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Obesity and High Blood Pressure: A Clinical Phenotype for the Insulin Resistance Syndrome in African Americans

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Abstract and Introduction

Abstract

The high prevalence of insulin resistance syndrome in African Americans predisposes this population to higher morbidity and mortality from cardiovascular disease. To test the hypothesis that the combination of obesity and high blood pressure (BP) represents the physical phenotype of insulin resistance syndrome, 337 African-American men and women aged 40-64 years were examined and classified into four groups (nonobese-normal BP, nonobese-high BP, obese-normal BP, obese-high BP), according to presence or absence of obesity and high BP. Mean values of glucose, insulin, lipids, urinary albumin excretion, and clamp-derived insulin sensitivity were determined for each group. Prevalence of prediabetes (24.4%), diabetes (19.2%), and insulin resistance syndrome (87.2%) were highest in the obese-high BP group ($p < 0.001$). Mean triglycerides, urinary albumin excretion, fasting glucose, fasting insulin, and insulin resistance were highest in the obese-high BP group ($p < 0.001$). Subjects with both obesity and high BP showed greater expression of lipid and glucose abnormalities, higher urinary albumin excretion, and greater prevalence of prediabetes, undetected type 2 diabetes, and insulin resistance syndrome.

Introduction

Both type 2 diabetes and obesity have been linked with high blood pressure (BP) and dyslipidemia in a clustering of metabolic abnormalities known as the insulin resistance syndrome (IRS). First described by Reaven in the 1988 Lecture,^[1] IRS has also been known as syndrome X, the metabolic syndrome, and dysmetabolic syndrome. There has been much debate over what criteria are best used for the diagnosis of IRS. In 2001, The National Cholesterol Education Program (NCEP) Adult Treatment Panel III (ATP III) proposed diagnostic criteria as three or more of the following metabolic abnormalities: waist circumference >102 cm (40 in) for men or >88 cm (34 in) for women, triglycerides ≥ 150 mg/dL, high-density lipoprotein (HDL) cholesterol level <40 mg/dL for men or <50 mg/dL for women, BP $\geq 130/85$ mmHg, and fasting glucose ≥ 110 mg/dL.^[2] In a 2003 position statement, the American College of Endocrinology adopted the ATP III guidelines for lipids and BP, but recommended broadening the criteria to include a definition of obesity on body mass index (BMI) and impaired glucose tolerance based on a 2-hour oral glucose tolerance test (OGTT). Analysis of data from the third National Health and Nutrition Examination Survey (NHANES) determined the prevalence of ATP III-defined IRS to range from 6.7% among persons aged 20-29 years to 43.5% among persons aged 60-69 years. In that report, more than 75% of African Americans had at least one metabolic abnormality typical of IRS.^[4]

Individuals with IRS experience a higher incidence of both diabetes and cardiovascular disease. Furthermore, IRS has been associated with higher cardiovascular and total mortality.^[5] Both hypertension and central adiposity have been shown to contribute to insulin resistance. However, not all patients with hypertension have insulin resistance. The purpose of this study was to test the hypothesis that the combination of obesity with high BP is the physical phenotype of IRS. We predicted that more persons with both obesity and high BP would meet the ATP III criteria for IRS and express more metabolic abnormalities of the IRS than subjects with either high BP alone or obesity alone.

Methods

Population

Participants in this cross-sectional study were drawn from a cohort of African-American men and women enrolled in investigations of BP, insulin sensitivity, and cardiovascular risk. This analysis examined 337 African Americans at average age of 32.1 ± 4.4 years. Written, informed consent was obtained from each participant at the time of enrollment at an institutionally approved protocol and consent form. Persons with known diabetes were excluded from initial enrollment. Female participants were evaluated during the follicular phase of the menstrual cycle to limit hormonal variability.

Procedure

Information on health status and current health behaviors was obtained from an enrollment interview. Anthropometric measurements of height and weight were obtained. BMI was calculated as weight (kilograms) divided by height (m squared). BP measurements were obtained from each subject following a 10-minute rest period in a seated position with auscultation with a mercury column sphygmomanometer. The average of two determinations of casual systolic (first phase) and diastolic (fifth phase) was used as the BP. An OGTT was conducted after a 12-hour overnight fast. A blood sample was obtained for serum lipids, insulin, and glucose, then 75 g glucose solution (Glucola; Ames Diagnostic, Elkhart, IN) was ingested. Blood samples were obtained at 30 minutes, 60 minutes, 90 minutes, and 120 minutes post-ingestion and were assayed for plasma insulin and glucose concentrations. A timed, overnight urine specimen was collected. Urine albumin was measured by radioimmunoassay (Double Antibody Assay KHADL; Diagnostic Products Corporation, Los Angeles, CA) and expressed as micrograms per minute. Urine creatinine was measured and urinary albumin excretion (UAE) was calculated in milligrams per gram creatinine.

