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Sex and Body Circumferences Associated with Serum Leptin in African American Adults

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Abstract

Objective: Cardiovascular disease (CVD) continues to be a leading cause of death for U.S. adults, especially African Americans (AA). Yet, few studies have examined a comprehensive set of metabolic health and health behavior factors related to CVD risk in this population. This study investigated the relationship between serum leptin and anthropometries (body mass index [BMI], circumferences [waist-WC, hip-HC, and waist/hip ratio W/H]), metabolic health (systolic and diastolic blood pressure [BP], serum lipids, glucose, and C-reactive protein [CRP]), and health behaviors (hours of sleep, physical activity) in midlife and older AAs.
Materials and Methods: Participants ($n = 89$, ≥45 years of age) were AAs in six churches in North Florida enrolled in a broader church-based longitudinal study. Anthropometric measurements, serum analyses, and self-reported items.
Results: Serum leptin was positively correlated with gender (being female) ($r = 0.623$, $p < 0.001$), BMI log transformed ($r = 0.469$, $p < 0.001$), WC ($r = 0.440$, $p < 0.001$), HC ($r = 0.658$, $p < 0.001$), use of BP medication ($r = 0.216$, $p < 0.05$), and serum CRP ($r = 0.277$, $p < 0.01$). Correlations by sex showed significant relationships for both men and women between leptin and BMI log transformed, WC, and HC. The final multiple regression model [$R^2 = 0.758$, $F(4, 66) = 55.871$, $p < 0.001$] showed that 75.8% of the variance in leptin was explained by being female ($\beta = 0.65$, $p < 0.001$), WC ($\beta = 0.26$, $p < 0.02$), and HC ($\beta = 0.28$, $p < 0.01$).
Conclusions: Findings more specifically delineate the variables associated with serum leptin in AAs, particularly WC and HC, and suggest greater attention to possible risk for leptin resistance in AA females. Clinical Trial Registration: This study is registered at www.clinicaltrials.gov NCT03339050.

Keywords: leptin, cardiovascular risk factors, body circumferences, African Americans, African American women

Introduction

Among noncommunicable diseases, cardiovascular disease (CVD) is one of the leading causes of death for both men and women in the United States. In particular, African Americans (AAs) have a higher risk for and mortality rates from CVD compared to non-Hispanic white men and women.[1] One key risk-factor for CVD is obesity. Non-Hispanic AAs have the highest prevalence rates for obesity compared to other ethnic/racial groups.[2] Although the distribution of body fat varies, AA women generally have more subcutaneous than visceral fat with the former distributed mostly in the gluteal region.[3] Leptin, a protein released mostly from adipose tissue (among other adipokines) and from enterocytes in the small intestine, as well as from bronchial epithelial cells and lung macrophages, has been linked to weight regulation[4] and immune homeostasis.[5] Studies show that leptin may have an important role in reducing body weight by regulating appetite and decreasing food intake and increasing energy expenditure via the hypothalamic axis.[4] However, studies also show that

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high serum leptin levels (hyperleptinemia) can create leptin resistance, failing to modulate appetite and food intake.[6] As reviewed previously, high serum leptin levels also have proinflammatory properties and, as such, are implicated not just in propagating obesity,[5,7] but also in atherogenesis, arterial stiffness, and myocardial infarction, thus increasing the risks for CVD development.[8] Leptin facilitates the secretion of other proinflammatory cytokines, namely interleukin 6 (IL-6) and tumor necrosis factor-alpha, which then further promote leptin secretion,[5] thus creating a perpetual cycle that maintains low-grade inflammation, which contributes to many noncommunicable diseases, including CVD.[8] Moreover, it was recently hypothesized that dysregulated leptin levels may compromise immune system in COVID-19 patients and worsen the outcomes of the infection.[9]

