The Metabolically Healthy But Obese Phenotype in African Americans

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Obesity has become one of the leading public health concerns in the United States and worldwide. While obesity is associated with the metabolic syndrome, some obese individuals do not possess the constellation of the metabolic abnormalities and are referred to as metabolically healthy but obese (MHO) persons. Limited data exist on the prevalence and characteristics of the MHO in African Americans. The authors studied 126 obese African Americans and defined the MHO phenotype as an individual with a body mass index $\geq$30 kg/m^2, high-density lipoprotein cholesterol $\geq$40 mg/dL, absence of type 2 diabetes mellitus, and absence of arterial hypertension. The correlates of the MHO phenotype with anthropometrical and metabolic indices were examined, as well as the effect of age on these correlates. Results showed that 36 (28.5%) of the individuals were identified with the MHO phenotype. Waist circumference (WC) and waist-to-hip ratio (WHR) were significantly lower ($P<.05$) in MHO than in non-MHO patients. While there were significant lower levels of low-density lipoprotein and triglycerides in MHO among patients younger than 40 years, the significance was lost among patients 40 years or older. This study indicates that increased WC and WHR may be early premetabolic syndrome markers in obese individuals and should warrant aggressive risk factor reduction therapy to prevent future development of related cardiovascular conditions. *J Clin Hypertens (Greenwich).* 2012;14:92–96. ©2011 Wiley Periodicals, Inc.

An estimated 1.1 billion adults worldwide are overweight or obese.[1] Obesity is a leading public health concern in the United States, where 65.7% of adults are either overweight or obese and 32.2% are obese.[2] The prevalence of cardiometabolic risk factors, namely insulin resistance, hypertriglyceridemia, hypertension, and diabetes is significantly higher among overweight and obese individuals. Some obese individuals, however, do not possess the constellation of metabolic abnormalities and have been dubbed as metabolically healthy but obese (MHO).[3] MHO individuals are insulin-sensitive, normotensive, and have normal lipid profiles[3,4] despite higher levels of body fat. Earlier studies suggest that they could represent as much as 20% of the obese population.[3,5,6] Wildman and colleagues[7] reported in a sample of 5440 participants from the National Health and Nutrition Examination Surveys (NHANES 1999–2004) that 51.3% of overweight and 31.7% of obese adults were metabolically healthy. Specifically, 29.2% of obese men and 35.4% of obese women were deemed metabolically healthy. The highest prevalence of MHO phenotypes was observed among non-Hispanic blacks and was estimated at 38.9%.[7]

Obesity, hypertension, and dyslipidemia are known cardiovascular (CV) disease risk factors as well as individual or collective components that define the metabolic syndrome. It is therefore important to identify youth and young adults at risk and intervene effectively in their early reversible stages.

Some studies have indicated that the MHO phenotype is characterized by less visceral adipose tissue.[8–10] Substantial evidence also suggests that African Americans have less visceral fat than whites at a similar body mass index (BMI).[11–15] This racial difference in body fat distribution has been observed in black children and adolescents.[16–18] There are, however, limited data on the prevalence and characteristics of the MHO phenotype in African Americans.

We therefore postulated that the prevalence of MHO phenotype may be higher in the African American obese population. Additionally, we determined which anthropometrical measure would be most useful for predicting the MHO phenotype among African American obese populations.

METHODS

The study consisted of 126 obese (BMI $\geq$30 kg/m^2) African American patients (114 women, 12 men) selected from a cohort of 518 obese patients who enrolled in a risk factor reduction program at Howard University Clinical Research Center. The 126 patients were selected because all parameters to be investigated were available for them.[19] Patients provided written consent approved by the institutional research board to participate in the study. There was no evidence of other CV disease (CVD) or peripheral vascular disease by history or physical examination in these patients.

