Published in final edited form as:

Transl Res. 2010 November ; 156(5): 302–308. doi:10.1016/j.trsl.2010.08.003.

Paradoxically High Adiponectin and the Healthy Obese Phenotype In Obese Black and White 16 year old Girls

John A Morrison, PhD¹, Charles J. Glueck, MD³, Stephen Daniels, MD, PhD⁴, Ping Wang, PhD³, Paul Horn, PhD⁵, and Davis Stroop, M Sc²

¹Division of Cardiology, Cincinnati Children's Hospital Medical Center, Cincinnati, OH

²Division Hematology Cincinnati Children's Hospital Medical Center, Cincinnati, OH

³Cholesterol Center, Jewish Hospital of Cincinnati, Denver CO

⁴Children's Hospital, Denver CO

⁵Department of Mathematical Sciences, University of Cincinnati

Abstract

Although adiponectin is inversely correlated with obesity, some obese adults without metabolic complications of obesity have paradoxically high adiponectin. Therefore, we assessed adiponectin-risk factor relations in 133 obese 16-year-old schoolgirls from a cohort of 448, focusing on paradoxically high adiponectin in obesity and the healthy obese phenotype. Median adiponectin (11.9 mg/L) in non-obese girls (BMI <24.6 kg/m²) was selected as a cutpoint to identify high adiponectin in obese girls. Of 90 black and 43 white obese girls (BMI = 24.6), 25 black (28%) and 13 white (30%) girls had paradoxically high adiponectin (>11.9). The 38 obese girls with adiponectin >11.9 vs the 95 obese girls with adiponectin ≤ 11.9 had higher median HDL cholesterol (54 vs 46 mg/dl, p=.0007) and ApoA1 (181 vs 164 mg/dl, p=.011), and lower insulin (14 vs 20 uU/ml, p=.0006). In the 133 obese girls, by stepwise regression, adiponectin category (>11.9, ≤ 11.9 mg/L) was a significant independent positive determinant of HDL cholesterol (partial R² = 8.4%, p = .001), and apolipoprotein A1 (partial R² = 4.1%, p = .025), and was inversely associated with fasting serum insulin (partial R² = 5.4%, p = .0074). By stepwise logistic regression in the 133 obese girls, adiponectin category (high vs. low) was a significant inverse explanatory variable for metabolic syndrome, odds ratio 0.20, 95% confidence intervals 0.04-0.95, p=.043. We conclude that paradoxically high adiponectin is associated with the healthy obese phenotype in obese adolescent black and white girls.

INTRODUCTION

The role of obesity in the pathogenesis of cardiovascular disease (CVD) is largely mediated through its co-morbid effects on major CVD risk factors, amplifying atherogenic risk factors (LDL-cholesterol, LDL apo B, systolic and diastolic blood pressure [SBP, DBP], triglycerides [TG], insulin, c-reactive protein, interleukin 1 and 6, tumor necrosis factor alpha), and lowering anti-atherogenic risk factors, HDL-cholesterol (HDL), and

© 2010 Mosby, Inc. All rights reserved.

Address correspondence to Charles J. Glueck MD, Cholesterol Center, ABC Building, 3200 Burnet Avenue, Cincinnati OH, 45229; phone 513-585-7945; fax 513-585-7950; cjglueck@health-partners.org.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

apolipoprotein A1 (ApoA1).^{1, 2} Centripetal obesity is associated with residual risk to CVD associated with obesity after accounting for the Framingham Risk Factor score.³

