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Race differences in the relation of vitamins A, C, E and β-carotene to metabolic and inflammatory biomarkers

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Abstract

Using archival data, we conducted a secondary analysis to examine race-differences in the relation of serum vitamins A, C, E and β-carotene to insulin resistance (IR), fasting insulin and glucose, high sensitivity C-reactive protein (hsCRP), and leukocyte count in 176 non-smoking, healthy, white and African American (AA) adults aged 18-65 years (48% women, 33% AA). We hypothesized that micronutrient concentrations would be associated with early risk markers of cardiometabolic diseases in a race-dependent manner. Fasting blood samples were analyzed for micronutrients, insulin, glucose, hsCRP, and leukocyte count. Insulin resistance was estimated using the homeostatic model assessment (HOMA). After adjusting for age, body mass index, gender, educational level, use of vitamin supplements, alcohol intake, leisure time physical activity, menopausal status, and total cholesterol, we observed that β-carotene was significantly associated with insulin resistance and fasting insulin in a race-dependent manner. Among AA, lower β-carotene levels were associated with higher estimates of insulin resistance and fasting insulin; whereas, these same associations were not significant for whites. Race also significantly moderated the relation of vitamin C to leukocyte count, with lower vitamin C being associated with higher leukocyte count only in AA but not whites. For all subjects, lower β-carotene was associated with higher hsCRP. In AA, but not whites, lower levels of β-carotene and vitamin C were significantly associated with early risk markers implicated in cardiometabolic conditions and cancer. Whether or not lower levels of micronutrients contribute uniquely to racial health disparities is a worthwhile aim for future research.

Keywords

Human; micronutrients; risk biomarkers; African Americans; whites

1. INTRODUCTION

Despite improvements in the overall health of the population of the United States, racial health disparities continue to pose a major challenge [1]. When comparing African Americans (AA) to whites, it is overwhelmingly evident that AA have worse health outcomes and higher mortality rates from type 2 diabetes and cardiovascular disease (CVD) [2-4]. Similarly, AA have a lower rate of survival for a variety of cancers [5, 6]. At this time,

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factors contributing to race-related differences are not well understood [7]. However, it has been postulated that racial health disparities may reflect race differences in the prevalence of obesity [8, 9], hypertension [10-12], hyperinsulinemia [13, 14], insulin resistance (IR) [15, 16], and inflammation [15, 17], which are factors implicated in heart disease, type 2 diabetes, and obesity-related cancers [18-22]. While the best risk models are successful in predicting disease-related outcomes, they fall short of fully explaining the underlying causes of racial health disparities [23].

It has been reported that cardiometabolic conditions and various forms of cancers are closely linked to dietary intake and blood levels of micronutrients [24-27]. To date, the most consistent findings have been reported for carotenoids where both dietary intake and serum concentrations have been inversely related to occurrence of type 2 diabetes [28, 29] and CVD mortality [30]. As suggested by a recent meta-analysis, lower levels of carotenoids are also associated with an increased risk of breast cancer [31], with recent evidence suggesting that this association is stronger when carotenoids are assessed in blood [32]. Low serum levels of β – carotene have also been associated with an increased risk of colon and colorectal cancers [33] and non-Hodgkin lymphoma [34]. In contrast, higher levels of β-carotene appear to be associated with an increased risk of prostate cancer [35]. For vitamins E and C, however, findings have been inconsistent, with some studies reporting inverse, albeit modest, associations with CVD [30, 36-38], type 2 diabetes [39, 40], and various forms of cancer [41, 42]. In light of these prior findings, the greater prevalence of cardiometabolic conditions, and some forms of cancers in AA, we examined whether the relation of serum micronutrient concentrations to early risk biomarkers differed in AA and whites. For the most part, prior studies either adjusted for the effects of race or did not include sufficient numbers of AA participants to conduct analysis [29, 43-45]. Interestingly, one study observed that the relation of serum β-carotene concentration to C-reactive protein (CRP) was moderated by race, although no additional details were provided [46]. More recently, one study suggested that the relation of a serum indicator of vitamin D mediates race-differences in the prevalence of insulin resistance in AA and whites [47].