Several definitions have been proposed to define the MHO phenotype.[3,4,7,20,21] In this study, we adopted the definition of Aguilar-Salinas and colleagues[20] for

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the MHO phenotype, described as an individual with the following characteristics: BMI $\geq$30 kg/m^2, high-density lipoprotein (HDL) cholesterol $\geq$40 mg/dL, absence of type 2 diabetes mellitus (DM) (ie, a random glucose concentration <200 mg/dL or a fasting glucose <126 mg/dL), and absence of arterial hypertension (ie, systolic blood pressure (SBP) <140 mm Hg and diastolic blood pressure (DBP) <90 mm Hg).

We obtained anthropometrical data (height, weight, waist circumference [WC], hip circumference, waist-to-hip ratio [WHR]) and metabolic profile (blood pressure [BP], body fat, fasting lipid profile, and glucose) for the selected patients. The WHR was calculated as the ratio of WC to hip circumference. The hip circumference was measured at the level of greater trochanter with the legs close together. WC was measured at the widest circumference at the level of umbilicus. The arm circumference of each participant was measured and fitted with an appropriately sized BP cuff. BP was measured in the left arm with appropriate large cuffs 3 times at 5-minute intervals after at least 5 minutes of rest, with the patient in the sitting position. Fasting blood samples to assess blood glucose and lipid profile were collected and immediately transported to the central laboratory (without freezing). Total cholesterol, HDL, and triglycerides were measured by enzymatic methods and low-density lipoprotein (LDL) was calculated using the Friedewald equation. Body fat was estimated by the BOD POD method (Life Measurement, Inc, Concord, CA).[22]

Clinical and demographic data are expressed as mean $\pm$ standard deviation or number (percentage). For the combined data, the Student *t* test was used to compare differences in mean for continuous outcomes, between MHO and non-MHO patients. Pearson chi-square test was used to compare differences in categoric outcomes. To examine the potential effect of age on study characteristics and the possible transition of MHO to non-MHO phenotype, data were further grouped by age according to age younger than 40 and 40 years and older. A 2-way factorial analysis was used to examine the effect of age and MHO status on anthropometric and metabolic characteristics. All analysis was performed using SPSS (SPSS, IBM, Armonk, NY) Significance was accepted at $P<.05$.

RESULTS

Table I presents demographic, anthropometric, and metabolic characteristics of the 126 patients. The mean BMI was 43.6$\pm$8.8kg/m^2 and the mean age was 41.5$\pm$10.8 years. A total of 36 (28.5%) patients were identified with MHO phenotype. MHO and non-MHO individuals were comparable for age, BMI, and percentage of body fat. Class III obesity (BMI $\geq$40 kg/m^2) was present in 21 (58.3%) MHO patients. Results showed that WC and WHR were significantly lower in MHO than non-MHO patients. In addition, LDL and triglycerides levels were significantly lower in the MHO group compared with the non-MHO group.

TABLE I . Demographic, Anthropometric, and Metabolic Characteristic of Obese Patients

Physical Characteristics	MHO (n=36)	Non-MHO (n=88)	*P* Value
Female sex, No. (%)	34 (94.40)	78 (88.60)	NS
Age, y	38$\pm$10.41	43$\pm$11.97	.06
[a]BMI, kg/m^2	43.63$\pm$8.66	43.47$\pm$8.99	.92
Body fat, %	50.06$\pm$5.56	50.49$\pm$4.03	.66
Waist circumference, cm	103.23$\pm$12.23	116.77$\pm$13.97	<.01
Waist-to-hip ratio, cm	0.75$\pm$0.048	0.86$\pm$0.044	<.01
[a]Fasting blood sugar, mg/dL	79.83$\pm$15.07	92.60$\pm$29.52	<.01
Total cholesterol, mg/dL	174.14$\pm$24.15	187.04$\pm$29.71	<.04
LDL cholesterol, mg/dL	96.33$\pm$21.81	112.40$\pm$25.75	<.01
[a]HDL cholesterol, mg/dL	63.64$\pm$9.57	50.41$\pm$13.11	<.01
Triglycerides, mg/dL	90.61$\pm$38.17	119.02$\pm$44.32	<.01
[a]Systolic BP, mm Hg	118.67$\pm$11.95	126.77$\pm$17.90	.01
[a]Diastolic BP, mm Hg	74.47$\pm$8.98	79.46$\pm$10.41	.02
Pulse pressure, mm Hg	44.19$\pm$11.46	48.78$\pm$16.25	.14

