

## Obesity Indicators and C - reactive Protein in African and Haitian Americans with and without Type 2 Diabetes

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### Abstract

**Purpose:** High sensitivity C-reactive protein (CRP) is a risk factor for cardiovascular disease based on finding in primarily non-Hispanic White populations. Obesity, another risk factor for cardiovascular disease, is higher in Blacks as compared to non-Hispanic Whites. The objective of this study was to assess the relationship between CRP, a marker of systemic inflammation, and obesity indicators by ethnicity, diabetes status and gender for two Black ethnicities.

**Methods:** Anthropometrics and venous blood were collected for African and Haitian Americans with and without type 2 diabetes in a cross-sectional study. A total of 434 participants; 190 African Americans, 244 Haitian Americans, met the inclusion criteria of CRP  $\leq 10$  mg/L. Main effects and interactions of ethnicity, diabetes status, gender, and each obesity indicator (waist circumference, waist-to-height ratio, and body mass index) were performed using General Linear Models.

**Results:** African Americans were more likely to be obese, have higher CRP, and smoke as compared to Haitian Americans. Haitian Americans has a lower rate of health care coverage than African American. Having a higher education level than Haitian Americans was a protective health factor for African Americans; whereas, Haitian Americans were protected by a higher percent married as compared to African Americans. All obesity indicators were associated with CRP. All differences in CRP by ethnicity and diabetes status were negated by obesity indicators. Being female was associated with higher CRP for waist circumference and BMI models. Adjusting for health insurance, smoking, marital status and education negated the relationship of gender and CRP for waist-to-height ratio.

**Conclusion:** Being African American as opposed to Haitian American was a greater risk factor for obesity and inflammation. Obesity was associated with elevated CRP levels in African and Haitian Americans regardless of diabetes status. Inflammation constitutes a serious health problem for minorities with high rates of obesity.

**Keywords:** African Americans; Haitian Americans; C-reactive protein; Body mass index; Waist circumference; Waist-to-height ratio; Type 2 Diabetes

### Introduction

Race/ethnicity and gender are risk factors for cardiovascular disease [1]. African Americans are more than six-time more likely to have coronary heart disease as compared to non-Hispanics Whites [2]. The fact that Blacks are at greater risk for cardiovascular disease, may be partially attributed to their higher rate of obesity (1.4) as compared to White, non-Hispanics (1.0) [3]. Along with race/ethnicity, obesity and systemic inflammation are risk factors for cardiovascular diseases. Waist circumference and body mass index (BMI), indicators of obesity, have predicted relative risk of coronary heart disease for men and women [4]. Albert and Ridker [5] reviewed numerous epidemiological studies and concluded that C-reactive protein (CRP), a sensitive measure of chronic, low-grade systemic inflammation, was positively associated with adverse cardiovascular events in adults. For

persons with diabetes, CRP was found to be an independent risk factor for coronary heart disease related deaths [5].

Most of the studies of CRP and cardiovascular risk were conducted primarily in Caucasian cohorts. High serum CRP was independently associated with the odds of type 2 diabetes for a primarily Caucasian cohort of women from the Nurses' Health Study [6]. In a cohort of primarily Caucasian men with diabetes from the Health Professionals Follow-up Study, high serum CRP was associated with increased risk of cardiovascular events, independent of blood lipids and glycated hemoglobin (A1C) [7]. In a representative sample of US adults, the odds of gender-adjusted high CRP was greater for those with diabetes as compared to those without diabetes even after adjusting for age, gender, BMI, race/ethnicity and education [8]. Although the investigators considered race/ethnicity, their focus was on the relationship between obesity and diabetes with elevated CRP. Adiposity is thought to play a role in CRP since adipose tissue is a major source of cytokines [9] and CRP is produced by the liver in

response to inflammatory cytokines such as interleukin-6 (IL-6) and tumor necrosis factor alpha (TNF $\alpha$ ) [10].