The euglycemic hyperinsulinemic clamp technique was used to measure insulin-stimulated glucose uptake.^[6,7] Each subject returned to the clinical research unit after a 12-hour overnight fast, at which time the euglycemic clamp procedure was conducted according to methods described previously.^[8] In brief, two peripheral venous catheters were placed for infusion and sample withdrawal. After determination of fasting plasma glucose concentration, hyperinsulinemia was established with a primed constant infusion of insulin according to the method of Rizza et al.^[7] to calculate the primed dose and infusion rate. The primed infusion rate was sufficient to achieve steady state hyperinsulinemia at 80-120% above fasting insulin levels with the goal of suppressing hepatic glucose production. Hyperinsulinemia was maintained for 120 minutes, during which time euglycemia was achieved using a variable infusion of 20% dextrose in water (20% Dextrose Injection USP; Abbott Laboratory, Abbott Park, IL). Insulin (Novolin R; Eli Lilly, Indianapolis, IN) was administered at the concentration of 1000 mU/mL in normal saline. The glucose infusion rate was adjusted by the negative feedback equation of DeFronzo et al.,^[6] according to plasma glucose sampled every 10 minutes.

The insulin-stimulated glucose uptake was computed as the mean glucose infusion during the final 60 minutes of the procedure and expressed as milligrams per kilogram per minute. Higher values of insulin-stimulated glucose uptake are indicative of greater insulin sensitivity. Because the level of steady state hyperinsulinemia achieved during the clamp procedure varied slightly among the cases, an index of insulin sensitivity was calculated by dividing the glucose infusion rate by the mean insulin level achieved during the final 60 minutes of steady state hyperinsulinemia. Because muscle tissue is more insulin resistant relative to adipose tissue, the measured insulin-mediated glucose uptake was adjusted for adiposity. Anthropometric measurements were used to estimate the fat-free mass,^[9,10] and the insulin-stimulated glucose uptake was calculated in milligrams per kilograms of fat-free mass per minute. The adjusted index of insulin sensitivity was also corrected for adiposity and expressed as milligrams per kilograms of fat-free mass per minute divided by mean insulin level.

The fasting serum sample from the OGTT was sent to the lipid research laboratory, where total cholesterol, HDL cholesterol, and triglyceride levels were analyzed with standard enzymatic methods and an automated analyzer (Model 704; Boehringer-Mannheim Diagnostics, Indianapolis, IN). HDL was isolated according to the method of Bachorik. LDL cholesterol was calculated by the Friedewald equation.^[12] Plasma glucose concentration was analyzed with the glucose oxidase technique (YS model 27; Glucostat, Yellow Springs, OH). Plasma insulin concentration was determined with a solid phase radioimmunoassay (Coat-a-Count; Diagnostic Products Corp., Los Angeles, CA). Coefficients of variation for inter- and intra-assay variability for glucose, insulin, and lipid assays were

Data Analysis

Subjects were classified into four groups according to the presence or absence of obesity and high BP (nonobese normal BP, nonobese high BP, obese normal BP, obese high BP). We defined obesity as BMI ≥ 30 . Hypertension was defined as a systolic BP ≥ 130 mm Hg or diastolic BP ≥ 85 mm Hg, according to the ATP III criteria.^[2] Subjects who were on antihypertensive medications were considered to have met the criteria for hypertension, even if their BP was controlled and currently measured $< 130/85$ mm Hg. To determine the relationship of hypertension and obesity to IRS, we examined the mean values of lipids, glucose, insulin, and measured insulin sensitivity in the four groups. A one-way analysis of variance was used to compare the group means. ATP III criteria were used to define IRS for subjects in each of the four BP groups. A subject had IRS if three or more of the following were present: obesity, HDL < 40 mg/dL for men or < 50 mg/dL for women, triglycerides ≥ 150 mg/dL, BP $\geq 130/85$ mm Hg, and fasting glucose ≥ 110 mg/dL or 2-hour

glucose ≥ 140 mg/dL. The proportion of subjects with IRS, prediabetes, and undiagnosed diabetes was compared among the four BMI-BP groups and analyzed using the Pearson χ^2 test.

Because ATP III criteria for BP and obesity were used to define the BMI-BP groups, the analysis was repeated for metabolic abnormalities of dyslipidemia and glucose intolerance, excluding obesity and high BP. Analysis of various categorical models (SAS PROC CATMOD, version 8.2; SAS Institute Inc., Cary, NC) was used to compare the distribution of metabolic abnormalities among the BMI-BP groups.