Higher serum leptin levels have been routinely found in AAs compared to other ethnic/racial groups. For example, a study that examined 47 novel protein markers of vascular disease measured in plasma in African Americans ($n = 1324$, mean age 63.5, 71% women) and non-Hispanic whites ($n = 1237$, mean age 58.9, 57% women) reported higher serum leptin and lower adiponectin levels in AAs compared to non-Hispanic whites.[10] Further, Azrad et al. compared longitudinally serum adiponectin and leptin levels in African American and non-Hispanic white premenopausal women in both overweight and normal-weight body mass index (BMI) categories. They found that AA women had higher leptin concentration even when their BMI was comparable at baseline to their non-Hispanic white counterparts and lower than 24 kg/m^2 (indicating their normal weight).[11]

Yet, the relationship between serum leptin and CVD risk factors in AA adults is understudied. Given the high rates of CVD and obesity as well as high serum leptin levels in AAs, it would follow that high serum leptin could be another risk factor for the development of CVD, and could be related to other CVD risk factors, including blood pressure (BP), BMI, central-body adiposity, serum lipids, glucose, and C-reactive protein (CRP), in this population. Indeed, the relationship between serum leptin and BMI in AA women was established in earlier studies,[12] and has been further supported in recent studies in broader populations.[13–15] Leptin was also positively associated with other CVD risk factors, including body circumferences,[16] BP,[17,18] cholesterol,[19] CRP,[20] and triglycerides,[21] with some conflicting findings. For example, one study showed glucose and cholesterol levels were not associated with leptin levels.[22] However, only two of these studies included AA adults.[18,20]

Of particular interest in our study was the relationship between serum leptin and the health behaviors, including hours of sleep and physical activity; both being linked to obesity and CVD risk.[23,24] Previous studies reported a positive relationship between serum leptin and loss of sleep[25,26] and an inverse relationship between serum leptin and physical activity in adolescents in Brazil and in adults in Japan and Iran.[27,28] In addition, napping during the day was associated with fewer hours of sleep in AA adults and with increased BMI and central adiposity.[23]

Few studies have investigated serum leptin in relationship to a comprehensive set of CVD risk factors in mid-life and older AA adults. Establishing a relationship between these factors in this population may help provide a more complete understanding of the role that leptin plays in CVD with implications for practice. Thus, the purpose of this study was to examine the relationship of serum leptin with selected CVD risk factors, including anthropometries (BMI, waist and hip circumferences), metabolic health factors (BP, serum glucose, lipids, and CRP), and health behaviors (hours of sleep and physical activity) in midlife and older AAs. Two demographic characteristics of interest in this study were age and sex. Age was of interest since few studies have examined leptin and CVD risk factors in older populations,[19] especially AAs. Sex was of interest considering the demonstrated higher leptin levels in women in general[29] and in AA women in particular, even when compared to their male counterparts and non-Hispanic white individuals.[12,30] Possible confounders in the study included use of medications (BP, cholesterol, and diabetes) and smoking status.

Materials and Methods

The data used for this article were from a broader church-based, quasi-experimental longitudinal study to reduce CVD risk in midlife and older AAs.[31–33] In brief, the study tested the effectiveness of an 18-month intervention developed using community-based participatory research approaches.[32] The data were collected from AA congregants (randomly sampled, stratified by age and sex) in six churches (three treatment, three comparison), in a two-county area in North Florida ($n = 221$, ≥45 years). For this study, the clinical subsample ($n = 89$) was used. The subsample was drawn at baseline from the overall sample, using the same procedure (randomly sampled, stratified by age and sex). All data, including clinical and self-report measures, were collected before the intervention. This study was approved by the Florida State University Institutional Review Board (2018.25585).

All data were collected from participants at the churches. Anthropometric and BP measurements were taken by trained staff in private rooms during clinical sessions held at the churches. During these sessions, self-administered questionnaires were used to collect the self-reported items. Participants needing assistance with the questionnaire were interviewed by trained staff. Fasting blood samples were taken at the churches in private rooms by trained staff.