Particularly in the class III obesity range, some subjects are free of the metabolic complications of obesity (increased insulin resistance [IR], low HDLC, high TG, high SBP and DBP), although their other clinical and laboratory characteristics are not different from equally obese subjects with obesity-related comorbidities.⁴⁻⁷ These individuals have been labeled the “metabolically healthy obese phenotype”. One factor associated with the healthy obese phenotype is adiponectin,⁸ a protein with a high-molecular-weight (HMW) multimer structure in the blood,^{9, 10} secreted by adipose tissue, having insulin sensitizing and anti-inflammatory effects and increasing HDLC. Martin et al¹¹ reported that adiponectin’s relationship with HDLC and triglycerides was present in lean adolescents, but strengthened with increasing adiposity. The adiponectin relationship with insulin, however, was only present among non-lean adolescents. Thus, Martin et al¹¹ concluded that heavier adolescents had a greater benefit from high levels of adiponectin than their lean counterparts. Jeffery et al¹² reported correlations between adiponectin and features of the metabolic syndrome in children.

Although adiponectin is inversely correlated with BMI, Aguilar-Salinas et al¹³ reported that 20% of cases with Class III obesity (BMI > 40 kg/m²) had adiponectin concentrations above the median value of subjects with normal BMI. Moreover, paradoxically high adiponectin levels have been reported by Vendrel et al in Class III obese subjects.¹⁴ One probable mechanism of the relatively high HDLC reported by Aguilar-Salinas et al¹³ in cases with Class III obesity lies in the strong inverse association between adiponectin and the fractional catabolic rate of ApoA1,¹⁵ a major structural apolipoprotein of high density lipoprotein. Using data on black and white girls in the Cincinnati Clinic of the NHLBI Growth and Health Study (NGHS) at mean age 16, our specific aim in the current study was to evaluate contributions of adiponectin to the healthy obese phenotype.

MATERIALS AND METHODS

The Study Population

In the NGHS,¹⁶ procedures followed were in accordance with the ethical standards of the Institutional Review Boards of the Centers, who approved the study. Signed informed consent was obtained from the girls’ parents or guardians and assent from the girls.

The NGHS has been described previously.¹⁷ Briefly, NGHS was a 10-year (1987-1997) multi-center cohort study to explicate origins of black-white disparities in obesity and its effects on CVD risk factors in women.¹⁷ Race was self-declared and enrollment was restricted to 9- and 10-year old girls from racially concordant households, to girls who said they were black or white and whose parents or guardians said that they were black or white, respectively. In ancillary projects, the Cincinnati clinic measured fasting insulin and adiponectin at Year 7, age 16 ± 1, in addition to the NGHS variables – lipid profiles, apolipoprotein A1 (ApoA1), systolic and diastolic blood pressure.¹⁶

Laboratory and Clinical Measurements

Methods for measurement of lipids, ApoA1, fasting serum insulin, height, weight, waist circumference, hip circumference, systolic and diastolic blood pressures have been previously described.¹⁷

The NGHS used BMI to assess overweight annually according to a standard protocol,¹⁷ as recommended by several expert panels¹⁸⁻²⁰ and waist circumference as an indicator of fat patterning.

Using criteria previously described,²¹ NGHS subjects having fasting blood glucose ≥ 126 mg/dl²² at Visit 1 (mean age 10) or type 1 diabetes mellitus (DM) at any time from mean age 10 through mean age 25 were excluded (n=7) from the analysis sample for this report. Diagnosis of type 1 DM was based on WHO criteria, fasting glucose ≥ 126 mg/dl, and self-reported diabetes with treatment by a physician.²² We did not have measurement of C-peptides as well as diabetes autoantibody levels, gold standard methods²³ to distinguish type 1 from type 2 diabetes.

Fasting serum insulin levels (competitive protein-binding radioimmunoassay) were measured after an overnight fast (≥ 8 hr).

Adiponectin

Adiponectin levels were determined by using a commercially available radioimmunoassay kit (Linco, St. Louis, MO). Following the approach of Aguilar-Salinas et al,¹³ we selected the median adiponectin (11.9 mg/L) in non-obese girls (BMI < 24.6 [the CDC 85th percentile for 16 year old girls])²⁴ to define “higher than expected” adiponectin in the obese girls (BMI ≥ 24.6) and assessed healthy phenotype factors -- higher HDL cholesterol, higher ApoA1, lower insulin, lower systolic blood pressure -- in obese girls with paradoxically high adiponectin.