Surprisingly, race differences in early risk factors of cardiometabolic conditions and some forms of cancer, such as hyperinsulinemia and insulin resistance, have not been associated with race differences in dietary intake [24], even when intake of fruits and vegetables has been reported to be higher for AA compared to whites [24, 48]. Those findings may explain the results of one meta-analysis that suggested that blood concentrations of micronutrients, relative to dietary assessment of intake, were more strongly associated with breast cancer risk [32]. Given the lack of evidence for the relation of early risk markers to dietary intake and the relative strength of the relation of blood concentrations to disease, we determined whether blood concentrations of micronutrients are associated with early markers of disease risk and whether these associations are race-dependent. More specifically, we examined the cross-sectional relationship of β-carotene, vitamin A, vitamin C, and vitamin E to metabolic and inflammatory biomarkers in a sample of apparently healthy, non-smoking community volunteers who self-identified as either white or AA. The data were derived from a study that examined the relation of psychosocial factors to early risk biomarkers of CVD and type 2 diabetes [49-52]. The aim of this secondary analysis, however, was to examine the relation of micronutrients to early risk biomarkers and whether these associations differed by race. We hypothesized that the relationship between micronutrient concentrations and early risk markers of cardiometabolic conditions would be race-dependent. Analyses focused on determining whether or not race moderated the relation of vitamin A, C, E and β-carotene to fasting insulin and glucose, estimation for insulin resistance, high sensitivity (hs) CRP and white blood cell count. Given the high prevalence of nutrition related cardiometabolic conditions among AA, we speculated that micronutrients would be more strongly associated with early risk markers in AA than in whites.

2. METHODS and MATERIALS

2.1 Participants and recruitment

Subjects in these analyses were 176, apparently healthy, adults (age: 18-65 years) that were recruited between 1999 and 2004 and self-identified as being white or AA. The 176 subjects in these analyses represent a subsample of 210 adults who enrolled in the initial study [53]. The remaining 34 subjects self-identified as being of another race or ethnicity. The procedures described in this article are the same as those used in the original study [53]. Individuals were initially screened for health criteria using a self-report health questionnaire and in-person interview. Inclusion criteria included the following: negative history and no current diagnosis of psychiatric conditions; no current or previous use of anti-depressant medications; and no chronic medical conditions, such as asthma, allergies, arthritis, diabetes, cancer, and cardiovascular diseases. Subjects who had a history of smoking were excluded. We excluded women if they reported use of oral contraceptives or hormone replacement therapy within the previous 6 months. This study was approved by the Institutional Review Board of Duke University and informed consent was obtained prior to the collection of data.

2.2 Protocol

Following an overnight fast, subjects reported to the laboratory. Subjects were instructed to not use prescription or over-the-counter medications, including low-dose aspirin, during the two-weeks prior to the study visit. On the day of the study visit, staff verified via interview that participants were free of acute infections, had not incurred any injuries, and had not undergone any medical/dental procedures two weeks prior, which are conditions known to increase hsCRP and other markers of inflammation. To minimize menstrual cycle effects, pre-menopausal women were studied during the follicular phase (days 4-9 of the menstrual cycle).

2.3 Biomarkers

Fasting blood samples were analyzed for vitamins A, C, E, β-carotene, lipids, and hsCRP. Blood samples used to assess micronutrients were drawn in chilled serum separator tubes containing Na-heparin. Careful attention was placed on protecting samples from light. Samples were immediately centrifuged and serum was transferred to an amber plastic transport tube. Due to issues with stability, analyses were performed on the day of sample collection. Samples were analyzed isocratically by reverse-phase high performance liquid chromatography (HPLC) with photodiode array detection. As previously noted, these data were collected between 1999 and 2004, a period of time during which a number of large intervention studies were examining the potential cardioprotective effects of vitamins A, C, E, and β-carotene [38, 54-57]. Thus, the selection of the micronutrient panel was based on those studies. For analysis of vitamin, 9 subjects had missing vitamin C values (4 whites, 5 AA), thus the vitamin C results are based on only 167 subjects (113 whites and 54 AA). For remaining micronutrients, analysis is based on 172 subjects (117 whites and 55 AA).

