given the higher prevalence of diabetes, hypertension, and dyslipidemia in the Indianapolis cohort, we expected to find elevated biomarkers for endothelial dysfunction in the Indianapolis cohort compared with the Ibadan cohort. Although the E-selectin and PAI-1 levels were in the normal range for a US population (28–296 μg/mL E-selectin, and 19–42 mg/mL PAI-1), we found no difference in E-selectin between the two female cohorts and nearly twice the level of PAI-1 in the Ibadan cohort. For the Ibadan group, two reasons may explain the higher PAI-1 levels: homocysteine and oxidative stress. Both cohorts had a high overall homocysteine level (normal US population 2.2–13.2 μmol/L). These higher homocysteine levels are unlikely due to low folate or vitamin B12 levels because both cohorts had normal serum folate and vitamin B12 levels for a US population (3–20 ng/mL folate and 200–900 pg/mL B12). These higher homocysteine levels could be due to polymorphisms in folate metabolism enzyme such as MTHFR. Regardless, homocysteine levels were higher in the men from Ibadan. In vitro, homocysteine levels increase PAI-1 expression in endothelial cells.[16] However, whether homocysteine regulates PAI-1 expression in vivo is unclear; some studies have and others have not observed a correlation between plasma homocysteine and PAI-1 levels.[17–20] Alternatively, elevated PAI-1 may be increased because of the higher levels of oxidative stress in the Ibadan group. PAI-1 expression is regulated by oxidative stress.[21,22]

Oxidative Stress

Why oxidative stress is higher in the Ibadan population is unclear. Numer-

Table 3. Partial correlation coefficients for PAI-1, E-selectin, C-reactive protein, and 8-isoprostane with other biomarkers among elderly African Americans in Indianapolis, Indiana, and Yoruba people in Ibadan, Nigeria

	Indianapolis				Ibadan			
	PAI-1	E-selectin	C-reactive protein	8-isoprostane	PAI-1	E-selectin	C-reactive protein	8-isoprostane
				Women				
8-isoprostane	−.01	.01	.02	1.00	.14*	−.08*	−.05	1.00
Cholesterol	−.03	.05	.05	−.02	−.03	.01	−.19*	−.05
Triglycerides	.11	.12	.09	.14	.02	.00	−.01	.08*
LDL cholesterol	−.10	.07	.01	−.08	−.02	.02	−.14*	−.08
HDL cholesterol	.08	−.11	.04	.05	−.06	.00	−.21*	−.01
Homocysteine	.07	.05	−.06	−.02	.03	−.08*	−.03	.06
Folate	.11	.06	−.04	−.01	−.02	.03	.00	−.08*
Vitamin B12	.03	.14	.02	.04	.05	.06	.06	.00
				Men				
8-isoprostane	.00	.07	−.09	1.00	.10	−.11*	−.02	1.00
Cholesterol	.06	−.01	−.18	−.19	−.04	.07	−.138	−.09
Triglycerides	.29*	.20	−.13	−.10	.03	.02	−.02	−.02
LDL cholesterol	−.02	−.04	−.17	−.14	−.01	.09	−.08	−.11*
HDL cholesterol	.00	−.08	.05	−.09	−.09	−.02	−.16*	.02
Homocysteine	−.06	.08	−.14	−.02	−.08	.04	−.01	.04
Folate	.03	−.08	.03	−.03	−.05	−.02	.12*	.07
Vitamin B12	−.04	−.09	−.03	.00	.02	.09	−.01	.10

PAI-1, plasminogen activator inhibitor type 1; LDL, low-density lipoprotein; HDL, high-density lipoprotein.
Note: Partial correlation was determined by adjusting for age, BMI, alcohol drinking, and smoking.
* P≤.05.

ous factors influence markers of lipid oxidation, including inflammation, obesity, and diet. Although numerous studies have demonstrated correlations between inflammation or obesity[22,23] with biomarkers for lipid oxidation, this probably does not explain the higher levels of 8-isoprostane in the Ibadan group, which had a considerably lower BMI than the Indianapolis cohort.

Diet may also contribute to the level of oxidative stress by amount of antioxidants or the type of food consumed. One possibility is that levels of antioxidants in the diet are lower. One study found that Ethiopians had lower levels of antioxidants than did a population in Norway,[24] which suggests that this may be one dietary contribution to the higher levels of lipid oxidation. We cannot eliminate this possibility since we did not measure levels of antioxidants such as vitamins C and E or uric acid. Alternatively, the Ibadan diet may contain more oxidized lipids or lipids that can be oxidized.

Previous studies have demonstrated that 8-isoprostane levels are influenced by diet. Increased consumption of fruits and vegetables are associated with decreases in 8-isoprostane,[25] and consumption of potatoes[26] or diets rich in n-6 fatty acids[27] are associated with increases in 8-isoprostane. Constituents in potatoes and other tubers, eg, glycoalkaloids or terpinoids, may increase oxidative stress,[28] or the methods of preparation may introduce oxidation products into diet. Since yam tubers (*Dioscorea Rotunda Poir*) are a major dietary constituent in Ibadan, this may account for the increase in oxidative markers. The increase in oxidative stress may also explain the higher levels of PAI-1.