Statistical Methods

Characteristics of the total cohort, and black-white comparisons (by Wilcoxon tests of difference, Hochberg-Benjamini²⁵ correction for multiple tests) are presented in Table 1.

In 133 obese girls with BMI ≥ 24.6 kg/m² (the CDC 85th percentile for 16 year old girls²⁴), comparisons between 38 girls with high adiponectin (>11.9 mg/L) and 95 girls with adiponectin ≤ 11.9 were made by Wilcoxon tests, Hochberg-Benjamini²⁵ correction, Table 2. In the 133 obese girls, univariate Spearman correlations of adiponectin with cardiovascular risk variables were calculated, Table 2.

Forward stepwise regression (significance level to enter [SLE] = 0.15, significance level to stay [SLS] = 0.05) was used to assess whether paradoxically high adiponectin (>11.9 mg/L) in obese 16-year-old girls would be protectively associated with the cardiovascular disease comorbidities conventionally associated with obesity. Dependent variables included HDLC, TG, LDLC, insulin, SBP, DBP, and ApoA1; explanatory variables included categorical adiponectin (>11.9 vs. ≤ 11.9 mg/L), race, age, BMI, waist circumference, hip circumference, waist/hip ratio, insulin, cigarette smoking and maturation stage, Table 3. Separately, forward stepwise regression was run for insulin as the dependent variable, with variables including categorical adiponectin (>11.9 vs. ≤ 11.9 mg/L), race, age, BMI, waist circumference, hip circumference, waist/hip ratio, cigarette smoking and maturation stage, Table 3.

The stepwise selection method is a modification of the forward selection technique. It begins with no variables in the model. For each explanatory variable, the F statistic that reflects its contribution to the model is calculated. The variable with the smallest p-value is entered in the model so long as the p-value is less than the significant level of entry threshold (SLE). The F statistic is then computed for each of the other variables with the current variable in the model. The variable with the smallest p-value less than the SLE is selected to enter the model. At this point the method deviates from the forward selection procedure. Each of the variables in the model is re-examined and the variable with the largest p-value is selected for possible removal from the model. The variable is removed if its p-value exceeds the significant level of staying (SLS). This removal process continues until all variables remaining have p-values less than the SLS. At this point the forward selection part of

process begins again examining variables for possible entry into the model. The stepwise process ends when no variables are added or removed. The default values for SLE and SLS are equal to 0.15, in the SAS ® statistical conservative software package version 9.1 (SAS Institute, Cary, NC). We used a slightly more statistically approach by setting SLS = 0.05, thus ensuring that the variables that remained in the model were statistically significant with a traditional alpha- level of 0.05. While having SLS < SLE can cause computational issues we had no such problems.

Stepwise logistic regression was carried out with metabolic syndrome (yes, no) ²⁶ as the dependent variable, and adiponectin category, race, age, insulin, cigarette smoking, and maturation stage as the explanatory variables, Table 4. Abnormal metabolic syndrome components were defined as follows: waist circumference our cohort's age-race-specific 90th percentile (also approximating NHANES III 16-year-old girls²⁷), HDLC 50 mg/dl, TG 110 mg/dl, SBP or DBP the age-height-adjusted 90th percentile,²⁷ and glucose 110 mg/dl.

To examine the possible effect of missing data on outcome variables in these analyses, we compared the current analysis sample (n=448) with the 417 Cincinnati NGHS girls studied at age 10, who were not included in the current analysis, either because they were not studied at age 16 (n=221), or had no adiponectin measured at age 16 (n=196). We also compared the current analysis sample (n=448) at age 16, with the 196 NGHS girls who were studied at age 16, but did not have adiponectin measured.

