Racial Differences in the Correlation Between Gonadal Androgens and Serum Insulin Levels

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OBJECTIVE — We previously demonstrated a direct correlation between serum insulin levels and gonadal androgens (testosterone and androstenedione) in a group of obese hyperandrogenic predominantly black women. Subsequent work by others in predominantly white women showed conflicting results. To examine these potentially important racial differences further, 14 premenopausal females from each ethnic group, of similar age, BMI, and waist-to-hip ratio, were studied.

RESEARCH DESIGN AND METHODS — We measured baseline gonadal androgens, dehydroepiandrosterone (DHEA), dehydroepiandrosterone sulfate (DHEAS), and leutinizing hormone (LH)/follicle-stimulating hormone ratio. Serum glucose, insulin, and C-peptide were measured at baseline and during a 2-h oral glucose tolerance test (area under the curve [AUC]). Insulin sensitivity was measured by glucose decrement during the first 15 min of an intravenous insulin tolerance test.

RESULTS — Simple correlation analysis revealed a significant direct correlation in blacks (but not whites) between gonadal androgens and AUC for glucose, insulin, and C-peptide. Race–by–covariate interaction models reinforced the simple correlation finding. Cholesterol level was also correlated to all androgens in blacks, but not in whites. We also found that whites had higher serum triglycerides and greater AUC glucose than blacks.

CONCLUSIONS — We conclude that there is a significant direct correlation between gonadal androgens and stimulated glucose, insulin, and C-peptide in blacks but not in whites. Thus, the previously reported direct correlation between gonadal hyperandrogenism and hyperinsulinemia may be a race-dependent phenomenon, hitherto an unreported observation. The implications of these findings are discussed.

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The association between hyperandrogenism and abnormal glucose homeostasis was first suggested by Achard and Thiers in 1921 when they described "diabetes in women with beards" (1). Several decades later in 1976, Kahn et al. (2) reported on syndromes in women with severe insulin resistance, ovarian hyperandrogenism, hyperinsulinemia, and acanthosis nigricans. In 1980, we (3) found a significant direct correlation between gonadal androgens (testosterone and androstenedione) and basal and glucose-stimulated insulin levels in a group of obese women with and without polycystic ovarian syndrome (PCOS), which was subsequently confirmed by others in obese (4,5) and nonobese (6) women and once again by us (7). Both our study subjects and those of Kahn et al. were predominantly black women.

Similar studies in predominantly white women showed conflicting results, with some showing a correlation (8–10) and others showing no correlation (11,12). We questioned if the correlation between gonadal androgens and insulin is a race-dependent phenomenon that might provide a practical marker for the black group, which is more susceptible to a variety of metabolic and cardiovascular diseases than the white population.

RESEARCH DESIGN AND METHODS

Study subjects

A total of 14 black premenopausal women between the ages of 18 and 39 years matched with 14 white premenopausal women of similar age and BMI were selected for this study. Race determination was based on the history of parents' and grandparents' ethnicity. All white women had positive ancestry for Caucasian ethnicity, excluding Latino, whereas black subjects were all from African-American ancestry, excluding Caribbean-American. None of the subjects had a history of diabetes in their immediate family.

All subjects underwent a complete history and physical examination including measurement of waist-to-hip ratio (WHR), as well as routine laboratory testing which consisted of a chemistry panel, complete blood count, thyroid function tests, and serum cortisol.

All subjects were in good health and had a stable weight for at least 6 weeks before the study. In addition, none had amenorrhea, oligomemorrhea, or significant hirsutism and they could not be classified clinically as having PCOS. None of the subjects had used estrogen and/or progesterone birth control agents or other forms of sex hormone therapy in the previous 6 weeks. Sex hormone measurements and metabolic

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Abbreviations: AUC, area under the curve; CV, coefficient of variation; DHEA, dehydroepiandrosterone; DHEAS, dehydroepiandrosterone sulfate; FSH, follicle-stimulating hormone; ITT, insulin tolerance test; LH, leutinizing hormone; OGTT, oral glucose tolerance test; PCOS, polycystic ovarian syndrome; RIA, radioimmunoassay; WHR, waist-to-hip ratio.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