Results

Data was available from 337 young adult African Americans. Subjects included 117 men and 220 women. Mean age at examination was 32.1 ± 4.1 years. This analysis included 133 nonobese subjects with normal BP, 48 nonobese subjects with high BP, 78 obese subjects with normal BP, and 78 obese subjects with high BP. As determined by the OGTT, 20.8% of subjects had prediabetes (impaired fasting glucose or impaired glucose tolerance) and 20 subjects (5.9%) had undiagnosed type 2 diabetes. Of the 337 subjects, 115 (34.1%) met the ATP III criteria for diagnosis of IRS.

[Table I](#) provides the gender distribution and mean age, BMI, and BP parameters for each of the four subject groups. Subjects with high BP ($\geq 130/85$ mm Hg) tended to be older. Mean age among subjects with high BP was 33 years, compared with 24.6 years among subjects with normal BP, a difference that was statistically significant at this sample size ($p < 0.001$). Among the nonobese persons, mean age averaged 24.6 and 25.2 in the normal and high BP groups respectively. Even in the absence of obesity, many of these subjects were overweight, with a BMI > 25 . Because the groups were defined by the presence or absence of obesity and high BP, both BMI and BP were statistically different among the groups. BMI was higher in the obese groups (37 vs. 25), and both systolic and diastolic BP was higher in the high BP groups (all $p < 0.001$). However, BMI was not statistically different between the two obese groups, and systolic or diastolic BP was not statistically different between the two high BP groups (all $p > 0.05$). The gender distribution was skewed with a higher percentage of women in the two obese groups ($p < 0.001$). This reflects the higher prevalence of obesity among African-American women compared with men.

[Table II](#) provides the mean values for lipids and OGTT measurements in each of the four groups. There was no significant difference in total cholesterol between the four groups. There was a statistically significant trend for linearity in LDL measurements, with higher LDL measurements in the obese with high BP group and lowest values in the nonobese with normal BP group ($p = 0.04$). HDL was lower among obese subjects with or without high BP compared with nonobese subjects ($p = 0.001$). Triglycerides were lowest in the nonobese with normal BP group. The presence of either high BP or obesity resulted in proportionate increases in triglyceride levels. When both obesity and high BP were present, the triglycerides were nearly 20 mg/dL higher than when either obesity or high BP was present alone. This difference in triglyceride measurements reached statistical significance ($p < 0.001$), with a significant trend for linearity ($p < 0.001$).

Both fasting and 2-hour glucose measurements from the OGTT were statistically different between groups (both $p < 0.001$). Fasting glucose was significantly higher in the groups with high BP compared with those with normal BP in both the nonobese and obese subjects ($p = 0.03$). The 2-hour glucose measurements rose from 111.9 mg/dL in the nonobese with normal BP to 144.4 mg/dL in the obese with high BP group ($p < 0.001$), with a statistically significant linear trend ($p < 0.001$). Similarly, the mean fasting insulin rose from 9.8 $\mu\text{U/mL}$ in the nonobese with normal BP group to 19.6 $\mu\text{U/mL}$ in the obese with high BP group, a difference that was statistically significant ($p < 0.001$) and showed a linear trend ($p < 0.001$).

IRS was absent in all nonobese subjects with normal BP. The presence of high BP alone was associated with 25% prevalence of IRS, and obesity alone was associated with 44.9% prevalence of the IRS. However, 87.2% of subjects with both high BP and obesity had at least one of the metabolic abnormalities and therefore fulfill the diagnostic criteria for IRS.

Figure 1 depicts the prevalence of prediabetes and type 2 diabetes in each of the BMI-BP groups. The prevalence of abnormal glucose tolerance in the form of diabetes or prediabetes was 15.8% in the nonobese with normal BP group. With the addition of high BP, the prevalence rose to 20.8%. In the obese population, the prevalence of abnormal glucose tolerance went from 32.1% in those with normal BP to 43.6% in those with high BP. The combination of obesity with high BP was associated with the highest prevalence of prediabetes or type 2 diabetes ($p < 0.001$). The prevalence of prediabetes and type 2 diabetes was lowest in the nonobese with normal BP group and increases significantly with the addition of obesity or high BP. The prevalence of type 2 diabetes in the obese with high BP group was 19.2%, compared with 0%-2.6% in all other groups ($p < 0.001$).