High sensitivity CRP was measured using an ultrasensitive, enzyme-linked, immunometric latex-enhanced assay (Diagnostic Products Corporation, Los Angeles, CA) using purified protein and polyclonal anti-CRP antibodies from Diagnostic Products Corporation (Los Angeles, CA). This system has a low detection threshold of < 0.10 mg/L with coefficients of variation ranging from 6.6% to 9.3%. Measurements of hsCRP were done on fasting venous blood samples collected between the hours of 8:30 AM and 9:30 AM while subjects were seated in a reclined position. Measures of fasting insulin, glucose and lipids (total, triglycerides, low density lipoprotein (LDL)) levels were conducted by the Duke University Clinical Laboratories. Estimated insulin resistance was calculated using the Homeostatic Model Assessment (HOMA-IR) [58] with the following equation: HOMA-IR =[fasting

glucose (mg/dl) X fasting insulin (unit/mL)]/405. HOMA-IR values have been positively associated with an increased risk of type 2 diabetes [59], CVD [60] and cancer [61-63].

2.4 Demographics

On the day of the study visit, subjects' heights and weights were measured and used to calculate BMI. Race was determined by self-report. Data were collected for vitamin supplement use, alcohol consumption, and leisure time physical activity. Vitamin supplement use was evaluated for the 6 months prior to the study visit. Alcohol consumption was classified using a modification of the scheme used by Albert et al. [64]: never/former (< 1 drink in past 12-months), infrequent (1-3 drinks/month), occasional (1-7 drinks/week), and regular (1-4 drinks/day). For the purpose of analysis, we combined the subjects who responded "occasional" and "regular." Leisure time physical activity was assessed by a yes/no response to the following question: "Do you exercise on a regular basis (2 or more hours/week)?". Educational attainment was defined as the highest level achieved. To confirm menopausal status and menstrual cycle phase, we assessed estradiol, progesterone, and follicular stimulating hormone (FSH).

2.5 Statistical Analyses

Statistical analyses were conducted using SAS 9.3 software (SAS Institute Inc., Cary, NC, USA). Tests of the hypothesis, that race moderates the relation of micronutrients to HOMA-IR, glucose, insulin, and hsCRP, were conducted using the SAS procedure for general linear models (PROC GLM). Guided by previous research, covariates were selected *a priori* and included in all models. Covariates included age, gender, body mass index (BMI), race, educational level, alcohol use, physical activity, vitamin supplement usage, menopausal status, and total cholesterol. For models predicting HOMA-IR, insulin, and glucose, log-transformed hsCRP was included as a covariate. Logarithmic transformation was performed on all micronutrient concentrations, HOMA-IR, fasting insulin, glucose, and CRP. Graphic and tabular means represent adjusted means or predicted means derived from multiple linear regression models.

Regression models included all covariates, main effects for vitamins A, C, and E and β-carotene, as well as the 2-way interactions between race and micronutrient levels (race X vitamin A, race X vitamin C, race X vitamin E, and race X β-carotene). A significant interaction suggests that race moderates the relation of vitamin level to biomarker, thus, significant interactions were followed by race-specific analysis that included the same set of covariates.

3 RESULTS

3.1 Bivariate Analyses

Data for demographic, biometric and clinical characteristics are presented by race with accompanying p-values for tests of race differences in Table 1. No race differences were observed for gender distribution, age, educational attainment, fasting triglycerides, glucose, and leisure time physical activity (> 2 hr/week). AA exhibited significantly higher BMI, fasting total cholesterol, high density lipoprotein (HDL) cholesterol, resting systolic and diastolic blood pressure (BP), fasting insulin, and estimated IR. No significant ethnic difference in the use of vitamin supplements was observed ($\chi^2(1) = 2.33$, ns), with approximately one-third of the total sample reporting regular use in the 6 months prior to study visit, which is a percentage of subjects consistent with recently published population reports of adults living in United States [65].

Analysis of vitamin concentrations, adjusting for vitamin supplement use, revealed no significant race differences in vitamin C, vitamin E, and β-carotene. African Americans, however, had significantly lower mean adjusted concentration of vitamin A ($p = .003$) (see Table 1). It is important to note that none of our subjects met National Center for Health Statistics (NCHS) criteria for at-risk status for serum retinol deficiency (< 20 μg/dL), vitamin C (< 2.0 mg/l), and vitamin E (< 5μg/ml) [66]. For β-carotene, subject levels were above 0.3 mol/L a level considered acceptable for adults.