RESULTS

The Cincinnati NGHS cohort included 872 girls, 7 of whom had type 1 diabetes mellitus, and were excluded from this analysis cohort. Of the remaining 865 girls, (429 white, 436 black) who had measures at mean age 10, 644 (311 white, 333 black) were assessed at mean age 16, and 448 (216 white, 232 black) had adiponectin measured. At NGHS study entry (mean age 10), the 448 girls in the current analysis sample did not differ (p>0.05) from the 417 not studied for age, weight, BMI, waist circumference, hip circumference, waist/hip ratio, lipids, insulin, glucose, SBP, DBP, and ApoA1. Similarly, at mean age 16, the 448 girls with measures of adiponectin did not differ (p>0.05) from the 196 girls whose adiponectin was not measured.

In 448 girls, mean (SD) and median adiponectin were 11.4 ± 4.9 mg/L and 10.9 mg/L, Table 1. Black girls had lower adiponectin than white girls (median 10.2 mg/L versus 11.6, p=.002, Table 1), which was marginally significant after covariance adjusting for BMI, p=.054.

Of the 448 girls, 315 were non-obese (BMI <24.6, the CDC 85th percentile for 16 year old girls²⁴), and their median adiponectin was 11.9 mg/L, which was used to categorize adiponectin for further analyses. Of the 448 girls, 133 (30%) were categorized as obese, having BMI ≥ 24.6 kg/m², Table 2. Of the 133 obese girls, 90 were black and 43 white. Of the 90 obese black girls, 25 (28%) had adiponectin > the median for non-obese girls (11.9 mg/L), as did 13 of 43 (30%) obese white girls.

The 38 obese girls with high adiponectin had higher HDL cholesterol and ApoA1 and lower fasting serum insulin than the 95 obese girls with adiponectin ≤ 11.9 , Table 2. In the 133 obese girls, adiponectin was inversely correlated with the waist/hip ratio, inversely correlated with insulin, and positively correlated with HDL cholesterol, Table 2.

In the 133 obese girls, categorical high adiponectin (>11.9 mg/dl) was a significant positive explanatory variable for HDLC (partial $R^2 = 8.4\%$, p=.0011) and for ApoA1 (partial $R^2 = 4.1\%$, p=.025), Table 3. Categorical high adiponectin was inversely associated with

insulin (partial $R^2 = 5.4\%$, $p = .007$), while waist and smoking were positively associated with insulin, Table 3.

By stepwise logistic regression, high adiponectin category was inversely associated with the presence of metabolic syndrome, as was black race, Table 4.

DISCUSSION

As summarized by Ziemke et al,⁸ adiponectin is a cardioprotective insulin sensitizer secreted by adipose tissue, which alters glucose metabolism and insulin sensitivity, and has antiinflammatory and antiatherogenic characteristics. Adiponectin levels are lower in subjects with obesity, metabolic syndrome, and cardiovascular disease.²⁸ Yan et al²⁹ reported that plasma adiponectin levels decreased with increasing obesity in Chinese children, and played an influential role in percent of body fat. Winer et al³⁰ reported that low levels of adiponectin in obese children were associated with higher levels of C-reactive protein, and with metabolic syndrome components. Unlike our study, none of the previous reports on adiponectin in children^{29,31} studied relationships between paradoxical high adiponectin in obese children and the healthy obese phenotype (higher HDLC, ApoA1, lower insulin). In the 133 obese girls in the current study, adiponectin category was positively and independently associated with HDL cholesterol and ApoA1 and was an independent negative predictor of insulin. The significant, independent, positive associations of paradoxically high adiponectin with HDLC and ApoA1 in obese girls probably are accounted for by the inverse association between adiponectin and ApoA1 fractional catabolic rate, independent of HDL, triglyceride content, or insulin sensitivity.¹⁵