Measurements

Anthropometries and BP. Height was measured without shoes to the nearest 0.1 cm using a Charder stadiometer (Issaquah, WA). Weight was measured in indoor clothing to the nearest 0.1 kg using a Tanita digital scale (Arlington Heights, IL) and BMI (kg/m^2) was calculated. The body circumferences (cm) were measured with a plastic, nonflexible circumference-measuring tape (Issaquah, WA) as the participant exhaled while standing in the upright position with feet together. The hip was measured at the largest protrusion around the buttocks and waist at the narrowest part of the torso, each three times and the average was included in the analysis.[34,35] The waist/hip (W/H) ratio was calculated as well. Three BP readings in the sitting position were taken using a digital device (A&D Medical, Miltitas, CA) on the nondominant arm, with the average calculated for the analyses.

Serum biomarkers. Overnight fasting blood samples were collected in red-top tubes (containing no coagulant); the red blood cells were separated by centrifugation and serum was stored at −80°C until further analyses. Serum lipids (total

cholesterol, low-density lipoprotein [LDL] cholesterol, high-density lipoprotein [HDL] cholesterol, and triglycerides) and glucose were analyzed by a contracting laboratory (Clinical Laboratory, Tallahassee Memorial Hospital, FL). Serum high-sensitive CRP (hs-CRP) and leptin were measured in our laboratory by immunoassays using the enzyme-linked immunosorbent assay (ELISA) kits (Enzo Life Sciences, Inc., Farmingdale, NY and ALPCO Diagnostics, Salem, NH, respectively), according to the manufacturers' instructions.

Self-reported data. Hours of sleep were assessed by the item, ''How many hours of sleep do you get per night?'' Age was assessed by the item, ''In what year were you born?'' and sex was coded as follows: female = 1, male = 0. Self-reported confounder items included BP medication (Are you on BP medications? Yes = 1, No = 0), cholesterol medication (Yes = 1, No = 0), diabetes medication (Yes = 1, No = 0), and smoking status (Do you currently smoke? Yes = 1, No = 0).

The Yale Physical Activity Survey (YPAS) was used to measure habitual physical activity and determine energy expenditure from activities such as daily tasks, yard work, exercising, and recreational activities.[36] In the YPAS, each activity is assigned an intensity code. The YPAS was scored by having participants report the number of minutes per day or week that they performed certain types of activities, and by multiplying the minutes per week of each activity by its intensity code. The resulting value described the energy (kilocalories, kcal) expended per week for that exercise in kcal/week and the sum of the kcal/week values for all activities generated the energy expended in a week.

Data analysis

SPSS software version 25.0 (SPSS, Inc., Armonk, NY, 2017) was used to perform descriptive analyses (frequencies and percentages) on all the variables with $p < 0.05$ deemed as significant. Normality tests were performed using Shapiro–Wilk tests. Serum leptin (ng/mL) was found to have a skewed distribution, and after removing two outliers, the skewness was found to be 0.266 with $p = 0.03$. BMI, which also was found to have a skewed distribution, was log transformed to reduce the skewness and was named BMI log transformed. A bivariate correlation analysis was performed on all variables to identify possible relationships between the variables. A stepwise linear regression with leptin as a dependent variable was then performed to determine the relationship between the independent variables found significant in the bivariate analysis (assuming that the bivariate association between serum leptin and the remaining independent variables were not suppressed).

Results

The majority of participants ($n = 89$) in this study were female (70.5%), were 50–63 years of age (53.3%), and were high school graduates or had some college (56.3%) (Table 1). For the total sample, hours of sleep ranged from 3.0 to 9.5 hours/night. About two thirds of the participants (65.1%) took BP medication, a third (32.5%) took cholesterol medication, and about a fifth (18%) took diabetes medication. Only a small percent (6.2%) currently smoked. Table 2 presents study variables by sex. Female and male participants had similar diastolic BP, serum CRP concentration, and number of hours of sleep. For both groups, BMI values reflected obesity and systolic BP and LDL exceeded normal levels. Male participants had significantly higher weight ($p < 0.01$) and glucose levels ($p < 0.01$) compared to females. In general, female participants were slightly older than males and had lower BMI, systolic BP, and serum LDL cholesterol, glucose, and triglyceride levels compared to male participants. In terms of significant differences, female participants had significantly higher serum HDL cholesterol levels ($p < 0.001$) and significantly lower waist/hip ratio ($p < 0.001$) than male participants. Most noteworthy, leptin levels for female participants (54.0 ± 21.9 ng/mL) exceeded those of male participants (18.5 ± 17.2 ng/mL) ($p < 0.001$) and were far outside of the normal range.