Univariate analysis controlling for use of vitamin supplements revealed that BMI was negatively correlated with concentrations of vitamin C ($r = −0.23$, $p = .003$) and β-carotene ($r = −0.22$, $p = .004$) but not with vitamin A or vitamin E. Race-specific analysis showed that for AA, BMI was significantly associated with vitamin C ($r = −0.35$, $p = .007$), β-carotene ($r = −0.28$, $p = .037$), and vitamin A (partial $r = 0.31$, $p = .02$) but not vitamin E. For whites, BMI was not associated with any of the micronutrients (all p-values > .05) although we did observe a marginally significant association between β-carotene and BMI ($r = −0.17$, $p = .080$).

We conducted multivariate analysis to determine if BMI was associated with micronutrient concentrations and whether this association was moderated by race. Regression analysis included age, gender, educational level, alcohol use, leisure time physical activity, vitamin supplements usage, and menopausal status as covariates. The BMI by race interaction did not significantly predict levels of any of the micronutrients. Adjusting for confounding factors revealed that BMI (= −0.04, $p = .01$) was significantly associated with β-carotene levels, and this association was independent of race. Consistent with results of univariate analysis, multivariate analysis revealed significant race differences ($F = 6.67$, $p = .01$) for vitamin A, with AA having lower concentrations. While results of univariate analyses suggested stronger associations between BMI and micronutrient concentrations in AA than whites, adjusting for potential confounding factors attenuated most of the associations between BMI and micronutrients. Consistent with results of univariate analysis, multivariate analysis revealed a significant race-related difference in vitamin A that was independent of BMI.

3.2 Interaction between serum micronutrients and ethnicity predicting insulin resistance, fasting insulin, and glucose

3.2.1 Insulin Resistance—Log-transformed HOMA-IR values were analyzed using multivariate general linear models adjusted for age, gender, BMI, vitamin supplement usage, alcohol consumption, leisure time physical activity, educational level, total cholesterol, menopausal status, and hsCRP. Inspection of the two-way interactions revealed that only the race X β-carotene interaction was significant ($p = .016$). The interactions between race and vitamin A, vitamin C, and vitamin E and the main effects of vitamin A, vitamin C, and vitamin E did not predict HOMA-IR.

We conducted race-specific analysis to determine the relation of log-HOMA-IR to β-carotene in whites and AA. The regression model included all covariates and micronutrients to examine the unique association of β-carotene to log-HOMA-IR. As shown in Figure 1, greater HOMA-IR was associated with lower β-carotene ($β = −0.253$, $p = .0398$). For whites, HOMA-IR was not associated with β-carotene ($β = −0.015$, $p = .84$).

3.2.2 Insulin and Glucose—The race X β-carotene interaction significantly predicted insulin level ($p = .021$). Neither the main effects of vitamins A, C, and E nor their interactions with race predicted fasting insulin (all $p > .05$). Decomposition of the race X β-carotene interaction revealed that for AA, higher fasting insulin was significantly associated

with lower β-carotene (β = −0.250, p = .028). In contrast, for whites, β-carotene (β = −0.034, p = .64) was not associated with fasting insulin.

For glucose, none of the interactions were significant and only the main effect of vitamin A approached significance (= .034, p = .06).

3.3 The relation of insulin resistance and fasting insulin to micronutrient concentrations as a function of adiposity

Given the significant race-difference in BMI and the observation that β-carotene concentrations were significantly associated with BMI in multivariate analysis, we tested the interactions of race X β-carotene and BMI X β-carotene for their effect on HOMA-IR, insulin levels, and glucose levels. First, we performed regression analysis that included the β-carotene X BMI interaction (as a continuous variable), with race as a covariate. Results showed that the BMI X β-carotene interaction significantly predicted HOMA-IR (= −0.034, p = .034) and fasting insulin level (= −0.58, p < .0001) with race included as a covariate.