Twenty-five of 90 obese black girls (28%) had paradoxically high adiponectin (>11.9 mg/L) as did 13 of 43 (30%) obese white girls, a finding congruent with the reports of Aguilar-Salinas et al¹³ and Vendrel et al¹⁴ in adults. Congruent with the report of Aguilar-Salinas in adults,¹³ paradoxical high adiponectin in the 133 obese girls in our cohort was positively associated with a metabolically healthy obese phenotype, positively associated with HDLC and ApoA1, and inversely associated with fasting serum insulin. In the study by Aguilar-Salinas of adults,¹³ 20% of all BMI Class 3 obese cases had paradoxically high adiponectin levels, and those subjects had lower plasma glucose, triglycerides, insulin, and higher HDLC compared to their peers with the same BMI.

Metabolic syndrome components associated with obesity include low HDLC, high triglycerides, high blood pressure, centripetal obesity, and impaired fasting glucose.²⁶ In the current study, in 133 obese girls, paradoxically high adiponectin was independently and inversely associated with the metabolic syndrome.

As described by Aguilar-Salinas et al,¹³ adults with the metabolically healthy obese phenotype are less insulin resistant and have a smaller waist circumference compared with obese control peers. In our study, obese adolescent girls with paradoxically higher adiponectin had higher HDLC and ApoA1 and lower insulin than equally obese girls with adiponectin below the median in non-obese children. To date, no potential mechanism has been demonstrated to explain the relative protection from obesity-related metabolic complications enjoyed by these subjects. Since a substantial proportion (30–70%) of the variability in plasma adiponectin levels is accounted for by genetic factors, variation in the adiponectin gene is a plausible explanation^{28, 32}

Limitations of our report include measurement of total adiponectin rather than the high molecular weight (HMW) form, which is more closely associated with markers of insulin sensitivity than is total adiponectin.^{13, 33}

Speculations

Since obesity tracks from childhood into young adulthood,^{34,36} we speculate that obese 16 year old girls with paradoxically high adiponectin will become obese young adults with paradoxically high adiponectin, which will remain as a cardioprotective positive determinant of HDL cholesterol and ApoA1, and a negative determinant for serum insulin. Metabolic syndrome is less likely to be present in obese adolescent girls with paradoxically high adiponectin, who have the healthy obese phenotype, and, speculatively, they may be less likely to have metabolic syndrome in young adulthood.

Acknowledgments

None of the authors had any substantive conflicts of interest. This research work was supported by NIH- HL55025, 48941, HL52911 and HL66430 (Drs Morrison and Daniels), and by the Lipoprotein Research Fund of the Jewish Hospital of Cincinnati (Dr Glueck)

Abbreviations

HDLC	High density lipoprotein cholesterol
ApoA1	apolipoprotein A1
BMI	body mass index
LDLC	low density lipoprotein cholesterol
SBP	systolic blood pressure
DBP	diastolic blood pressure
TG	triglyceride