The results of the bivariate correlation analysis in the entire population (both women and men) showed that serum leptin was significantly and positively related to sex (being female) ($r = 0.623$, $p < 0.001$), BMI log transformed ($r = 0.469$, $p < 0.001$), waist circumference ($r = 0.440$, $p < 0.001$), hip ($r = 0.658$, $p < 0.001$) circumference, BP medication use ($r = 0.216$, $p < 0.05$), and serum CRP ($r = 0.277$, $p < 0.05$)

Table 1. Characteristics of Participants

Variables[a]	*Participants* n	*Participants* %
Age categories (years)		
45–49	14	18.1
50–56	19	24.7
57–63	22	28.6
64–70	12	15.6
71–77	7	9.1
78–85	3	3.9
Sex		
Female	55	70.5
Male	23	29.5
Education		
Some high school	5	6.3
High school graduate	22	27.5
Some college	23	28.8
Bachelor's degree	14	17.5
Master's degree	15	18.8
Other	1	1.3
Hours of sleep (average per night)		
3.0–5.5	12	15.0
6.0–7.0	48	60.0
7.5–9.5	20	25.0
BP medication		
Yes	54	65.1
No	29	34.9
Cholesterol medication		
Yes	29	32.5
No	60	67.5
Diabetes medication		
Yes	16	18.0
No	73	82.0
Currently smoking		
Yes	5	6.2
No	76	93.8

[a]Sample size ranged from $n = 77$ to $n = 89$ due to missing data.
BP, blood pressure.

Table 2. Selected Variables of Participants by Sex

Variables	*Females*[a] *Mean ± SD*	*Males* *Mean ± SD*	*All participants* *Mean ± SD*	*Normal range*
Age (years)	59.2 ± 9.7	57.8 ± 9.5	58.6 ± 9.7	—
Height (cm)	163.1 ± 7.8	174.5 ± 11.2	166.5 ± 9.9	—
Weight (kg)*	91.53 ± 23.5	108.8 ± 32.4	96.5 ± 26.8	—
BMI (kg/m^2)	34.2 ± 7.7	35.5 ± 9.0	34.7 ± 8.1	≤24
Waist (cm)	101.6 ± 16.6	109.6 ± 18.3	104.1 ± 17.4	≤88 f,[a] ≤102 m[a]
Hip (cm)	118.4 ± 14.1	114.9 ± 15.1	117.3 ± 14.4	<108 f,[a] <105 m[a]
Waist-hip ratio**	0.85 ± 0.08	0.95 ± 0.05	0.88 ± 0.09	≤0.85 f,[a] ≤0.90 m[a]
Systolic BP (mmHg)	131.0 ± 19.7	133.3 ± 14.1	132.1 ± 18.5	≤120
Diastolic BP (mmHg)	81.4 ± 11.4	81.0 ± 12.2	81.3 ± 11.6	≤80
HDL CHOL (mg/dL)**	53.2 ± 14.1	41.6 ± 11.1	49.7 ± 14.7	>39
LDL CHOL (mg/dL)	117.5 ± 28.6	127.5 ± 31.8	118.6 ± 29.1	≤99
Total CHOL (mg/dL)	188.6 ± 37.5	186.9 ± 33.6	185.5 ± 35.5	100–200
Triglycerides (mg/dL)	83.9 ± 57.2	88.5 ± 44.9	85.2 ± 53.7	≤149
Glucose (mg/dL)*	98.8 ± 21.6	122.1 ± 55.6	105.4 ± 34.4	65–99
CRP (mg/dL)	0.6 ± 0.8	0.6 ± 0.8	0.6 ± 0.8	≤1
Leptin (ng/mL)**	54.0 ± 21.9	18.5 ± 17.2	44.6 ± 26.3	4.7–23.7
YPAS (kcal/week)	5523.4 ± 5238.3	6010.2 ± 7208.4	5957.4 ± 6037.4	—
Sleep (hours per night)	6.8 ± 1.0	6.4 ± 1.2	6.7 ± 1.1	—

BMI, body mass index; CRP, C-reactive protein; f, females; HDL CHOL, high-density lipoprotein cholesterol; LDL CHOL, low-density lipoprotein cholesterol; m, males; Total CHOL, total cholesterol; YPAS, Yale Physical Activity Survey score (reflecting energy expenditure).