Differences in CRP were found across gender and race in a large multiethnic sample of adults between ages 30 and 65 years [11]. Blacks and women had higher CRP levels as compared to Whites and men; adjustment for obesity (BMI) negated this association for Black men, only [11]. Few studies examined the combined effect of race/ethnicity and obesity on CRP. Wee and colleagues [12] studied whether Blacks and Mexican Americans differed compared to White non-Hispanics by obesity indicators with respect to CRP in a nationally representative US sample of adults. They found only Mexican women in the largest category of waist circumference had higher CRP levels than women of other racial groups [12]. These investigators found higher BMI was associated with higher CRP regardless of ethnicity, comparing Black non-Hispanics, Mexicans, Hispanic (other than Mexican) and White non-Hispanics [12].

Blacks have been combined as a single group in most epidemiological studies and there are relatively few studies assessing health outcomes for Haitian Americans as compared to African Americans. In the context of the literature, we examined three proxy measures for obesity: BMI, waist circumference, and waist-to-height ratio by ethnicity and diabetes status with CRP for two Black ethnicities. Specifically, it was hypothesized that individuals with type 2 diabetes will have higher CRP levels than those without type 2 diabetes in consideration of obesity indicators. Since no data exist for CRP levels among Haitian Americans, it was hypothesized that their CRP levels will differ from African Americans.

## Materials and Methods

### Participants

This cross-sectional study was conducted on African American and Haitian Americans with and without type 2 diabetes. Two mailing lists (with and without type 2 diabetes) of addresses were purchased from Knowledge Base Marketing, Inc., Richardson, TX 75081. The randomly generated lists were used to recruit participants from Miami-Dade and Broward Counties, Florida. Knowledge Base Marketing, Inc. did not have addresses for Haitian Americans; therefore, recruitment came from community based sources. Over a 1-year period, 7,550 letters were mailed to African Americans with and without type 2 diabetes. From delivered letters, 4% (n=256) responded, and 259 Haitian Americans were recruited from the community based sources. Eligible participants were invited to the Human Nutrition Laboratory at Florida International University (FIU). The study was approved by the Institutional Review Board at FIU. The purpose and protocol of the study were explained, and written consent was obtained before the start of the study. A total of 700 participants (Haitian Americans =253; African Americans =248) had complete data. The final sample size (N=434; 190 African Americans, 244 Haitian Americans) included participants with CRP  $\leq$  10 mg/dL. Participants were  $\geq$ 35 years of age, male and female, not pregnant or lactating, and with no other conditions associated with elevated CRP (e.g. gout, arthritis, CHD, lupus, stroke).

### Measures

Subjects were asked to fill out standard questionnaires on site. Trained interviewers who were bilingual in English and Creole were present to administer the questionnaires. The questionnaire contained

structured questions to gather information on each participant's demographics, smoking history, and anthropometric measurements, diabetes status, diabetes care (for diabetes only), anthropometric measurements and nutritional variables. Height and weight were measured using a SECA balance scale (Seca Corp, Columbia, MD). BMI was calculated as weight in kg/height in m<sup>2</sup>. Waist circumference (WC) to the nearest 0.1 cm was measured horizontally with a non-stretchable measuring tape placed midway between the 12th rib and iliac crest at minimal respiration to determine central obesity [13]. Waist-to-height ratio was calculated as the waist circumference divided by height in cm. Body mass index (BMI), calculated as the weight (kg) divided by square of height (m<sup>2</sup>). A 20 ml venous blood was collected from each subject after an overnight fast (at least 8 hours) by a certified phlebotomist using standard laboratory techniques. Blood samples were collected into 2 tubes: K2EDTA to analyze A1C and the second a vacutainer Serum Separator Tube (SST) for analysis of glucose. After complete coagulation (30–45 minutes), the SST was centrifuged at 2,500 RPM for 30 minutes. The serum was transferred from the spun SST into 3 labeled plastic tubes: the first tube was used for glucose analysis, and the second tube was stored at  $-70^{\circ}\text{C}$  to be used later for High-sensitivity CRP (hs-CRP). Glucose levels were measured by hexokinase enzymatic methods by Laboratory Corporation of America, Miami, FL (LabCorp<sup>®</sup>). Hs-CRP was analyzed at the Vascular Disease Intervention and Research Laboratory, Edmond, OK using Immulite method. The Immulite assay is a 2-site chemiluminescent enzyme immunometric assay with one monoclonal and one polyclonal anti-CRP antibody. A 1:100 manual dilution of the antibody provides a measurable range of 0.1–500 mg/L [14].