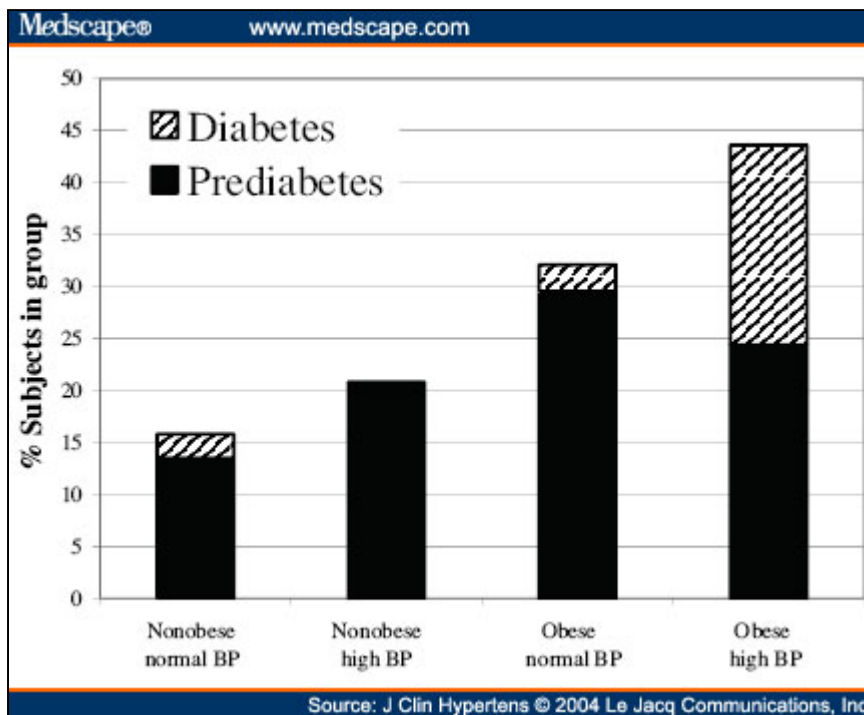


Figure 1. Prevalence of prediabetes and undiagnosed type 2 diabetes in each of the four body mass index-blood pressure (BP) groups.

Of the 337 subjects, 283 returned and underwent a euglycemic hyperinsulinemic clamp. Figure 2 shows the mean sensitivity as measured by the euglycemic hyperinsulinemic clamp. M was lower in the obese groups compared with nonobese groups ($p < 0.001$). When corrected for both adiposity and the steady state insulin level achieved, the difference becomes even more striking. In addition, high BP in the absence of obesity results in decreased insulin sensitivity (14.3 mg/kg fat-free mass/min/ μ U insulin \times 1000), a difference that is statistically significant ($p = 0.02$). The insulin sensitivity is further reduced in both groups with obesity to 6.5 with normal BP and 6.6 with high BP ($p < 0.001$).

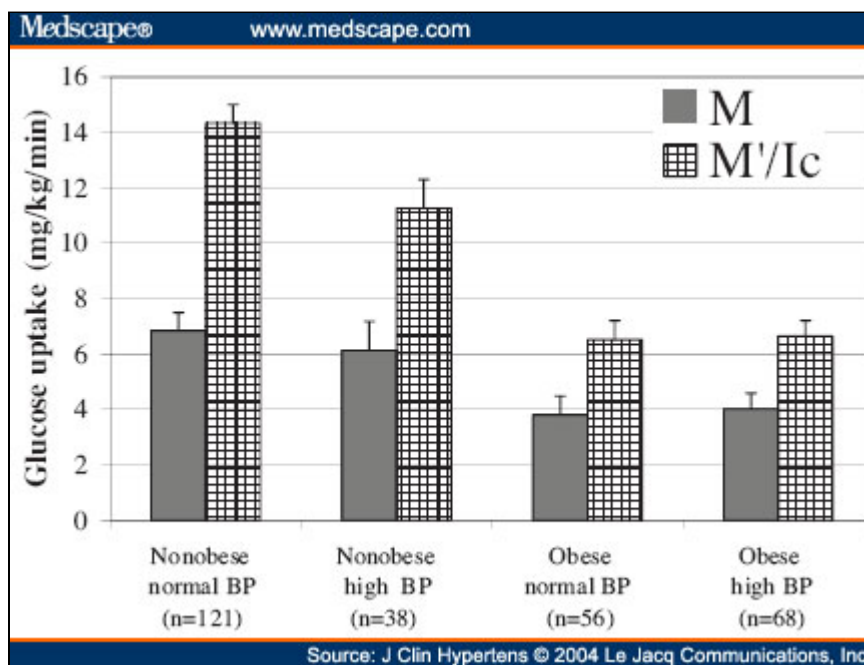


Figure 2. Mean insulin sensitivity as measured by euglycemic hyperinsulinemic clamp in each body mass index-blood pressure (BP) group. M=mean \pm standard error for measured glucose uptake (in mg/kg/min); M'/Ic=glucose uptake corrected for adiposity and level of steady-state clamp hyperinsulinemia (mg/kg fat-free mass/min/ μ U).