Having established the significance of the BMI by β-carotene interaction, we then conducted analysis to evaluate whether the β-carotene by race interaction was due, in part, to the effect of carotene and BMI. If these analyses revealed that the β-carotene X race interaction was no longer significant, the results would suggest that our initial observation of a race by β-carotene interaction was likely due to race being a proxy for BMI. Conversely, if the β-carotene by BMI interaction was no longer significant, then it would suggest that BMI served as a proxy for race. Results indicated that when both BMI X β-carotene and race X β-carotene interactions were included in the model, the effects of both interactions lost significance for HOMA-IR (p's > .05). Analysis of fasting insulin, however, revealed that both the β-carotene X race and the β-carotene X BMI interactions remained significant (p's < .05), thus suggesting that the effects of these interactions were independent in predicting insulin levels.

3.4 The relation of inflammatory biomarkers to micronutrient concentrations in whites and African Americans

Using the same analytic approach, we examined the moderating effect of race on the relationship between micronutrients, leukocyte count, and hsCRP. None of the 2-way interactions were significant at the 0.05 level. We then examined the main effects of micronutrients on hsCRP. Higher hsCRP was significantly associated with lower β-carotene (β = −0.30, p = .007). There was a non-significant trend for a positive association between hsCRP and vitamin E (= 0.64, p = .064). No other micronutrient was related to hsCRP levels.

For leukocyte count, the race X vitamin C interaction (p < .0001) and race X vitamin A interaction (p = .021) were significant. Post-hoc analyses revealed that for AA, a higher leukocyte count was significantly associated with lower vitamin C (β = −1.73, p = .0001), where in whites, leukocyte count was not associated with vitamin C (β = 0.075, p = .76). This was not the pattern observed for vitamin A where for whites, but not AA, higher leukocyte count was associated with higher vitamin A concentrations (= 1.18, p = .024). For the total sample, higher leukocyte count tended to be associated with lower β-carotene concentration (β = −0.396, p = .072), although the association only approached significance.

4. DISCUSSION

The current findings are consistent with our hypothesis that the relation of micronutrient concentrations to early risk biomarkers of cardiometabolic conditions is moderated by race. In a sample of healthy, non-smoking adult men and women, we found statistically

significant race-related differences in the relationship of fasting levels of serum micronutrients to early markers of disease risk. For AA, lower β-carotene concentrations were associated with greater IR and elevated fasting insulin. For whites, however, we found no such relationships. These observations were noted in the presence of no significant race differences in β-carotene concentrations and were independent of the effects of other measured micronutrients and potential confounders such as BMI, age, alcohol use, leisure time physical activity, educational level, fasting total cholesterol, menopausal status, and hsCRP. In addition, race also moderated the relation of vitamin C and vitamin A to leukocyte count, a measure of inflammation. While whites and AA did not differ in mean level of vitamin C, lower vitamin C concentrations were associated with higher leukocyte count in AA but not whites. Conversely, higher levels of vitamin A were associated with higher leukocyte count in whites but not in AA. Lastly, lower β-carotene concentrations were associated with higher levels of hsCRP in both races, a relation that has been previously reported [67, 68]. Combined, our observations suggest that race is a key moderator of the relation of β-carotene and vitamin C to early risk markers and that race differences may explain, in part, the previously reported lack of an association between micronutrients and early biomarkers [69]. More importantly, the observation that lower levels of β-carotene were significantly associated with HOMA-IR and greater inflammation suggests that for AA, β-carotene may be an important early marker of risk given the synergistic effects of inflammation and insulin resistance on progression of both coronary artery disease [70] and cancer [18]. Our findings complement recent evidence suggesting that serum 23 [OH] D levels mediate the increased prevalence of IR among AA [47].

Given the novelty of our findings, it is important that we stress that the study sample included only nonsmokers with no evidence of vitamin deficiencies in any of our participants. Similar to large intervention studies, such as the β-carotene and Retinal Efficacy Trial (CARET) [71], we assessed smoking history via self-report and interview and not with an objective measure such as cotinine levels. Thus, these findings may not be generalized to smokers, a speculation consistent with recent findings suggesting that β-carotene is associated with the metabolic syndrome only in nonsmokers [72, 73]. Given that insulin resistance is a principle component of the metabolic syndrome, it is likely that race differences observed in the current study likely would not be applicable to smokers.