Table 1—*Clinical, metabolic, and hormonal profiles of study subjects*

	Black women	White women	*P*
n	14	14	—
Age (years)	32.4 ± 1.8	32.9 ± 1.9	0.8617
BMI (kg/m^2)	34.7 ± 1.7	33.2 ± 1.4	0.5091
WHR	0.81 ± 0.02	0.82 ± 0.02	0.8140
Waist circumference (cm)	92.6 ± 3.07	99.1 ± 3.78	0.1945
Glucose			
Fasting (mmol/l)	4.99 ± 0.13	5.28 ± 0.12	0.1247
AUC (mmol · l^{-1} · 2 h^{-1})	819.7 ± 41.0	962.3 ± 36.8	0.0154
Insulin			
Fasting (pmol/l)	124.8 ± 30.6	102.6 ± 15.0	0.5218
AUC (pmol · l^{-1} · 2 h^{-1})	91,082 ± 23,915	67,851 ± 8,178	0.3717
C-peptide			
Fasting (pmol/l)	0.74 ± 0.11	0.83 ± 0.09	0.4863
AUC (pmol · l^{-1} · 2 h^{-1})	271.5 ± 31.6	298.8 ± 19.9	0.4807
Cholesterol (mmol/l)	4.86 ± 0.29	5.05 ± 0.23	0.6179
Triglycerides (mmol/l)	0.83 ± 0.08	1.37 ± 0.25	0.0457
Testosterone (nmol/l)	1.79 ± 0.40	1.50 ± 0.29	0.5649
Androstenedione (nmol/l)	5.51 ± 0.74	5.55 ± 0.70	0.9655
DHEA (nmol/l)	13.76 ± 1.86	14.80 ± 2.97	0.7666
DHEAS (μmol/l)	4.31 ± 0.68	5.56 ± 1.14	0.3543
LH/FSH ratio	1.44 ± 0.27	1.09 ± 0.15	0.2618
K_{ITT}	3.95 ± 0.41	3.32 ± 0.29	0.2280

Data are means ± SEM.

studies were conducted during the follicular phase based on menstrual history.

The study was conducted at the Clinical Research Center of the University of Tennessee College of Medicine, Memphis, and was approved by the Institutional Review Board. All subjects gave written informed consent before joining the study.

Metabolic profile studies

Oral glucose tolerance test. All subjects were instructed to maintain three regular meals a day that constituted a high-carbohydrate (~300 g/day) diet for 3 days prior to the test. The subjects were then requested to arrive at the research center at 7:00 A.M. after a 12- to 14-h fast. An oral glucose tolerance test (OGTT) was performed between 8:00 and 9:00 A.M. using 75 g of glucose solution. Blood samples were drawn at −15, 0, 30, 60, 90, and 120 min of glucose ingestion for measurement of glucose, insulin, and C-peptide. The areas under the curve (AUCs) were calculated according to Tai (13).

Measurement of insulin sensitivity by insulin tolerance test. Glucose disposal in response to intravenous administration of insulin was measured for assessing insulin sensitivity by the method of Bonora et al. (14). In addition to its simple technique, the insulin tolerance test (ITT) has been shown to be safe and reproducible and its index (K_{ITT}) correlates very closely with the *M* values obtained by the euglycemic-hyperinsulinemic clamp in diabetic and nondiabetic subjects (15–17). The test was performed after an overnight fast by injecting 0.1 U of regular insulin per kilogram of body weight as an intravenous bolus. Blood samples were drawn at −15, 0, 3, 6, 9, 12, and 15 min after insulin injection followed by glucose injection at 20 min to prevent blood glucose fall. K_{ITT} was calculated according to the formula $0.693/t_{1/2}$. The plasma glucose $t_{1/2}$ was calculated from the slope of the least-squares analysis of glucose concentration between 3 and 15 min of intravenous insulin injection, when glucose concentration is linearly decreased.

Basal hormonal profile studies. On the same day, before OGTT, two blood samples were drawn 15 min apart (then pooled), for measurement of total testosterone, androstenedione, leutinizing hormone (LH), follicle-stimulating hormone (FSH), dehydroepiandrosterone (DHEA), dehydroepiandrosterone sulphate (DHEAS), estradiol, cortisol, prolactin, and lipid profile.

Analytical methods

Plasma glucose was measured by the glucose oxidase method using a Beckman analyzer (Beckman, Brea, CA). Plasma immunoreactive insulin and C-peptide were measured by radioimmunoassay (RIA) methods. The interassay of coefficient of variation (CV) for both assays was <8%. Plasma FSH, LH, prolactin, and cortisol were measured by double antibody RIAs using ^{125}I-labeled hormones. The inter- and intra-assay CVs for these assays were <12%. Plasma testosterone, androstenedione, and DHEAS and DHEA were measured by specific RIAs using reagents obtained from Radioassay System Laboratories (Carson, CA), Pentex (Santa Monica, CA), and Corning (Medford, MA), respectively. The inter- and intra-assay CVs for these assays were <10%.