Figure 3 shows the mean urine albumin excretion per gram creatinine in each group from an overnight urine colle

performed at the time of the clamp procedure. Nonobese subjects with normal BP had the lowest UAE. In the pre-high BP, the mean UAE increased to 7.1 mg/g creatinine, a difference that was not statistically significant at this size ($p=0.16$). In the presence of both obesity and high BP, UAE increased to 17.6 mg/g creatinine, a statistically significant difference compared with nonobese and obese subjects with normal BP ($p<0.001$, $p=0.006$, respective

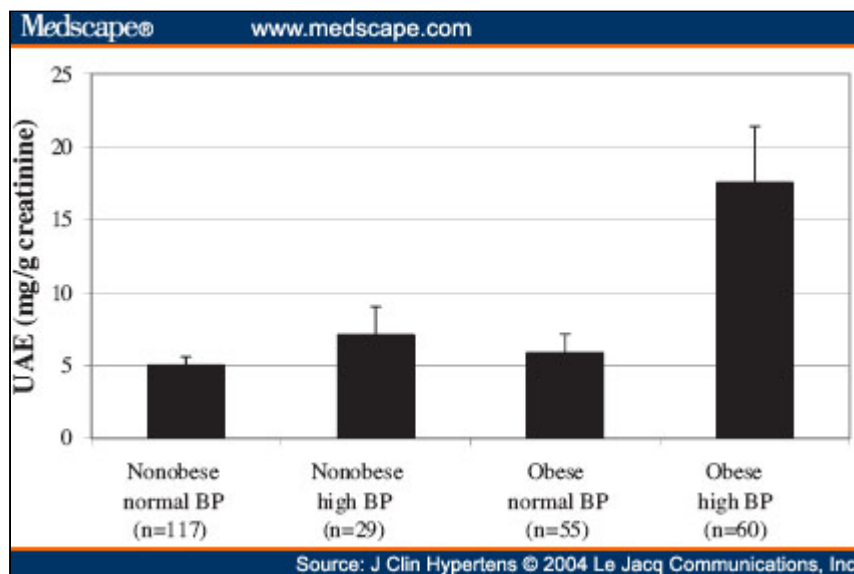


Figure 3. Bars represent the mean \pm standard error of urinary albumin excretion (UAE) in mg/g creatinine for each body mass index-blood pressure (BP) group.

The distribution of subjects within each group by number of coexisting metabolic abnormalities (low HDL level, high triglycerides, or abnormal glucose tolerance) is presented in Figure 4. The distribution of metabolic abnormalities significantly skewed with a greater number of abnormalities in the subjects with obesity ($p<0.001$) and/or high BP ($p=0.006$). There was no significant interaction between obesity and high BP ($p=0.40$) and thus the combination of obesity and high BP does not seem to cause a negative synergistic effect, but rather seems to be the combined linear effect of each factor of obesity and high BP.

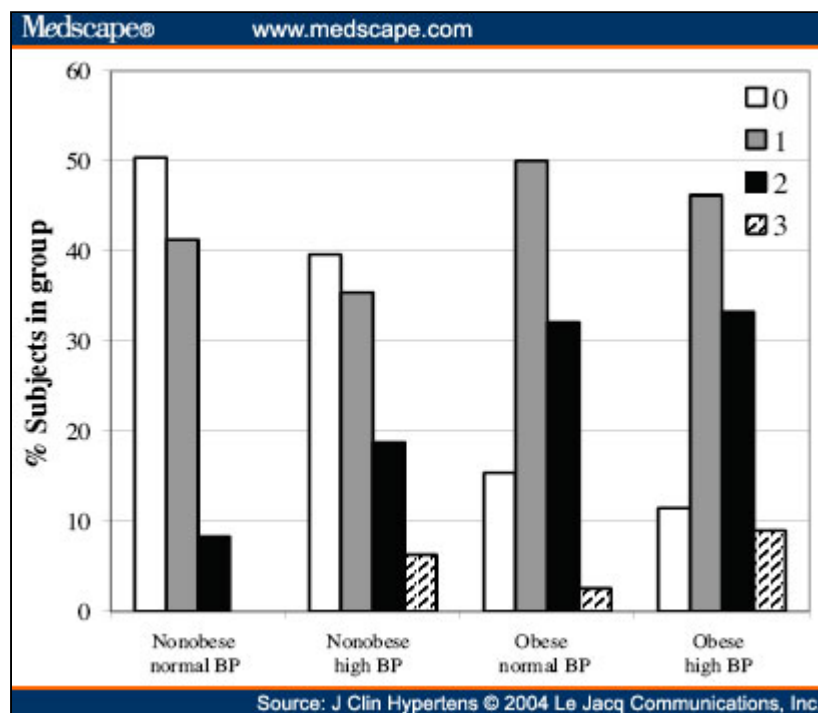


Figure 4. Distribution of subjects by number of insulin resistance syndrome-associated metabolic abnormalities present (body mass index and blood pressure [BP] excluded). White bar=percentage of subjects with no metabolic abnormalities; gray bar=percentage of subjects in each body mass index-BP group with one metabolic abnormality; black

bar=percentage of subjects with two metabolic abnormalities increases in subjects with high BP, obesity, or both; striped bar=percentage of subjects with three metabolic abnormalities is greatest in the obese with high BP group.