### Statistical Analysis

SPSS (Version 21.0, Chicago, IL) was used for statistical analysis and  $P < .05$  was considered significant. Prior to analysis, all continuous variables were tested for linearity and normality using QQ plots and the Kolmogorov-Smirnov Test. Variables were transformed to achieve normality, when needed. CRP and all obesity indicators (waist circumference, body mass index (BMI) and weight-to-height ratio) were natural logarithm transformed. Descriptive statistics were run comparing sociodemographics and biomarkers for participants by diabetes status and ethnicity using the student t-test. General Linear Models were run with the natural logarithm of CRP as the dependent variable. Models tested main effects, 2- and 3-way interactions of diabetes status, ethnicity, and gender with CRP. Clinically important adjustment variables: age, smoking, education, marital status, and health insurance were used. Other covariates considered, such as physical activity, fatty acid intake, and dietary fiber were not included since they were not significantly correlated with CRP. Energy (Kcal/d) was not used as a covariate since it was highly collinear with all of the obesity indicators.

### Results

The general characteristics of the study population by ethnicity are shown in Table 1. Compared with African Americans, Haitian Americans were older, had lower obesity measures, lower CRP, less percent of current smokers, higher percent married, and had a lower percent with health care coverage. Both ethnicities were compared by diabetes status in Table 2. As compared to those free of diabetes, those with type 2 diabetes were older, had higher obesity measures, higher CRP and had a higher percent with less than a high school education.

Independent t-test by ethnicity (data not shown) indicated that females had higher waist circumference and BMI than males, but that males had a higher waist to height ratio. In addition CRP levels were higher for females (2.9±2.3) as compared to males (2.3±2.2), P=.007. To assess the effect of ethnicity, diabetes status, and gender with obesity indicators on CRP, separate models were run (Table 3). Since the 2-and 3-way interactions were not significant, final models included main effects with each obesity indicator, adjusted for age,

smoking, marital status, education, and health insurance. All differences in CRP by ethnicity and diabetes status were negated by obesity indicators. The proposed hypothesis that CRP levels would be higher for persons with diabetes independent of obesity was not supported. The second hypothesis, that Haitian Americans and African Americans would have different CRP levels was supported in the reduced model. Once obesity measures were added, the difference in CRP levels between these ethnicities was no longer significant.

Variable	Haitian Americans	African Americans	P
	Means ± SD		
Age (yrs)	56.2 ± 11	53.1 ± 9.2	.002
Waist circumference (cm)	97.7 ± 12	106.5 ± 17	<.001
Body mass index (BMI) (kg/m <sup>2</sup> )	29.0 ± 5.0	32.5 ± 7.3	<.001
Waist-to-height ratio	.597 ± .08	.629 ± .11	.001
C-reactive protein (CRP) (mg/dL)	2.20 ± 2.0	3.13 ± 2.4	<.001
	N (% within ethnicity)		
Gender (females)	125 (51.2)	85 (44.7)	.179
Type 2 diabetes (yes)	130 (53.3)	100 (52.6)	.893
Current smoker (yes)	15 (6.1)	75 (39.5)	<.001
Education (< high school)	119 (48.8)	31 (16.3)	<.001
Currently married/cohabitating (yes)	154 (63.1)	52 (27.4)	<.001
Health insurance in past year (yes)	225 (51.2)	147 (77.4)	<.001

**Table 1:** General characteristics of the study population by ethnicity

Variable	Without diabetes	With type 2 diabetes	P
	Means ± SD		
Age (yrs)	52.8 ± 9.8	56.6 ± 10	<.001
Waist circumference (cm)	97.7 ± 13	105 ± 16	<.001
Body mass index (BMI) (kg/m <sup>2</sup> )	29.3 ± 5.4	31.6 ± 7.0	<.001
Waist-to-height ratio	.585 ± .08	.634 ± .10	<.001
C-reactive protein (CRP) (mg/dL)	2.29 ± 2.1	2.89 ± 2.4	<.001
	N (% within diabetes status)		
Gender (females)	95 (46.6)	115 (50.0)	.475
Ethnicity (Haitian American)	114 (55.9)	130 (56.5)	.893
Current smoker (yes)	44 (21.6)	46 (20.0)	.687
Education (< high school)	56 (27.5)	94 (40.9)	.006
Currently married/cohabitating (yes)	98 (48.0)	108 (47.0)	.822
Health insurance in past year (yes)	121 (59.3)	151 (65.7)	.173