Abbreviations: BMI, body mass index; BP, blood pressure; HDL, high-density lipoprotein; LDL, low-density lipoprotein; NS, not significant. [a]Indicates parameters that were part of the definition of metabolically healthy but obese (MHO) phenotype.[20]

Table II presents results of analysis by age category. Results showed that patients in the younger-than-40 group have a higher prevalence of the MHO phenotype compared with those 40 years or older (36.5% vs 23.0%, $P<.01$). Analysis from the 2-way factorial analyses showed no interaction of age and MHO status on WC and WHR. Results showed consistent and significant lower measurement in WC and WHR in the MHO group compared with the non-MHO group. There were, however, interaction effects of metabolic parameters. Among patients younger than 40, results showed significantly lower levels of LDL and triglycerides in MHO than the non-MHO individuals. However, there were no statistically significant differences in blood glucose or the BP components.

In contrast, among patients 40 years or older, there were no significant differences in LDL and triglyceride levels between MHO and non-MHO individuals. However, there were statistically significant differences in the blood glucose and BP components. While the reversal of significance in these metabolic indices from patients younger than 40 years to 40 years or older is not clear from this study, they do suggest that even in an ''obese healthy population,'' dyslipidemia may precede diabetes and the time-dependent changes needed for the development of the hypertension components qualifying for the metabolic syndrome; thus, the MHO state appears to be transient and therefore treatable.

TABLE II. Anthropometric and Metabolic Characteristics by Age Group

Age Category	Physical Characteristics	MHO	Non-MHO	*P* Value
Age <40 y		n=19	n=33	
	Body fat, %	50.00±4.36	49.00±4.24	.67
	Waist circumference, cm	105.00±14.08	114.00±12.78	.04
	Waist-to-hip ratio	0.75±0.05	0.85±0.04	<.01
	[a]Fasting blood sugar, mg/dL	78.21±9.18	90.30±32.71	.12
	Total cholesterol, mg/dL	166.11±26.32	181.06±24.28	.08
	[a]HDL cholesterol, mg/dL	62.95±9.47	44.82±10.95	<.01
	LDL cholesterol, mg/dL	91.37±24.25	112.63±20.24	.01
	Triglycerides, mg/dL	82.32±36.23	115.53±51.96	.03
	[a]Systolic BP, mm Hg	117.68±11.14	116.91±14.05	.84
	[a]Diastolic BP, mm Hg	74.26±8.36	76.50±10.12	.45
	Pulse pressure, mm Hg	43.42±11.37	40.41±9.83	.36
Age ≥40 y		n=17	n=57	
	Body fat, %	49.55±6.89	50.89±3.88	.37
	Waist circumference, cm	100.82±9.61	118.45±14.53	<.01
	Waist-to-hip ratio	0.76±0.03	0.88±0.04	<.01
	[a]Fasting blood, sugar, mg/dL	81.65±19.88	93.84±28.84	.03
	Total cholesterol, mg/dL	183.12±18.27	190.63±32.39	.38
	[a]HDL cholesterol, mg/dL	64.41±9.91	53.93±13.32	.01
	LDL cholesterol, mg/dL	101.88±18.27	112.28±28.29	.16
	Triglycerides, mg/dL	99.88±39.22	120.86±40.40	.08
	[a]Systolic BP, mm Hg	119.76±13.05	133.15±17.36	.01
	[a]Diastolic BP, mmHg	74.71±9.89	81.50±10.26	.03
	Pulse pressure mm Hg	45.06±11.84	54.36±17.38	.05

Abbreviation: HDL, high-density lipoprotein. [a]Indicates parameters that were part of the definition of metabolically healthy but obese (MHO) phenotype.[20] Results showed significant age by MHO-status interaction effects of low-density lipoprotein (LDL), triglycerides, and blood pressure (BP) components.