At this time, the exact physiological and biochemical mechanisms for the relation of β-carotene to an IR/secretion profile in AA but not whites are unknown. One possibility is adiposity. In univariate analysis, micronutrient concentrations were associated with BMI, an association that has been previously reported [74-76]. However, with the exception of the interaction between β-carotene to BMI, the remaining associations were attenuated once confounding factors were included in the analysis. Thus, it was important to determine if race-differences in the relation of β-carotene to insulin and IR remained significant when the β-carotene by BMI interaction was included in the model. Results of the concomitant testing of the interactions revealed that for HOMA-IR, the independent effect of each interaction was attenuated. For insulin, however, both interactions remained significant. Combined, these findings suggest that the observed race-related differences in the relation of β-carotene to metabolic factors are complex and may involve BMI in predicting insulin resistance but not fasting insulin.

We also observed significant associations between lower vitamin C and higher leukocyte count in AAs and not whites, as well as an association between lower β-carotene and higher CRP that was independent of race. It has been suggested that antioxidant micronutrients provide protection against oxidative damage via inactivation of reactive oxygen species (ROS), reduction of lipid peroxidation, and reduction of cholesterol uptake implicated in formation of atherosclerotic lesions. Each of these actions are thought to inhibit the onset

and progression of atherosclerosis and type 2 diabetes [77-79], as well as certain types of cancer [41, 80]. The benefits of vitamin C may also be due, in part, to its effects on increasing immune cell proliferation and activity, as well as protecting cells from oxidative DNA damage. Thus, among AA, lower serum vitamin C may contribute to inflammation via increased production of ROS.

It is interesting to note that serum levels of micronutrients have been associated with self-reports of dietary intake in a race dependent manner. Arab et al. [81] showed that dietary intake of carotenoids was correlated with serum levels in whites, but not AA, suggesting the possibility of metabolic or pharmacokinetic differences in micronutrient processing between the two races. Such observations argue for the importance of measuring serum concentrations of β-carotene, since dietary intake appears to not be a reliable measure of circulating levels in AA. Interestingly, previous studies have shown that relative to whites, AA have a greater intake of fruits and vegetables [24, 48], an observation that is inconsistent with the increased burden of IR among AA [24].

At this time, we can only speculate on the putative mechanisms underlying our findings, and specifically, those with regards to β-carotene. One possibility is the enzyme β-carotene monooxygenase (BCMO)-1 which converts β-carotene to vitamin A [82, 83]. In this study, whites and AA exhibited equivalent levels of β-carotene. Yet AA had significantly lower levels of vitamin A, relative to whites, alluding to potential differences in the conversion of β-carotene to vitamin A. Interestingly, evidence from one study has suggested that BCMO-1 exhibits variation in activity among ethnic groups [84]. Moreover, recent evidence stemming from a mouse model with a disruption on the BCMO-1 gene showed that, compared to wild-type mice, the BCMO-1 −/− knockout mouse exhibited lower levels of vitamin A but no difference in β-carotene levels, even when both groups were fed a diet supplemented with β-carotene [85]. In that same study, when animals were fed a high fat diet, the BCMO-1 −/− mice, relative to C57BL/6 control mice, gained significantly more weight and showed greater increases in serum cholesterol ester levels [85]. Interestingly, in our study, AA subjects had significantly higher mean BMI and fasting cholesterol with lower vitamin A levels, which were significantly associated with higher BMI, an association not found in whites. Thus, it may be that the race-related difference in BCMO-1 gene expression is an important mechanism underlying our findings of race-related differences in the relation of β-carotene to early metabolic risk markers. Gene-diet interactions have been previously reported, and while this is an emerging research area, it points to the possibility that the effect of diet is dependent upon genetic phenotypes [86].