**Table 2:** General characteristics of the study population by diabetes status

Model	Independent Variables	Coefficient (95%CI)	SE	P
Model 1	Body mass index (kg/m <sup>2</sup> )	1.83 (1.3, 3.2)	.25	<.001
Ethnicity	Haitian American	-.19 (-.42, -.04)	.12	.107
	African American (reference)	-	-	-
Diabetes status	Without diabetes	-.12 (-.29, .07)	.09	.230
	With diabetes (reference)	-	-	-
Gender	Female	.22(.03, .41)	.10	.022
	Male (reference)	-	-	-
Model 2	Waist circumference (cm)	2.79 (2.1, 3.4)	.33	<.001
Ethnicity	Haitian American	-.15 (-.37, .07)	.12	.181
	African American (reference)	-	-	-
Diabetes status	Without diabetes	-.05 (-.23, .13)	.09	.600
	With diabetes (reference)	-	-	-
Gender	Female	.29 (.11, .48)	.09	.022
	Male (reference)	-	-	-
Model 3	Waist-to-height ratio	2.8 (2.2, 3.5)	.33	<.001
Ethnicity	Haitian American	-.21 (-.43, .007)	.11	.057
	African American (reference)	-	-	-
Diabetes status	Without diabetes	-.05 (-.23, .13)	.09	.606
	With diabetes (reference)	-	-	-
Gender	Female	.11 (-.08, .30)	.10	.269
	Male (reference)	-	-	-

Models were adjusted for age, smoking, education, marital status, and health insurance.

**Table 3:** General Linear Models for the effect of ethnicity, diabetes status, and gender with obesity indicators on C-reactive proteins

## Discussion

These findings suggest that a high CRP level is related to obesity indicators for both Black ethnicities, Haitian and African Americans. Although African Americans had higher CRP levels as compared to Haitian Americans, this association was no longer significant, adjusting for obesity. Females had higher CRP than males, even when adjusting for obesity; however, once demographics were taken into account, gender was no longer associated with CRP. In addition, obesity indicators, waist circumference and BMI by race/ethnicity interactions were not associated with CRP in our study; however, waist circumference interacted with ethnicity and gender in predicting CRP levels in a nationally representative US sample [12]. Using BMI as an obesity indicator the investigators found higher BMI was significantly associated with higher CRP regardless of race/ethnicity for the national sample which agreed with our findings for both Haitian and African Americans. Conversely, Khera et al [11] found CRP levels that differed by race and gender were still significant even after adjusting for BMI for a multiethnic, large probability sample of participants

from Dallas County, Texas. Despite the ethnic differences found in CRP levels, BMI was associated with CRP, independent of age in a multiethnic study of women [15]. Allowing for BMI as a confounder, these investigators found African ancestry to be independently associated with higher CRP as compared to Caucasian women; albeit, ethnic differences in CRP were substantially attenuated when adjusting for BMI [15]. Another possible confounder between race and obesity indicators with CRP levels could be due to differences in the type and amount of fat present for a given BMI or waist circumference. Stevens et al [16] found different health outcomes, such as diabetes, hypertension, and hyperlipidemia were found to have different associations with BMI by race for African American and Caucasian women. The investigators stated BMI cutoffs had different equivalent risk by race for different health outcomes and risk estimates [16]. Visceral adipose tissue, associated with metabolic abnormalities, has been found to be lower in African American men and women as compared to Caucasian men and women for a given BMI or waist circumference [17]. Racial/ethnic differences in visceral fat suggest obesity indicators such as waist circumference and BMI may over- or

under-estimate health risk for certain groups and cutoffs may need to be specific by race/ethnicity [16,17].