Statistical analysis

Data were analyzed using the SAS System for Windows release 6.12. To determine group equivalence, black and white mean differences were examined by Student's *t* test for independent groups with $\alpha = 0.05$. Results of these comparisons are presented in Table 1.

Preliminary analysis revealed that the study's androgen, insulin, and C-peptide measures were not distributed normally in their original metric but were normal following natural log transformation. Consequently, before further analysis, the androgen, insulin, and C-peptide measures were log-transformed. The glucose distributions could not be differentiated from normal and were not transformed.

To estimate the extent of relationship of androgens with insulin level and metabolic variables, Pearson correlation coefficients were computed for blacks and whites separately and jointly. Results are shown in Tables 2–4. Race–by–androgen interaction mixed models were constructed using SAS Proc Mixed to investigate ethnic differences that appeared in the simple correlations. BMI pairs were retained as a random blocking variable, and waist circumference was included as a continuous covariate in all models. Consequently, all models included BMI, waist circumference, race, and a race-by-androgen interaction term. Tables 5 and 6 organize the resulting race-by-androgen slopes for blacks and whites separately. Table 7 presents results of testing ethnic differences in the slopes. Tables 5–7 also present results of modeling cholesterol as a function of androgens as well as modeling the study's insulin and metabolic variables as a function of cholesterol. Since waist measurement had been documented for only 22 of the 28 subjects, the mixed model analyses are based on fewer subjects than the correlation analysis.

All significant tests reported for these models were conducted as Type III tests.

RESULTS

Demographic, metabolic, and hormonal profiles

The ethnic groups did not differ significantly in mean age, BMI, or WHR (Table 1). Although waist circumference in whites was greater than in blacks, the difference was not significant. Mean fasting glucose, insulin, C-peptide, cholesterol, serum testosterone, androstenedione, DHEA, DHEAS, and LH/FSH ratio were all comparable. Insulin sensitivity (K_{ITT}) in the two groups was not significantly different. The only significant differences among the two groups were higher fasting serum triglycerides and OGTT AUC for glucose in the white compared with the black group (Table 1). No subject had impaired glucose tolerance, diabetes, or hypertriglyceridemia.

Correlation analysis

Correlational results are depicted in Tables 2–4 for black women alone, white women alone, and the combined groups, respectively. The results clearly demonstrate the presence of ethnically specific effects. The following cogent points emerge from these tables.

Fasting glucose and AUC for insulin and C-peptide were significantly positively correlated with testosterone in the black group. A similar pattern, but not quite reaching significance, was also observable for fasting insulin and AUC glucose. Further, androstenedione level was significantly positively correlated with AUC for glucose, insulin, and C-peptide in the black group.

Cholesterol was significantly positively correlated with androstenedione, DHEA, and DHEAS and nearly significantly correlated with testosterone in black women.

When the two ethnic groups were combined, significant positive correlations for fasting cholesterol and AUC for insulin and C-peptide with androstenedione and testosterone were observable. In addition, fasting C-peptide was significantly positively correlated with androstenedione.

WHR was significantly positively correlated with androstenedione and DHEA in the white group and not in the black group. The correlation of WHR with androstenedione and DHEA in the combined group remained significant but not as strongly as was found for the white group alone.

Table 2—*Correlations of serum testosterone, androstenedione, DHEA, and DHEAS with insulin levels and metabolic profiles of black women*

	Log testosterone		Log androstenedione		Log DHEA		Log DHEAS	
	r	*P*	*r*	*P*	*r*	*P*	*r*	*P*
Fasting glucose	0.54	0.0445	0.48	0.0846	0.24	0.4069	0.14	0.6325
Log fasting insulin	0.53	0.0502	0.38	0.1831	0.16	0.5847	0.03	0.9157
Log fasting C-peptide	0.49	0.0882	0.52	0.0709	0.30	0.3286	−0.09	0.7623
AUC glucose	0.53	0.0532	0.69	0.0061	0.57	0.0319	0.38	0.1797
Log AUC insulin	0.74	0.0025	0.71	0.0042	0.13	0.6670	−0.05	0.8622
Log AUC C-peptide	0.61	0.0269	0.68	0.0113	0.25	0.4138	−0.16	0.5946
Cholesterol	0.50	0.0675	0.58	0.0307	0.72	0.0035	0.69	0.0062
Triglycerides	0.27	0.3554	0.30	0.3038	0.17	0.5700	−0.05	0.8701
K_{ITT}	−0.15	0.6787	−0.24	0.5033	−0.11	0.7711	−0.26	0.4663
WHR	0.24	0.4174	0.22	0.4557	0.17	0.5627	0.18	0.5349
Waist circumference	0.29	0.3585	0.23	0.4669	0.53	0.0736	0.54	0.0678