Discussion

The results of this study show a strong association between the phenotype of obesity plus high BP with the metabolic abnormalities of IRS. HDL is lower in the obese groups with and without high BP, while both LDL and triglycerides are highest in subjects with both obesity and high BP. Both fasting and 2-hour glucose by OGTT were highest in the subjects with both obesity and high BP. Subjects in the group with obesity and high BP had significantly greater prevalence of glucose intolerance and previously undetected diabetes. Microalbuminuria is a trait considered by some to be another characteristic of IRS.¹³⁻¹⁵ Our data also show significantly greater UAE in subjects with both obesity and high BP. Subjects with both obesity and high BP tended to have more concurrent metabolic abnormalities consistent with IRS. Therefore, according to ATP III criteria, approximately 87% of subjects with obesity and high BP had at least one metabolic abnormality and fulfilled the criteria for IRS.

IRS consists of a cluster of metabolic and physiologic abnormalities that cosegregate within an individual. The original definition of the syndrome, first called syndrome X by Reaven in 1988,^[1] included hypertension, glucose intolerance, hypertriglyceridemia, and low HDL level. Since then, several other abnormalities have been associated with IRS, including central adiposity, dyslipidemia, insulin resistance, hyperuricemia, fibrinolysis, hemostasis, inflammation, and microalbuminuria. Presence of IRS is associated with increased mortality and morbidity from coronary heart disease and cardiovascular disease.^[5,15-17] Furthermore, risk of coronary heart disease and cardiovascular disease are elevated in the presence of only one to two risk factors for IRS.^[17]

Multiple studies have used factor analysis to investigate the clustering of variables considered to be part of IRS.^[14] These studies have included subjects of multiple races ranging in age from adolescence to late adulthood. While results vary slightly according to the study population, all analyses have found two or more independent factors or clusters of abnormalities. Insulin resistance, obesity, elevated plasma glucose, and dyslipidemia have generally been found to load onto one factor, while hypertension and insulin resistance have been found to load onto a separate second factor. In some of these studies, insulin measurements contribute across multiple separate factors, which suggests that insulin resistance could be the core abnormality of IRS. A recent study by Ford^[20] of 6868 subjects, of which 1834 were African American, identified three separate factors contributing to the insulin resistance syndrome in subjects aged 20-44 years. In this study, HDL cholesterol level, triglycerides, insulin, and waist circumference were found to load together onto Factor 1; systolic blood pressure, waist circumference, and uric acid were found to load onto Factor 2; and glucose and UAE were found to load onto Factor 3. Factor analysis conducted by Hanley et al.^[18] identified two factors, a metabolic factor that loaded with BMI, glucose, insulin sensitivity, HDL cholesterol level, and triglyceride level and a BP factor that loaded with systolic and diastolic blood pressure. These studies all suggest that BP acts separately from the metabolic factors to contribute to IRS.

Triglyceride levels have been reported to be lower in both male and female African Americans compared with age-matched whites.^[22,23] Similarly, HDL levels have been reported to be higher in African Americans than whites.^[22] African Americans still have higher rates of heart disease and mortality from cardiovascular disease.^[24] While high triglycerides and low HDL levels are less prevalent, hypertension, obesity, and type 2 diabetes are more prevalent in African Americans than whites.^[25-27] This suggests that obesity, diabetes, insulin resistance, and high BP rather than high triglycerides and low HDL cholesterol levels may be the major determinants of IRS in African Americans. Alternatively, the relatively low prevalence of elevated triglycerides and low HDL cholesterol levels raise the question of whether the threshold for the effects of dyslipidemia is lower in African Americans.