[a]Sample was $n = 77$ due to 12 participants not disclosing sex.

[b]Normal values are tentative and depend on height.

*$p < 0.01$, **$p < 0.001$.

(Table 3). There were no significant relationships between serum leptin and hours of sleep, physical activity, or any of the other examined variables (including W/H). Of note, hours of sleep was negatively associated with total cholesterol ($r = -0.305$, $p < 0.01$), triglycerides ($r = -0.267$, $p < 0.01$), and LDL ($r = -0.253$, $p < 0.05$). YPAS was negatively associated with systolic BP ($r = -0.241$, $p < 0.05$), while smoking was positively associated with both systolic ($r = 0.335$, $p < 0.01$) and diastolic BP ($r = 0.245$, $p < 0.05$) (Table 3). Because of the sex differences, separate correlation analyses were performed for men and women. For males, leptin was significantly associated with hours of sleep ($r = 0.474$, $p < 0.05$), BMI log ($r = 0.465$, $p < 0.05$), current smoking ($r = 0.545$, $p < 0.01$), waist circumference ($r = 0.841$, $p < 0.001$), and hip circumference ($r = 0.830$, $p < 0.001$). Similar results were noted for females, with leptin significantly related to hours of sleep ($r = -0.310$, $p < 0.05$), BMI log ($r = 0.706$, $p < 0.001$), waist circumference ($r = 0.626$, $p < 0.001$), and hip circumference ($r = 0.671$, $p < 0.001$). However, for females, there was a significant relationship between leptin and serum CRP ($r = 0.375$, $p < 0.01$), but no significant relationship between leptin and current smoking.

In the initial multiple stepwise regression analysis, all independent variables, including confounders, that were significantly related to leptin (sex, BMI log-transformed, hip and waist circumferences, BP medication, serum CRP, and current smoking) in the bivariate analyses were entered with leptin as the dependent variable. The results showed that 67% of the variance in leptin was accounted for in the model [$R^2 = 0.67$, $F(1, 65) = 64.570$, $p < 0.001$] (Table 4). In Model 1, hip circumference was the only significant variable, and in Model 2, hip circumference and sex (being female) were statistically significant (Table 4). Both waist circumference and BMI log transformed approached significance in Model 2. A subsequent analysis (Model 3) was conducted, which included both significant and marginally significant independent variables (sex, hip and waist circumferences, BMI log transformed) from Models 1 and 2. The results showed that 75.8% of the variance in leptin was explained by this model [$R^2 = 0.758$, $F(4, 66) = 55.871$, $p < 0.001$] with sex (being female), hip circumference, and waist circumference statistically significant. BMI log transformed was no longer significant in this model (Table 4).

Discussion

This study examined the relationship between serum leptin and selected cardiovascular risk factors in midlife and older AAs. Specifically, the relationship between serum leptin and anthropometries (BMI, circumferences [waist, hip, W/H]), metabolic health (BP, serum glucose, lipids, and CRP), and health behaviors (physical activity, hours of sleep) were examined. Very strong bivariate correlations were noted between serum leptin and sex (being female), anthropometries, as well as serum CRP. The results of the stepwise multiple regression analyses were similar showing that sex, hip circumference, and waist circumference were the strongest predictors of serum leptin. These results suggest that hip circumference and waist circumference have unique independent contributions to the serum leptin level in these AA women and may indicate the state of leptin dysregulation and resistance.