Inflammation

C-reactive protein levels did not differ between the men in the two cohorts but they did in the women. This was unexpected given the prevalence of obesity, diabetes, and cardiovascular disease in the Indianapolis cohort. As seen in other studies, African American women had the highest C-reactive protein levels. Nevertheless, the levels were very high as a C-reactive protein level >3 mg/dL is considered an increased risk factor for cardiovascular events in middle-aged populations. However, the clinical significance of this finding is unclear because unlike in younger cohorts, C-reactive protein may not be predictive of cardiovascular events in the elderly.[29]

Limitations

A number of limitations may influence our results and interpretation of the data. As pointed out, many of the biomarkers tested are influenced by diet, and we do not have detailed individual dietary histories on all of the study participants. Pharmacologic treatment of the various co-morbidities would also influence these biomarkers, and we do not have sufficient information on medication use in Ibadan. The net effect of medication use in African Americans would, if anything, lessen the reported differences in biomarkers, as in the case with the statins. Diabetes is based on self-report or family member report and may be an underestimation

in Ibadan, where 86% of the cohort has no formal education at all. Alcohol use is based on self-report or report by a family member; this information is limited as it does not provide information about quantity or pattern of alcohol use. The Yoruba in this cohort are primarily Muslim, and they drink alcohol in less quantity and frequency than do non-Muslim Nigerians. The African Americans are predominantly conservative Christians, and alcohol use may be underreported because of social pressures. The effect of this variable in lipids and homocysteine is the same in the two populations. Finally, the clinical significance or predictive value of the biomarkers employed, although validated in younger populations, may be different in the elderly, such as those studied here.

Conclusions

Biomeasures associated with cardiovascular disease risk differ between these two cohorts. As anticipated, lipid levels were lower in the Yoruba than in African Americans, which may in part be attributed to differences in diet. Oxidative stress appears to be higher in the Yoruba than in African Americans, which may also be related to dietary factors. The effect of differences in biomeasures for cardiovascular risk on the rates of cardiovascular disease, dementia, or other morbidities between the two populations remains to be determined.

ACKNOWLEDGMENTS

This study was supported by the National Institute on Aging grant RO1AGO9956-14, The Indianapolis-Ibadan Dementia Project. We thank the elders of Idikan, Ibadan, and Indianapolis, Indiana, for their continued participation.