National population data show that the prevalence of type 2 diabetes increased from 8.9% among participants in the 1980 NHANES to 12.3% among participants in the 1988-1994 NHANES.^[25] In addition, the prevalence of obesity is increasing. The 1988-1994 NHANES found a 22.8% prevalence of obesity, which increased to 30.5% by 1999-2000. In our study, we found the prevalence of prediabetes ranged from 12.9% in the nonobese normal BP group to 29.5% in the obese normal BP group. In the subjects with obesity and high BP, the prevalence of prediabetes was 24.4%. However, in this group the prevalence of undiagnosed diabetes was 19.9%, which is much higher than the prevalence in the general population. Subjects with both obesity and high BP had undiagnosed diabetes almost as frequently as prediabetic persons. Persons with IRS frequently have an elevated 2-hour glucose on OGTT in the presence of normal fasting glucose. In a sample of young adult African Americans, more prediabetes was detected by the 2-hour plasma glucose than the fasting plasma glucose. Screening for diabetes or prediabetes with the measurement of only fasting plasma glucose measurement fails to identify many persons with impaired glucose tolerance. For this reason, the American College of Endocrinology currently recommends OGTT for screening for IRS.^[3]

Due to the increasing rates of obesity and diabetes, identification of IRS is important for management of premature cardiovascular events. Lifestyle and pharmacologic interventions can improve insulin sensitivity and improve the metabolic components of IRS. Both high BP and obesity are traits easily determined in a physician's office. We fo

87% of our African-American subjects with both obesity and high BP possessed at least one other metabolic abnormality and met the ATP III criteria for diagnosis of IRS. Subjects with the clinical phenotype of obesity plus high BP also had the highest rates of previously undetected diabetes. Because these data are only on African Americans, generalizability will be limited. However, this clinical phenotype is easily identified, and subjects with both obesity and high BP from a given group may have increased rates of treatable metabolic abnormalities.

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Tables

Table I. Mean Parameters of Each Body Mass Index (BMI)-Blood Pressure (BP) Group

Medscape®		www.medscape.com			
	NONOBESE NORMAL BP	NONOBESE HIGH BP	OBESE NORMAL BP	OBESE HIGH BP	
n	133	48	78	78	
Age (years)	31.2±4.1	33.2±5.4	31.6±4.0	33.5±4.3	
Women (%)	61.7	39.6	78.2	74.4	
BMI	24.6±3.3	25.2±3.3	36.6±5.4	37.3±6.9	
SBP (mm Hg)	113±9	141±13	118±8	143±13	
DBP (mm Hg)	72±9	91±14	74±10	92±11	
SBP=systolic blood pressure; DBP=diastolic blood pressure					
Source: J Clin Hypertens © 2004 Le Jacq Communications, Inc.					

Table II. Mean Metabolic Measures From Lipid and Oral Glucose Tolerance Testing

Medscape®		www.medscape.com				P VALUE	
MEASURE	NONOBESE NORMAL BP	NONOBESE HIGH BP	OBESE NORMAL BP	OBESE HIGH BP	GROUP	LINEAR	
Total cholesterol [†] (mg/dL)	176±39	184±44	174±31	186±40	0.15	0.18	
LDL [†] (mg/dL)	107±33	115±34	111±28	118±41	0.13	0.04	
HDL [†] (mg/dL)	53±16	52±23	45±11	46±14	0.001	<0.001	
Triglycerides ^{††} (mg/dL)	72±29	91±42	91±40	110±65	<0.001	<0.001	
Fasting glucose [‡] (mg/dL)	90.7±10.6	94.6±10.0	97.2±23.9	105.0±21.4	<0.001	<0.001	
2-Hour glucose [‡] (mg/dL)	111.9±33.2	116.4±26.4	132.5±47.0	144.4±53.7	<0.001	<0.001	
Fasting insulin ^{‡‡} (μU/mL)	9.8±9.0	10.1±6.8	16.2±8.7	19.6±18.9	<0.001	<0.001	
Prediabetes or diabetes (%)	15.8	20.5	32.1	43.6	<0.001*		
Prevalence IRS (%)	0.0	25.0	44.9	87.2	<0.001*		
BP=blood pressure; LDL=low-density lipoprotein; HDL=high-density lipoprotein; IRS=insulin resistance syndrome; *Pearson's χ^2 test; [†] to convert total, LDL, and HDL cholesterol in mg/dL to mmol/L, multiply by 0.0259; ^{††} to convert triglycerides in mg/dL to mmol/L, multiply by 0.0113; [‡] to convert glucose in mg/dL to mmol/L, multiply by 0.0555; ^{‡‡} to convert insulin in μU/mL to pmol/L, multiply by 6.94							
Source: J Clin Hypertens © 2004 Le Jacq Communications, Inc.							