Our results are consistent with earlier, yet, rare studies in AAs showing a positive relationship between serum leptin and adiposity, especially in AA women.[12] These findings are also similar to studies in other ethnic/racial groups. For example, in a study conducted in Mexico to determine the relationship between serum leptin and metabolic syndrome (MetS) in obese female and male workers ($n = 204$, 20–56

Table 3. Correlation Analysis for All Participants

	Age	*BMI Log*	*Waist*	*Hip*	*W/H*	*SBP*	*DBP*	*LDL CHOL*	*HDL CHOL*	*Total CHOL*	*Glucose*	*CRP*	*Leptin*	*TG*	*Sleep*	*YPAS*	*Smoke*	*Educ level*	*Sex*	*BP Meds*	*CHOL Meds*	*Diabetes Meds*
Age	—																					
BMI Log	–0.222*	—																				
Waist	–0.251*	0.761**	—																			
Hip	–0.338**	0.760**	0.784**	—																		
W/H	–0.011	0.314**	0.645**	–0.040	—																	
SBP	0.163	–0.060	0.134	–0.134	0.049	—																
DBP	–0.340**	–0.021	0.038	0.035	0.040	0.680***	—															
LDL CHOL	0.023	0.123	0.102	0.041	0.124	–0.079	0.099	—														
HDL CHOL	0.178	–0.219*	–0.272	–0.272*	–0.414**	–0.085	–0.103	0.064	—													
Total CHOL	0.091	–0.005	0.000	–0.043	0.055	–0.102	0.042	0.898***	0.383***	—												
Glucose	–0.036	0.410***	0.245*	0.121	0.258*	0.124	0.008	0.150	–0.042	0.118	—											
CRP	–0.081	0.200	0.243*	0.268*	0.068	0.113	–0.250*	–0.124	0.078	–0.053	0.044	—										
Leptin	–0.154	0.469***	0.440***	0.658***	–0.100	–0.016	0.146	–0.076	0.143	–0.022	–0.129	0.277*	—									
TG	0.002	–0.068	0.031	–0.187	0.298**	0.024	0.039	0.074	–0.214*	0.367***	0.065	0.044	0.099	—								
Sleep	0.189	–0.136	–0.139	–0.057	–0.160	0.062	–0.048	–0.253*	0.030	–0.305**	–0.131	–0.105	0.105	–0.267**	—							
YPAS	–0.024	0.126	0.042	0.212	–0.175	–0.241*	–0.122	–0.056	0.079	–0.073	–0.018	–0.031	–0.093	–0.017	0.092	—						
Smoke	–0.124	0.087	0.048	0.019	0.017	0.335**	0.245*	–0.158	0.070	–0.100	–0.070	0.041	–0.007	0.009	0.069	0.091	—					
Educ level	–0.092	–0.084	0.063	0.058	0.038	–0.135	–0.064	–0.108	–0.047	–0.116	–0.097	0.026	–0.026	–0.019	0.113	0.051	–0.119	—				
Sex	0.067	–0.073	–0.214	0.113	0.486***	–0.057	0.013	–0.165	0.371***	0.021	–0.293**	0.032	0.623***	–0.039	0.157	–0.038	–0.060	–0.062	—			
BP Meds	–0.302**	–0.270*	0.127	0.155	0.029	0.071	–0.108	0.202	0.133	0.122	0.107	0.112	0.216*	0.098	0.086	–0.021	0.078	–0.161	–0.060	—		
CHOL Meds	0.289	0.100	0.229	0.071	0.294	0.228	–0.038	–0.341*	–0.079	–0.256	0.052	0.428**	–0.014	0.025	–0.032	0.005	0.131	0.100	0.111	0.298	—	
Diabetes Meds	0.197	0.013	0.046	–0.025	0.116	0.124	–0.101	–0.316**	–0.093	–0.296**	0.200	0.107	–0.069	0.013	0.092	–0.110	0.130	–0.060	–0.089	0.279**	0.291	—

BP Meds, blood pressure medications; CHOL Meds, cholesterol medications; DBP, diastolic blood pressure; Diabetes Meds, diabetes medications; Hip, hip circumference; SBP, systolic blood pressure; Sleep, hours of sleep per night; TG, triglycerides; Total CHOL, total cholesterol; W/H, waist/hip ratio; Waist, waist circumference.