REFERENCES

1. Yarnell JW, Patterson CC, Thomas HF, Sweetnam PM. Comparison of weight in middle age, weight at 18 years, and weight change between, in predicting subsequent 14 year mortality and coronary events: Caerphilly Prospective Study. *J Epidemiol Community Health*. 2000; 54:344–8. [PubMed: 10814654]
2. Suadicani P, Hein HO, von Eyben FE, Gyntelberg F. Metabolic and lifestyle predictors of ischemic heart disease and all-cause mortality among normal weight, overweight, and obese men: a 16-year follow-up in the Copenhagen Male Study. *Metab Syndr Relat Disord*. 2009; 7:97–104. [PubMed: 19032035]
3. Dhaliwal SS, Welborn TA. Central obesity and multivariable cardiovascular risk as assessed by the Framingham prediction scores. *Am J Cardiol*. 2009; 103:1403–7. [PubMed: 19427436]
4. Karelis AD, Faraj M, Bastard JP, et al. The metabolically healthy but obese individual presents a favorable inflammation profile. *J Clin Endocrinol Metab*. 2005; 90:4145–50. [PubMed: 15855252]
5. Karelis AD, Rabasa-Lhoret R. Inclusion of C-reactive protein in the identification of metabolically healthy but obese (MHO) individuals. *Diabetes Metab*. 2008; 34:183–4. [PubMed: 18329310]
6. Janssen I. Heart disease risk among metabolically healthy obese men and metabolically unhealthy lean men. *Cmaj*. 2005; 172:1315–6. [PubMed: 15883406]
7. Karelis AD, Brochu M, Rabasa-Lhoret R. Can we identify metabolically healthy but obese individuals (MHO)? *Diabetes Metab*. 2004; 30:569–72. [PubMed: 15671927]
8. Ziemke F, Mantzoros CS. Adiponectin in insulin resistance: lessons from translational research. *Am J Clin Nutr*. 2010; 91:258S–61S. [PubMed: 19906806]
9. Scherer PE. Adipose tissue: from lipid storage compartment to endocrine organ. *Diabetes*. 2006; 55:1537–45. [PubMed: 16731815]

10. Liang KW, Lee WJ, Lee WL, Ting CT, Sheu WH. Decreased ratio of high-molecular-weight to total adiponectin is associated with angiographic coronary atherosclerosis severity but not restenosis. *Clin Chim Acta*. 2009; 405:114–8. [PubMed: 19397903]
11. Martin LJ, Woo JG, Daniels SR, Goodman E, Dolan LM. The relationships of adiponectin with insulin and lipids are strengthened with increasing adiposity. *J Clin Endocrinol Metab*. 2005; 90:4255–9. [PubMed: 15870125]
12. Jeffery AN, Murphy MJ, Metcalf BS, et al. Adiponectin in childhood. *Int J Pediatr Obes*. 2008; 3:130–40. [PubMed: 19086185]
13. Aguilar-Salinas CA, Garcia EG, Robles L, et al. High adiponectin concentrations are associated with the metabolically healthy obese phenotype. *J Clin Endocrinol Metab*. 2008; 93:4075–9. [PubMed: 18682512]
14. Vendrell J, Broch M, Vilarrasa N, et al. Resistin, adiponectin, ghrelin, leptin, and proinflammatory cytokines: relationships in obesity. *Obes Res*. 2004; 12:962–71. [PubMed: 15229336]
15. Verges B, Petit JM, Duvillard L, et al. Adiponectin is an important determinant of apoA-I catabolism. *Arterioscler Thromb Vasc Biol*. 2006; 26:1364–9. [PubMed: 16574896]
16. Morrison JA, Glueck CJ, Horn PS, Schreiber GB, Wang P. Pre-teen insulin resistance predicts weight gain, impaired fasting glucose, and type 2 diabetes at age 18–19 y: a 10-y prospective study of black and white girls. *Am J Clin Nutr*. 2008; 88:778–88. [PubMed: 18779296]
17. Obesity and cardiovascular disease risk factors in black and white girls: the NHLBI Growth and Health Study. *Am J Public Health*. 1992; 82:1613–20. [PubMed: 1456335]
18. Barlow SE, Dietz WH. Obesity evaluation and treatment: Expert Committee recommendations. The Maternal and Child Health Bureau, Health Resources and Services Administration and the Department of Health and Human Services. *Pediatrics*. 1998; 102:E29. [PubMed: 9724677]
19. Cole, T. Weight-stature indices to measure underweight, overweight, and obesity. In: Hines, JH., editor. *Anthropometric assessment of nutritional status*. Wiley-Liss; New York: 1991. p. 83–111.
20. Kuczmarski RJ, Ogden CL, Guo SS, et al. 2000 CDC Growth Charts for the United States: methods and development. *Vital Health Stat* 11. 2002;1–190. [PubMed: 12043359]
21. Morrison JA, Glueck CJ, Horn PS, Wang P. Childhood predictors of adult type 2 diabetes at 9- and 26-year follow-ups. *Arch Pediatr Adolesc Med*. 164:53–60. [PubMed: 20048242]
22. Alberti KG, Zimmet PZ. Definition, diagnosis and classification of diabetes mellitus and its complications. Part 1: diagnosis and classification of diabetes mellitus provisional report of a WHO consultation. *Diabet Med*. 1998; 15:539–53. [PubMed: 9686693]
23. Dabelea D, Bell RA, D'Agostino RB Jr. et al. Incidence of diabetes in youth in the United States. *Jama*. 2007; 297:2716–24. [PubMed: 17595272]
24. Kuczmarski RJ, Ogden CL, Grummer-Strawn LM, et al. CDC growth charts: United States. *Adv Data*. 2000;1–27. [PubMed: 11183293]
25. Hochberg Y, Benjamini Y. More powerful procedures for multiple significance testing. *Stat Med*. 1990; 9:811–8. [PubMed: 2218183]
26. Morrison JA, Friedman LA, Wang P, Glueck CJ. Metabolic syndrome in childhood predicts adult metabolic syndrome and type 2 diabetes mellitus 25 to 30 years later. *J Pediatr*. 2008; 152:201–6. [PubMed: 18206689]
27. Li C, Ford ES, Mokdad AH, Cook S. Recent trends in waist circumference and waist-height ratio among US children and adolescents. *Pediatrics*. 2006; 118:e1390–8. [PubMed: 17079540]
28. Menzaghi C, Ercolino T, Di Paola R, et al. A haplotype at the adiponectin locus is associated with obesity and other features of the insulin resistance syndrome. *Diabetes*. 2002; 51:2306–12. [PubMed: 12086965]
29. Yan WJ, Wu J, Mo J, Huang CW, Peng LW, Xu L. [Plasma levels of adiponectin and tumor necrosis factor-alpha in children with obesity]. *Zhongguo Dang Dai Er Ke Za Zhi*. 2009; 11:47–50. [PubMed: 19149923]
30. Winer JC, Zern TL, Taksali SE, et al. Adiponectin in childhood and adolescent obesity and its association with inflammatory markers and components of the metabolic syndrome. *J Clin Endocrinol Metab*. 2006; 91:4415–23. [PubMed: 16926246]
31. Jeffery AN, Murphy MJ, Metcalf BS, et al. Adiponectin in childhood. *Int J Pediatr Obes*. 2008;1–11. [PubMed: 18608628]