Table 3—*Correlations of serum testosterone, androstenedione, DHEA, and DHEAS with insulin levels and metabolic profiles of white women*

	Log testosterone		Log androstenedione		Log DHEA		Log DHEAS	
	r	*P*	*r*	*P*	*r*	*P*	*r*	*P*
Fasting glucose	−0.18	0.5321	0.06	0.8485	−0.10	0.7216	−0.30	0.2935
Log fasting insulin	0.01	0.9661	0.08	0.7748	0.05	0.8761	−0.11	0.7071
Log fasting C-peptide	−0.01	0.9874	0.21	0.5194	0.24	0.4465	−0.07	0.8341
AUC glucose	−0.17	0.5672	−0.29	0.3142	−0.40	0.1526	−0.40	0.1596
Log AUC insulin	0.35	0.2146	0.09	0.7659	0.09	0.7609	−0.04	0.9027
Log AUC C-peptide	0.37	0.2420	0.27	0.3972	0.31	0.3321	0.07	0.8378
Cholesterol	0.15	0.6264	0.15	0.6162	−0.06	0.8384	0.13	0.6738
Triglycerides	−0.18	0.5454	0.27	0.3547	0.30	0.2990	−0.23	0.4294
K_{ITT}	−0.06	0.8642	0.02	0.9486	−0.03	0.9409	0.35	0.3218
WHR	0.31	0.2776	0.67	0.0087	0.68	0.0073	0.13	0.6563
Waist circumference	−0.14	0.7066	0.21	0.5515	0.44	0.1973	0.01	0.9828

Table 4—*Correlations of serum testosterone, androstenedione, DHEA, and DHEAS with insulin levels and metabolic profiles of white plus black women*

	Log testosterone		Log androstenedione		Log DHEA		Log DHEAS	
	r	*P*	*r*	*P*	*r*	*P*	*r*	*P*
Fasting glucose	0.28	0.1482	0.27	0.1611	0.00	0.9987	−0.06	0.7402
Log fasting insulin	0.33	0.0817	0.23	0.2309	0.09	0.6590	−0.06	0.7578
Log fasting C-peptide	0.34	0.0964	0.40	0.0488	0.22	0.2884	−0.04	0.8325
AUC glucose	0.26	0.1871	0.21	0.2764	−0.06	0.7438	−0.00	0.9961
Log AUC insulin	0.62	0.0004	0.45	0.0169	0.10	0.6050	−0.05	0.7820
Log AUC C-peptide	0.53	0.0064	0.51	0.0085	0.24	0.2549	0.00	0.9825
Cholesterol	0.40	0.0382	0.40	0.0383	0.25	0.2038	0.38	0.0487
Triglycerides	−0.01	0.9663	0.23	0.2378	0.22	0.2538	−0.12	0.5385
K_{ITT}	−0.11	0.6446	−0.13	0.5837	−0.01	0.9775	0.05	0.8247
WHR	0.26	0.1897	0.44	0.0190	0.47	0.0110	0.15	0.4429
Waist circumference	0.15	0.5013	0.26	0.2361	0.46	0.0292	0.22	0.3169

Table 5—*Race-by-covariate slopes in insulin level and metabolic profile models controlling for waist circumference of black women*

	Log testosterone		Log androstenedione		Log DHEA		Log DHEAS		Cholesterol	
	β	*P*	β	*P*	β	*P*	β	*P*	β	*P*
Fasting glucose	0.74	0.0193	0.62	0.1218	0.07	0.8701	−0.02	0.9681	0.06	0.7508
Log fasting insulin	1.02	0.0617	0.55	0.3867	0.08	0.9153	−0.69	0.3193	−0.03	0.9110
Log fasting C-peptide	0.20	0.0635	0.22	0.0690	0.18	0.2055	−0.19	0.1849	0.07	0.2284
AUC glucose	152.32	0.0847	296.63	0.0022	238.97	0.0359	93.05	0.4183	117.45	0.0109
Log AUC insulin	1.37	0.0001	1.14	0.0032	0.34	0.4939	−0.44	0.3717	0.18	0.3716
Log AUC C-peptide	0.49	0.0067	0.49	0.0125	0.23	0.3123	−0.32	0.2061	0.13	0.2000
Cholesterol	0.48	0.1080	0.62	0.2057	3.03	0.0139	4.69	0.0073	—	—