The strength of our study rests upon a number of factors, one of which is stringent methodological controls. This is most notable in including only participants who were healthy, non-smoking, non-medicated, and limiting female subjects to those not using exogenous hormones (either oral contraceptives or hormone replacement therapy). We implemented these methodological constraints so as to reduce the sources of error variance that are frequently controlled for in statistical models employed in studies with considerably larger samples. Our aim was to allow for statistical models to include tests of effects commensurate with sample size while recognizing the possibility that results may have limited generalizability. Smoking status was determined by self-report and interview and not serum cotinine level, an objective measure of smoking status. Nevertheless, we are relatively confident that all participants were non-smokers. To control for the effects of female sex hormones on inflammatory biomarkers, blood samples were collected during the follicular phase (days 5-9) when sex hormones are at their nadir. Implementing these methodological constraints and statistically adjusting for other potential confounders such as socioeconomic and lifestyle factors adds to the strength of the study. Although sample size was small

compared to large population studies, our sample size was sufficient to replicate many findings previously reported by larger studies.

Nevertheless, our study has several limitations. Most notable are the cross-sectional design and the lack of a dietary intake tool. The design of our study did not allow for tests of causality among the variables of interest. Thus, we could not determine if low concentrations of β-carotene and vitamin C precede the development of IR, hyperinsulinemia, and inflammation as a result of increased oxidative stress or vice-versa. We also did not collect dietary histories to assess energy intake. It is widely accepted that serum concentrations of micronutrients reflect dietary intake and supplementation. As noted in the preceding section, recent findings by Arab et al. suggest that the strength of the relation of dietary carotenoid intake to serum β-carotene concentration is significantly lower in AA relative to whites [87]. In that study, Arab et al. attributed their findings to differences in dietary reporting or genetic differences between races, possibilities that can be tested in future studies. Interestingly, results of another study suggest that race-related dietary differences do not account for the higher prevalence of IR and hyperinsulinemia in AA, particularly since AA reported greater intake of fruits and vegetables [24].

To our knowledge, the current findings are the first to show that the relationship between β-carotene and vitamin C levels and early risk markers of chronic diseases are moderated by race. Lower levels of β-carotene and vitamin C were associated with elevated risk markers in AA but not in whites, despite the fact that we observed no race differences in serum levels of these micronutrients. Our findings complement recent evidence suggesting that lower serum vitamin D may account, in part, for the greater prevalence of IR and hyperinsulinemia in AA [47]. Thus, we hypothesize that micronutrients may contribute in multiple ways to racial disparities in incidence of CVD and type 2 diabetes. The current paper suggests that even when there are no differences in serum levels (implying no difference in dietary intake or serum uptake), there still may be differences in how micronutrients confer protection from or vulnerability to disease.

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Abbreviations

AA	African American
HOMA	homeostatic model assessment
IR	insulin resistance
CVD	cardiovascular disease
hsCRP	high sensitivity C-reactive protein