We did not find any differences in CRP by diabetes status accounting for obesity. Diabetes is another confounder in assessing the relationships among BMI, race/ethnicity and CRP. BMI has a strong correlation with CRP and may introduce a low grade of inflammation in a person with excess body fat, which can be an underlying factor in the pathogenesis of type 2 diabetes [6,7]. Huffman and colleagues [18] reported obesity was more associated with CRP in persons without as opposed to with type 2 diabetes in Cuban American adults. The investigators attribute diabetes medications as partially explaining their unexpected results since some oral hypoglycemic agents have been shown to reduce CRP levels [19,20]. Obesity may have been confounded by diabetes complications in assessing CRP differences for those with diabetes as compared to controls. Sarangi et al, [21] found higher CRP levels for the group with hypertension and retinopathy ( $5.8 \pm 2.13$  mg/ml) disease as compared to the group without complications ( $5.2 \pm 1.16$ ) in non-obese Asian Indian males with type 2 diabetes ( $N = 80$ ) ( $P = .019$ ). The investigators also compared CRP levels in the combined group with diabetes ( $5.1 \pm 2.59$ ) with the control group (free of diabetes) ( $1.7 \pm .54$ ) ( $P = .001$ ).

Another possible confounder in assessing CRP differences across diabetes status and ethnicity could be genetic differences. The production of paraoxonase-I activity (PON 1), an enzyme functioning with high-density lipoprotein cholesterol (HDL-C) helps to protect low-density lipoprotein cholesterol (LDL-C) from oxidation, is influenced by genetic and environmental factors and may differ in persons with T2D [22]. Lower PON 1 ( $199 \pm 39$  vs.  $258 \pm 60$  U/L,  $P < 0.05$ ) and higher CRP ( $5.8 \pm 4.9$  vs.  $3.2 \pm 1.1$  mg/L,  $P < 0.05$ ) was found in a group with T2D and diabetic retinopathy on oral antiglycemic agents as compared to controls free of diabetes in Asian Indian male and female outpatients ( $N=54$ ) [22]. Even though both PON 1 and retinopathy have been associated with oxidative stress, there were no significant differences between the T2D groups with and without diabetic retinopathy [22].

Components of diet as well as overall diet quality may have been associated with CRP for our sample. Although we did not adjust for overall diet quality, we tested association with several notable dietary components known to be associated with CRP levels. The normalized variables for dietary fiber and CRP levels were not correlated for our participants. Our sample had lower than recommended dietary fiber intake regardless of diabetes status. A systematic review indicated in six out of seven intervention trials higher fiber dosages significantly lowered CRP from baseline to completion [23]. The relationship between saturated fatty acid intake and CRP was not significant for our participants. Studies comparing dietary saturated fatty acid and CRP levels have been inconsistent. The ratio of saturated to polyunsaturated fatty acids intake was associated with higher CRP levels for men but this relationship was not significant for women in a study of a Portuguese population ( $N=395$ ) [24].

## Limitations

The strength of this study was the comparison between two Black ethnicities in terms of diabetes status, obesity markers, and CRP which to our knowledge has not been assessed; albeit, the study has several limitations. The cross-sectional design of this study could not establish causality. Participants were from Miami-Dade County, Florida and may not be representative of African Americans and Haitian

Americans throughout the entire state or country. BMI, waist circumference, and waist-to-height ratio are proxy measures of obesity. Even though we eliminated participants with CRP levels above 10 mg/dL; we assumed our participants' CRP levels measured cardiovascular inflammation. By using this threshold, we increased the likelihood of cardiovascular inflammation; however, some cases may have been attributed to non-cardiovascular inflammation.

## Conclusions

Although African Americans had higher levels of CRP as compared to Haitian Americans, we found all indicators of obesity, BMI, waist circumference and waist-to-height ratio to be associated with high CRP levels regardless of ethnicity or diabetes status, adjusting for confounders. Being female was associated with higher CRP when adjusting confounders and two of the obesity indicators, BMI and waist circumference, but not waist-to-height ratio. To its merit, this study differentiated cardiovascular risk factors among two Black ethnicities that have been assessed as one group in many epidemiological studies.

## Practical Application

Inflammation constitutes a serious health problem for minorities with high rates of obesity. Target interventions aimed at improving health behaviours to reduce obesity could help in reducing inflammation and potential cardiovascular diseases in this population. Future studies should be conducted in other ethnic/racial groups which include comparisons of obesity indicators with CRP and other inflammatory markers.

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