REFERENCES

1. Gaziano TA. Cardiovascular disease in the developing world and its cost-effective management. *Circulation*. 2005;112(23):3547–3553.
2. Gu D, Reynolds K, Wu X, et al. Prevalence of the metabolic syndrome and overweight among adults in China. *Lancet*. 2005; 365(9468):1398–1405.
3. Alberts M, Urdal P, Steyn K, et al. Prevalence of cardiovascular diseases and associated risk factors in a rural black population of South Africa. *Eur J Cardiovasc Prev Rehabil*. 2005; 12(4):347–354.
4. Sekikawa A, Horiuchi BY, Edmundowicz D, et al. A "natural experiment" in cardiovascular epidemiology in the early 21st century. *Heart*. 2003;89(3):255–257.
5. Steyn K, Sliwa K, Hawken S, et al. Risk factors associated with myocardial infarction in Africa: the INTERHEART Africa study. *Circulation*. 2005;112(23):3554–3561.
6. Reitz C, Tang MX, Luchsinger J, Mayeux R. Relation of plasma lipids to Alzheimer disease and vascular dementia. *Arch Neurol*. 2004; 61(5):705–714.
7. Luchsinger JA, Reitz C, Honig LS, Tang MX, Shea S, Mayeux R. Aggregation of vascular risk factors and risk of incident Alzheimer disease. *Neurology*. 2005;65(4):545–551.
8. Kivipelto M, Ngandu T, Fratiglioni L, et al. Obesity and vascular risk factors at midlife and the risk of dementia and Alzheimer disease. *Arch Neurol*. 2005;62(10):1556–1560.
9. Hendrie HC, Osuntokun BO, Hall KS, et al. Prevalence of Alzheimer's disease and dementia in two communities: Nigerian Africans and African Americans. *Am J Psychiatry*. 1995; 152(10):1485–1492.
10. Szwast S, Hendrie HC, Lane KA, et al. Statin use reduces cognitive decline in elderly African Americans. Mechanism of action is unclear. *Neurology*. 2007;69(19):1873–1880.
11. NDS Software: Created with Nutrition Data System for Research (NDS-R), Database Version 4.02 30 1999 Regents of the University of Minnesota.
12. Olusanya EO. *Manual on Food Consumption Surveys in Developing Countries*. Ibadan (Nigeria): Ibadan University Press; 1977.
13. Hendrie HC, Murrell J, Gao S, Unverzagt FW, Ogunniyi A, Hall KS. International studies in dementia with particular emphasis on populations of African origin. *Alzheimer Dis Assoc Disord*. 2006;20(3 Suppl 2): S42–6.
14. Hall KS, Murrell J, Ogunniyi A, et al. Cholesterol, APOE genotype and Alzheimer's disease: an epidemiological study of Nigerian Yoruba. *Neurology*. 2006;66:223–227.
15. Evans RM, Emsley CL, Gao S, et al. Serum cholesterol, APOE genotype and the risk of Alzheimer disease in a population-based study of African Americans. *Neurology*. 2000;54: 240–242.
16. Midorikawa S, Sanada H, Hashimoto S, Watanabe T. Enhancement by homocysteine of plasminogen activator inhibitor-1 gene expression and secretion from vascular endothelial and smooth muscle cells. *Biochem Biophys Res Commun*. 2000;272(1):182–185.
17. Balasa VV, Gruppo RA, Glueck CJ, et al. The relationship of mutations in the MTHFR, prothrombin, and PAI-1 genes to plasma levels of homocysteine, prothrombin, and PAI-1 in children and adults. *Thromb Haemost*. 1999; 81(5):739–744.
18. Mezzano D, Munoz X, Martinez C, et al. Vegetarians and cardiovascular risk factors: hemostasis, inflammatory markers and plasma homocysteine. *Thromb Haemost*. 1999;81(6): 913–917.
19. de Valk-de Roo GW, Stehouwer CD, Lambert J, et al. Plasma homocysteine is weakly correlated with plasma endothelin and von Willebrand factor but not with endothelium-dependent vasodilatation in healthy postmenopausal women. *Clin Chem*. 1999;45(8 Pt 1): 1200–1205.
20. Schreiner PJ, Wu KK, Malinow MR, et al. Hyperhomocysteinemia and hemostatic factors: the Atherosclerosis Risk in Communities study. *Ann Epidemiol*. 2002;12(4):228–236.
21. Vulin AL, Stanley FM. Oxidative stress activates the plasminogen activator inhibitor type 1 (PAI-1) promoter through an AP-1 response element and cooperates with insulin for additive effects on PAI-1 transcription. *J Biol Chem*. 2004;278(24):25172–25178.
22. Keaney JF Jr, Larson MG, Vasan RS, et al. Obesity and systemic oxidative stress: clinical correlates of oxidative stress in the Framingham Study. *Arterioscler Thromb Vasc Biol*. 2003;23(3):434–439.
23. Urakawa H, Katsuki A, Sumida Y, et al. Oxidative stress is associated with adiposity and insulin resistance in men. *J Clin Endocrinol Metab*. 2003;88(10):4673–4676.
24. Madebo T, Lindtjorn B, Aukrust P, Berge RK. Circulating antioxidants and lipid peroxidation products in untreated tuberculosis patients in Ethiopia. *Am J Nutr*. 2003;78(1): 117–122.
25. Thompson HJ, Heimendinger J, Sedlacek S, et al. 8-Isoprostane F2alpha excretion is reduced in women by increased vegetable and fruit intake. *Am J Nutr*. 2005;82(4):768–776.
26. Lasheras C, Gonzalez S, Huerta JM, et al. Food habits are associated with lipid peroxidation in an elderly population. *J Am Diet Assoc*. 2003;103(11):1480–1487.
27. Turpeinen AM, Basu S, Mutanen M. A high linoleic acid diet increases oxidative stress in vivo and affects nitric oxide metabolism in humans. *Prostaglandins Leukot Essent Fatty Acids*. 1998;59(3):229–233.
28. Rajendran S, Parasakthy K, Deepalakshmi PD, Devaraj SN. Oxidative stress in rat liver and lung induced by furanoterpenoids isolated from *Fusarium solani* infected sweet potatoes. *Indiana J Exp Biol*. 1996;34:57–60.

29. Sattar N, Murray HM, McConnachie A, et al. C-reactive protein and prediction of coronary heart disease and global vascular events in the Prospective Study of Pravastatin in the Elderly at Risk (PROSPER). *Circ.* 2007;115(8):981–989.

AUTHOR CONTRIBUTIONS

Design concept of study: Baiyewu, Gao, Ogunniyi, Gureje, Unverzagt, Smith-Gamble, Evans, Dickens, Hendrie, Hall

Acquisition of data: Baiyewu, Ogunniyi, Gureje, Taylor, Murrell, Unverzagt, Smith-Gamble, Evans, Dickens, Hendrie, Hall

Data analysis and interpretation: Deeg, Baiyewu, Gao, Ogunniyi, Shen, Gureje, Taylor, Unverzagt, Smith-Gamble, Evans, Hendrie, Hall

Manuscript draft: Deeg, Baiyewu, Gao, Ogunniyi, Shen, Gureje, Murrell, Evans, Hendrie, Hall

Statistical expertise: Gao, Shen, Evans

Acquisition of funding: Unverzagt, Evans, Hall

Administrative, technical, or material assistance: Deeg, Baiyewu, Ogunniyi, Gureje, Taylor, Murrell, Smith-Gamble, Evans, Hendrie, Hall

Supervision: Deeg, Baiyewu, Ogunniyi, Gureje, Smith-Gamble, Evans, Dickens, Hendrie