*$p < 0.05$, **$p < 0.01$, ***$p < 0.001$.

Table 4. Multiple Regression Models with Serum Leptin as Dependent Variable and Selected Independent Variables (Predictors)

Predictors	β	t-*value*	*Significance* (p-*value*)	R^2	*Adjusted* R^2	F
Model 1				0.380	0.371	40.457***
Hip	0.616	6.361***	0.001			
Excluded						
Female	0.558	8.036***	0.001			
BMI log	0.015	0.090	0.921			
Waist	–0.231	–1.455	0.151			
BP Meds	–0.153	–1.578	0.119			
CRP	0.100	0.998	0.322			
Currently smoking	0.112	0.358	0.120			
Model 2				0.689	0.679	64.570***
Hip	0.564	8.113***	0.001			
Female	31.024	8.036***	0.001			
Excluded						
BMI log	0.204	1.941	0.057			
Waist	0.236	1.874	0.066			
BP Meds	–0.084	–1.202	0.066			
CRP	0.112	1.575	0.120			
Currently smoking	0.025	0.358	0.722			
Model 3				0.772	0.758	55.871***
Hip	0.282	2.428**	0.018			
Female	0.656	9.648***	0.001			
Waist	0.264	2.281*	0.026			
BMI log	0.126	1.267	0.210			

*$p < 0.05$, **$p < 0.01$, ***$p < 0.001$.

years of age), significant associations between serum leptin and several MetS indicators, including BMI and waist circumference, were found.[15] Further, in a study to evaluate the relationship between leptin levels and MetS components in normal and obese females ($n = 136$, 20–60 years) in Saudi Arabia, a strong positive correlation between leptin and hip circumference and BMI was found. Even after adjusting for BMI, a positive association between leptin and hip circumference remained.[15] Finally, similar to other studies,[11] our results showed a strong association between serum leptin and sex (being female) which remained significant in all regression analyses.

Although the utility of waist circumference as a major indicator for CVD risk is widely accepted, it is not the case with hip circumference. For example, the results from Quebec Family Study[37] showed independent but opposing effects of waist and hip circumferences on CVD risk in over 700 men and women of French descent living in Quebec City (Canada). In that study, waist circumference was positively associated with some of the CVD risk factors (*e.g.*, serum lipids). However, hip circumference showed independent and opposite relationships. Similarly, a prospective study in almost 3000 Danes reported that large hip circumference had independent and protective effects on CVD risk and mortality in women but not in men.[38] Anatomically, while waist circumference almost solely reflects the accumulation of visceral fat and a small amount of subcutaneous fat, the hip circumference reflects accumulation of mostly subcutaneous fat and gluteal muscle, as well as the size of bone structure (pelvic width), thus not necessarily negatively influencing CVD risk. In our study, however, hip circumference showed positive correlation with leptin and CRP and negative with HDL cholesterol, each important mediators of CVD risk. Also, hip circumference was the strongest predictor of leptin in regression analyses, even after adjusting for BMI, waist circumference, and sex. Therefore, it seems that hip circumference may have a different role in CVD risk in AA adults compared to other ethnic/racial groups, a unique finding of this study.

Somewhat surprising was the lack of significant associations between leptin and CRP in the regression analysis, despite the significant positive relationship in the bivariate analysis. These findings are in contrast to the results in the Spruijt-Metz et al.[20] study that investigated AA and Latina (female) children ($n = 51$) and found that leptin was significantly associated with CRP regardless of ethnicity. Each of these variables alone indicates a strong relationship between body adiposity and low-grade chronic inflammation.[7] However, the molecular interaction between leptin and CRP is complex and implies that leptin may regulate CRP expression, while CRP may modulate leptin action,[39] the issues beyond the scope of this article.