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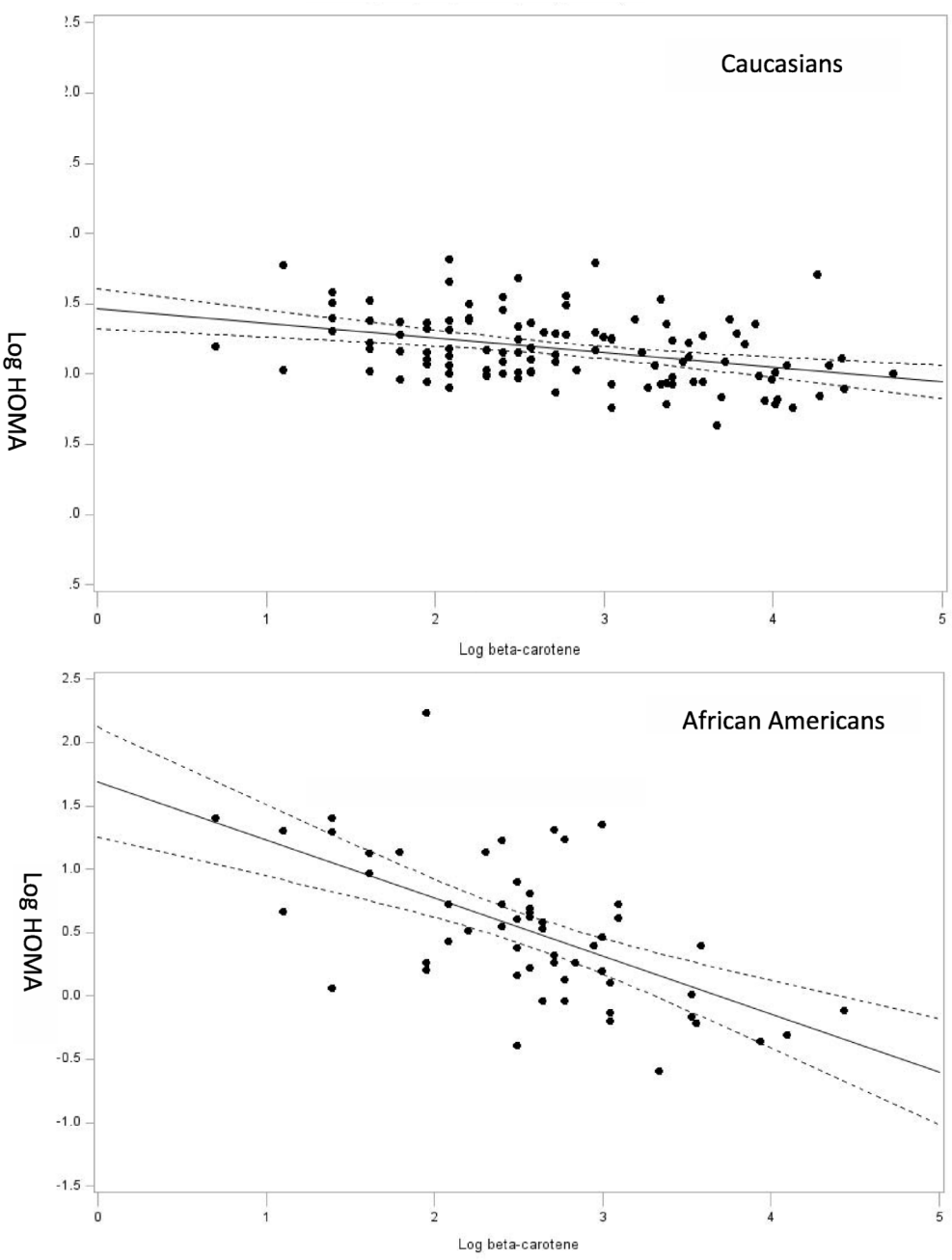

Figure 1.
Illustrated are scatterplots with regression line (95% confidence interval) for the relation of HOMA-estimated insulin resistance and β-carotene concentration for African Americans and whites. Regression lines are adjusted for all covariates in the model.

Table 1

Participant Characteristics

	Caucasian	African American	Race Difference (p-value)
Gender (% female)	42	57	NS
Age, years	29.6	29.2	NS
BMI, kg/m^2	24.4	28.5	<.0001
Total Cholesterol (mg/dL)	167.4	179.2	.047
HDL Cholesterol (mg/dL)	48.0	52.7	.01
Triglycerides (mg/dL)	98.6	82.7	NS
Fasting Glucose (mg/dL)	85.8	85.6	NS
Fasting Insulin (mcU/mL)	6.53	10.04	.0004
Insulin Resistance (units)	1.40	2.21	.0005
Systolic Blood Pressure (mmHg)	106.6	116.1	.0083
Diastolic Blood Pressure (mmHg)	61.1	67.0	<.0001
Education level (%)			NS
Less than High School	0.9	0	
High School Graduate	6.9	5.1	
Some College	31.9	34.5	
College Graduate	19.8	34.5	
Post-College	40.5	25.9	
Use of Vitamin Supplements (%)[a]			NS
Yes	38.8	27.6	
No	61.2	72.4	
Leisure Time Physical Activity (%) [b]			.03
Yes	86.2	72.9	
No	13.8	27.1	
Micronutrient Levels [c]			
vitamin A (μg/dL)	53.2	44.3	<.0001
vitamin C (mg/dL)	0.91	0.99	NS
vitamin E (mg/L)	11.1	10.5	NS
β-carotene (μg/dL)	17.1	14.0	NS
C-reactive protein (mg/L)	0.99	1.92	<.0001

Continuous parametric results are given as Mean (SD); categorical results as percentage; and continuous non-parametric results as median (95% confidence interval); NS = not significant

[a] in past 6 months;

[b] 2 hours/week or more;

[c] adjusted for multivitamin use