DISCUSSION

To our knowledge, this is the first study to examine the MHO phenotype in African Americans. Higher BMI has been associated with increased CV risk in numerous studies.[23,24] There are studies suggesting that the value of the metabolic status of obese patients is more important for their further CV risk stratification. This study examined the prevalence of the MHO phenotype in African Americans. From our analysis, we could speculate that the MHO phenotype might be merely an early stage of the metabolic syndrome, with the potential to amplify with aging and become fully expressed over time as individuals accumulate more cardiometabolic risk determinants including central adiposity, insulin resistance, glucose intolerance, dyslipidemia, and hypertension.

We expected that an age-related difference might exist as metabolic risk factors appear increasingly prevalent or worsen as an individual ages.[25] Multiple mechanisms underlying the development of the MHO phenotype have been proposed including an earlier onset of obesity (younger than 20 years of age),[3] less visceral adipose tissue,[4,26] less ectopic fat accumulation in the liver, normal to high levels of insulin sensitivity,[27] and lower inflammation state as suggested by low C-reactive protein (CRP) levels.[28] The strong contribution of CRP has been documented in a study by Karelis and Rabasa-Lhoret,[29] where MHO women were found to have 92.7% lower CRP levels than those ''at risk'' and was suggested as a metabolic marker for the identification of MHO patients. Moreover, studies have indicated that MHO patients have no increased risk for development of CVD or type 2 diabetes,[21,30] and this evidence has prompted debate as to the need for aggressive management of this ''benign'' obesity.

In adults, pattern of excess adipose tissue distribution, rather than the total fat, may be important in conferring CV risk to the obese population. If deposited in the abdomen or visceral adipose tissue, it is considered to be associated with more adverse metabolic complications. That is why fat distribution (measured as WC) is used as one factor for the metabolic syndrome components.[31] WC has been considered as a better index of visceral adipose tissue than WHR and therefore has been advocated as a ''supplemental vital sign'' for every patient.[32] In our study, WC was found to be significantly lower in MHO individuals across both age subgroups, underlying the importance of WC in predicting the MHO phenotype. However, this finding is not consistent with some studies that suggest the lack of relationship between WC and an atherogenic lipid profile in severely obese individuals (BMI ≥40 kg/m^2).[33,34]

The WHR is gaining popularity as a surrogate marker of atherogenic risk. Indeed, in a number of studies, the WHR performed better than WC in predicting CVD.[35,36] Worldwide, WHR has shown a graded and highly significant association with myocardial infarction risk.[37]

Similarly, in a number of studies focusing on African Americans fat distribution in relation with CVD risk, WHR was associated with increase in CVD prevalence in blacks.[38,39] Our results support the measurement of WHR as a valuable tool to predict metabolic abnormalities in morbidly obese African Americans across different age groups.

LIMITATIONS

Our study findings are limited by the relatively small sample size and the preponderance of female sex. Larger studies are therefore required to confirm our findings. This study, however, is perhaps the first study to examine the MHO phenotype in African Americans. Moreover, this study sheds light on the fact that elevated WC and WHR measurements in obese individuals may indicate metabolic abnormality and should warrant aggressive risk factor reduction therapy to prevent development of CV complications in the future.

CONCLUSIONS

Our study suggests that the measurement of WC and WHR is perhaps a more sensitive index of the precursors of the metabolic syndrome than other components or anthropometric measures and should warrant aggressive reduction through appropriate therapeutic lifestyle changes such as diet and exercise to prevent future development of related CV conditions.

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