Mixed model analysis

Mixed model race–by–covariate interaction results controlling for waist circumference are depicted in Tables 5 and 6 for black and for white women, respectively. Differences in race–by–covariate slopes are shown in Table 7. In these tables, β is the ram regression slope. As in the simple correlational results presented above, nearly all significant findings are associated with black women. The following cogent points emerge from these models.

Significant positive relationships are identifiable for AUC of insulin and AUC C-peptide and glucose with testosterone and for AUC of insulin and C-peptide with androstenedione in black (Table 5) but not in white women (Table 6). Only in the case of the relationship between fasting glucose and testosterone do both groups exhibit a significant association. For that relationship, black women demonstrate a significant positive association while white women exhibit a significant negative association. The association between AUC glucose and testosterone follows a similar pattern but is not significant for either ethnic group.

Comparisons of black with white race–by–covariate slopes (Table 7) reveal that the associations of fasting and AUC glucose and AUC insulin with testosterone are significantly greater in black than in white women. The relationship of AUC glucose with androstenedione is also significantly greater in blacks. AUC insulin follows a similar pattern but just fails to reach significance for androstenedione. Blacks also have documentably stronger relationships between AUC glucose and DHEA and between AUC glucose and cholesterol.

The positive association noted for fasting cholesterol with gonadal and adrenal androgens in black but not in white women (Tables 2 and 3, respectively), when controlled for waist circumference in a race–by–covariate interaction analysis (Tables 5 and 6), is no longer significant for the gonadal androgens. Apparently, waist circumference confounds and at least partially accounts for the observed simple race-specific relationship between cholesterol and gonadal androgens.

CONCLUSIONS — Our earlier findings (3) (based on six obese normal and eight obese PCOS subjects without controlling for race) regarding the presence of direct correlations between gonadal androgens (testosterone and androstenedione) and stimulated insulin levels were confirmed in the present study in the black women with a larger number of subjects. The present study further extends these observations to include cholesterol, C-peptide, and stimulated glucose levels that were not investigated and demonstrated previously.

The whites did not exhibit any significant correlation between gonadal androgens and insulin but did demonstrate positive correlation between WHR and androstenedione and DHEA. The presence of correlation between gonadal androgens and insulin is in agreement with three previous studies (8–10) and in disagreement with two others (11,12).

It is apparent that glucose, glucose-stimulated C-peptide, and insulin are significantly associated with testosterone and androstenedione in blacks but not in whites (Tables 5 and 6). This finding suggests that correlations between gonadal androgens, insulin, and glucose are in fact a valid race-dependent phenomenon.

Recent studies by various groups have demonstrated a smaller amount of visceral fat in blacks than in whites with comparable BMIs (18–21). We have also confirmed these findings by magnetic resonance imaging in a subset (six pairs) of our subjects (22). Because waist circumference may be a better surrogate for visceral adiposity than WHR (21), in the absence of visceral fat

Table 6—*Race-by-covariate slopes in insulin level and metabolic profile models controlling for waist circumference of white women*

	Log testosterone		Log androstenedione		Log DHEA		Log DHEAS		Cholesterol	
	β	*P*	β	*P*	β	*P*	β	*P*	β	*P*
Fasting glucose	−1.56	0.0351	−0.30	0.5424	−0.60	0.0919	−0.48	0.1118	−0.06	0.7811
Log fasting insulin	−0.52	0.6708	0.30	0.7081	0.11	0.8382	−0.45	0.3325	0.58	0.0563
Log fasting C-peptide	−0.11	0.6492	0.08	0.5821	0.08	0.3839	−0.07	0.4672	−0.04	0.5229
AUC glucose	−355.37	0.0899	−80.26	0.3957	−111.69	0.1569	−115.82	0.1385	−9.10	0.8381
Log AUC insulin	0.34	0.4102	0.09	0.8234	0.23	0.5275	−0.13	0.6834	0.16	0.4441
Log AUC C-peptide	0.50	0.1821	0.25	0.2686	0.27	0.1083	−0.02	0.8836	−0.05	0.6018
Cholesterol	0.97	0.1334	0.88	0.1565	1.30	0.2380	2.09	0.0190	—	—