Although the significant relationship between leptin and BP existed in the bivariate analysis, this relationship was not evident in the regression analysis. This is contrary to the previous studies reporting a positive association between serum leptin and hypertension in the United States adults.[17,18] One possible reason for the lack of significance in this study was that 65.1% of our participants were taking BP medication, resulting in average BP of 132.1/81.3 mmHg, the values slightly above the elevated level. There was no significant relationship between leptin and serum glucose levels, the latter having great variability, ranging from 47 to 326 mg/dL

(average of 105.4 ± 34.4 mg/dL) and indicating that some participants had alarmingly high levels (only ~18% were taking diabetes medication). This might have influenced the results. Similarly, there was no significant association between leptin and serum lipids, which is in contrast to previous studies.[19,21] However, about 32% of participants were taking lipid-lowering medications, probably resulting in on-average normal total cholesterol, triglycerides, and HDL cholesterol (Table 2) and influencing the results.

With regard to the health behavior variables, neither hours of sleep nor physical activity was significantly associated with leptin. The lack of association with leptin and hours of sleep in our study was in contrast to other studies showing increasing leptin levels with loss of sleep in various populations.[25] One reason might be that most of our participants reported getting adequate sleep (average of 6.7 hours per night). In previous studies, the participants were experiencing sleep restrictions.[25] The survey administered in our study did not have a question about sleep loss, thus future studies may need to probe more deeply to determine sleep patterns in relationship to serum leptin in midlife and older AAs. Interestingly, in the bivariate analysis in this study, hours of sleep was significantly and negatively associated with total cholesterol, LDL, and triglycerides, which is in agreement with previous studies.[40,41] With regard to physical activity, other studies reported an inverse relationship between leptin and physical activity in various populations, with those more active having lower levels of leptin.[27] In this study, we used the YPAS, which is a validated self-report measure for physical activity in older adults. The overall YPAS energy expenditure (5957.4 ± 6037.4 kcal/week) was within the range of previous studies assessing selected broader populations of older adults (*i.e.*, 2313 + 2277 kcal/week, retirement home residents; 8125 + 4125 kcal/week, community center participants).[42] However, we did not analyze the YPAS in relationship to energy expenditure by dimension of physical activity, which might give a more accurate picture, especially in view that AAs participate less in vigorous physical activity.[1]

This study's major strength is that it contributes to the limited knowledge base on the relationship of serum leptin and a comprehensive set of CVD risk factors in midlife and older AAs. Of note is that the analysis also included selected health behaviors of sleep and physical activity in addition to established confounding factors. However, there are several limitations to this study, including the relatively small number of participants, its cross-sectional nature, and a narrow geographical region. In addition, health behavior measures were self-reported, possibly introducing some bias. Future studies should incorporate a larger number of participants, more in-depth measures for sleep, and a more thorough analysis of physical acivity, including objective measures such as accelerometry.

Conclusions

Our results show that serum leptin was significantly positively associated with sex (being female) hip circumference and waist circumference, as well as with CRP (although only in bivariate analysis) in the midlife and older AAs. These findings suggest that an increase in hip circumference and an increase in waist circumference have unique independent contributions to an increase in serum leptin and that AA females are particularly at risk. Taken together, our findings point out the contribution of adiposity in general and central and hip obesity in particular to higher leptin levels in AA adults and the risk of leptin resistance in this population.

This study has implications for practice. Excess adiposity can be a sign of high serum leptin and thus leptin resistance would lead to disrupted appetite/satiety regulation. In addition, excess circulatory leptin promotes higher inflammatory state,[5] thus contributing to obesity and onset of CVD,[8] which are particularly relevant in midlife and older AA adults, especially women. This study suggests that, in providing care for this population, health professionals need to monitor serum leptin in relationship to excess adiposity. The positive relationship between BMI and leptin is well established, but this study suggests that hip circumference and waist circumference have an even stronger influence and need to be considered as an additional clinical measure. Finally, this study points out the need to provide more specific monitoring of health care for AA women, which may in general reduce CVD risk and related diseases in this population.

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Authors' Contributions

O.C. conceived and wrote the article under the guidance of P.A.R., J.L.L., and J.Z.I. K.W. assisted with data analysis and I.Y.-C. read drafts of the article.

Disclaimer

The content is solely the responsibility of the authors and does not necessarily represent the official views of NIMHD.

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