References

1. Reaven GM. Role of insulin resistance in human disease. *Diabetes*. 1988;37:1595-1607.
2. Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. Executive summary of the Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). *JAMA*. 2001;285:2486-2497.
3. Einhorn D, Reaven GM, Cobin RH. American College of Endocrinology position statement on the insulin resistance syndrome. *Endocr Pract*. 2003;9:240-252.
4. Ford ES, Giles WH, Dietz WH. Prevalence of metabolic syndrome among US adults: Findings from the Thi

- National Health and Nutrition Examination Survey. *JAMA*. 2002;287:356-359.
5. Lakka HM, Laaksonen DE, Lakka TA, et al. The metabolic syndrome and total and cardiovascular disease in middle-aged men. *JAMA*. 2002;288:2709-2716.
 6. DeFronzo R, Tobin J, Andres R. Glucose clamp technique: a method for quantifying insulin secretion and resistance. *Am J Physiol*. 1979;237:E214-E223.
 7. Rizza RA, Mandarino LJ, Geric JE. Dose-response characteristics for effects of insulin on production and utilization of glucose in man. *Am J Physiol*. 1981;240:E630-E639.
 8. Falkner B, Kushner H, Tulenko T, et al. Insulin sensitivity, lipids, and blood pressure in young African Americans. *Arterioscler Thromb Vasc Biol*. 1995;15:1798-1804.
 9. Wormsley J. A comparison of the skinfold method with extent of 'overweight' and various height-weight relationships in the assessment of obesity. *Br J Nutr*. 1977;38:271-284.
 10. Heymsfield S, McManus C, Stevens V, et al. Muscle mass: reliable indicator of protein-energy malnutrition and outcome. *Am J Clin Nutr*. 1982;35:1192-1199.
 11. Bachorik PS, Walkner RE, Virgil DG. High-density-lipo-protein cholesterol in heparin-MnCl₂ supernates determined with the Dow enzymic method after precipitation of -Mn²⁺ with HCO₃. *Clin Chem*. 1984;30:839-842.
 12. Friedwald WT, Levy RI, Frederickson DS. Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. *Clin Chem*. 1972;18:499-502.
 13. Kim YI, Kim CH, Choi CS, et al. Microalbuminuria is associated with the insulin resistance syndrome independent of hypertension and type 2 diabetes in the Korean population. *Diabetes Res Clin Pract*. 2001;52:145-152.
 14. Groop L, Ortho-Melander M. The dysmetabolic syndrome. *Curr Control Trials Cardiovasc Med*. 2002;3:2-1
 15. Isomaa B, Almgren P, Tuomi T. Cardiovascular morbidity and mortality associated with the metabolic syndrome. *Diabetes Care*. 2001;24:683-689.
 16. Wilson PW, Kannel WB, Silbershatz H, et al. Clustering of metabolic factors and coronary heart disease. *A Intern Med*. 1999;159:1104-1109.
 17. Malik S. Importance of number of metabolic syndrome risk factors in predicting cardiovascular disease and mortality in U.S. persons. American Heart Association's Scientific Sessions 2003. Available at: <http://www.sessionsonline.org/viewByDayMon.asp> Accessed on November 11, 2003.
 18. Hanley AJG, Karter AJ, Fester A, et al. Factor analysis of metabolic syndrome using directly measured insulin sensitivity: the Insulin Resistance Atherosclerosis Study. *Diabetes*. 2002;51:2642-2647.
 19. Meigs JB, D'Agostino RB, Wilso OW, et al. Risk variable clustering in the insulin resistance syndrome: the Framingham Offspring Study. *Diabetes*. 1997;46:1594-1600.
 20. Ford ES. Factor analysis and defining the metabolic syndrome. *Ethn Dis*. 2003;13:429-437.
 21. Chen W, Srinivasan SR, Elkasabany A, et al. Cardiovascular risk factors clustering features of insulin resistance syndrome (syndrome X) in a biracial (black-white) population of children, adolescents, and young adults: the Bogalusa Heart Study. *Am J Epidemiol*. 1999;150:667-674.
 22. Hutchinson RG, Watson RL, Davis CE, et al. Racial differences in risk factors for atherosclerosis: the ARIC Study. *Angiology*. 1997;48:279-290.
 23. Hall WD, Clark LT, Wenger NK, et al., for the African-American Lipid and Cardiovascular Council (AALCC). Insulin resistance syndrome in African Americans: a review. *Ethn Dis*. 2003;13:414-428.
 24. Clark LT, Ferdinand KC, Flack JM, et al. Coronary heart disease in African Americans. *Heart Dis*. 2001;3:9
 25. Harris MI, Flegal KM, Cowie CC, et al. Prevalence of diabetes, impaired fasting glucose, and impaired glucose tolerance in U.S. adults: the Third National Health and Nutrition Examination Survey, 1988-1994. *Diabetes*. 1998;21:518-524.
 26. Burt VL, Whelton P, Roccella EJ, et al. Prevalence of hypertension in the US adult population: results from the National Health and Nutrition Examination Survey, 1988-1991. *Hypertension*. 1995;25:305-313.
 27. Flegal KM, Carroll MD, Ogden CL, et al. Prevalence and trends in obesity among US adults, 1999-2000. *JAMA*. 2002;288:1723-1727.

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