Table 7—*Differences in race-by-covariate slopes in insulin level and metabolic profile models controlling for waist circumference (black versus white)*

	Log testosterone		Log androstenedione		Log DHEA		Log DHEAS		Cholesterol	
	β	*P*	β	*P*	β	*P*	β	*P*	β	*P*
Fasting glucose	2.29	0.0067	0.92	0.1561	0.67	0.2090	0.46	0.3784	0.12	0.6723
Log fasting insulin	1.54	0.2471	0.25	0.8110	−0.03	0.9692	−0.24	0.7659	−0.61	0.1117
Log fasting C-peptide	0.32	0.2467	0.14	0.4611	0.09	0.5758	−0.12	0.4688	0.11	0.1868
AUC glucose	507.69	0.0299	376.89	0.0122	350.65	0.0137	208.87	0.1359	126.55	0.0447
Log AUC insulin	1.02	0.0413	1.05	0.0693	0.11	0.8493	−0.31	0.5985	0.01	0.9585
Log AUC C-peptide	−0.01	0.6691	0.24	0.4111	−0.03	0.9017	−0.30	0.3228	0.18	0.1840
Cholesterol	−0.49	0.4497	−0.26	0.7415	1.12	0.1114	2.60	0.1114	—	—

measurement in all of our subjects we analyzed our data using race–by–covariate interaction models controlling for waist circumference rather than WHR. This analysis showed a positive correlation between gonadal androgens and insulin in the black group, but not in the white group.

As to the effect of gonadal androgens on insulin level and vice versa, the controversy is not yet settled, because there are data supporting both theories (23). However, to our knowledge, excess DHEA level has not been associated with hyperinsulinemia, and in fact many studies demonstrate an opposite effect of DHEA on insulin from that of testosterone (24–28) with the possible existence of a servomechanism for control of circulating DHEA by insulin (29). Our studies clearly show that correlation between insulin and gonadal androgens in black women goes hand-in-hand with C-peptide, suggesting a positive effect of these androgens on insulin secretion. Hyperandrogenism is also associated with reduced clearance and metabolism of insulin (9,30,31); therefore, both increased insulin secretion and its decreased clearance may result in hyperinsulinemia as a result of gonadal hyperandrogenism. It thus appears that androgenism in general and gonadal androgenism in particular exhibit distinct racial relationships with insulin, C-peptide, and glucose levels. It is, therefore, tempting to hypothesize that hyperandrogenism is associated with insulin level only in blacks, inasmuch as insulin, C-peptide, and glucose are increased by increasing androgen levels in blacks but not in whites. Examination of the insulin-to-glucose ratio, as a marker of insulin resistance, from Table 1 indicates a tendency (although not significant) for higher values in blacks (111.11) than in whites (70.5) for comparable WHR and BMI. As shown by many studies (20,32–35), increased insulin resistance has been associated with greater susceptibility to diabetes, insulin resistance, and cardiovascular diseases (36,37). Whether smaller visceral adiposity in blacks than in whites for the same BMI and WHR is a compensatory and protective mechanism against such conditions as coronary artery disease (18,21,38) is an intriguing possibility, but needs further investigation.

Our study also confirms previous observations (18,19,21) that white women have higher AUC for glucose and higher serum triglycerides than black women. Furthermore, we note that AUC glucose is consistently positively correlated with serum testosterone, androstenedione, DHEA, and DHEAS in our sample of black women but negatively correlated in our sample of white women, even though a number of the associations fail to reach statistical significance. These patterns remain even after controlling for waist circumference.

In summary, our study demonstrates significant racial differences in the associations of serum glucose, insulin, and C-peptide levels with serum testosterone and androstenedione. Nearly all associations reaching statistical significance in this study were specific to black women, a hitherto unreported phenomenon. Simple correlation results were reinforced by mixed models that controlled for waist circumference.

Our study further implies that waist circumference may be an important variable affecting fasting cholesterol, as well as fasting insulin and C-peptide, in blacks. Lower levels of visceral fat in black than in white women with comparable BMI may thus be a protective mechanism for this ethnic group. Further studies with a larger number of subjects looking into these possibilities are necessary to elucidate the underlying mechanisms for these ethnic differences.

Results of metabolic studies with mixed sex and ethnicity and wide age ranges must be interpreted with caution, inasmuch as subtle but important metabolic differences related to age, sex, and ethnicity could be blunted or abolished as a result of the heterogeneity of study subjects.

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