32. Menzaghi C, Trischitta V, Doria A. Genetic influences of adiponectin on insulin resistance, type 2 diabetes, and cardiovascular disease. *Diabetes*. 2007; 56:1198–209. [PubMed: 17303804]
33. Halperin F, Beckman JA, Patti ME, et al. The role of total and high-molecular-weight complex of adiponectin in vascular function in offspring whose parents both had type 2 diabetes. *Diabetologia*. 2005; 48:2147–54. [PubMed: 16091909]
34. Ventura AK, Loken E, Birch LL. Developmental trajectories of girls' BMI across childhood and adolescence. *Obesity (Silver Spring)*. 2009; 17:2067–74. [PubMed: 19424165]
35. Silventoinen K, Kaprio J. Genetics of Tracking of Body Mass Index from Birth to Late Middle Age: Evidence from Twin and Family Studies. *Obes Facts*. 2009; 2:196–202. [PubMed: 20054225]
36. Herman KM, Craig CL, Gauvin L, Katzmarzyk PT. Tracking of obesity and physical activity from childhood to adulthood: the Physical Activity Longitudinal Study. *Int J Pediatr Obes*. 2009; 4:281–8. [PubMed: 19922043]

Mean $\pm$ SD and median adiponectin, and cardiovascular disease risk variables in 488 girls from the National Growth and Health Study at mean age 16 years

Table 1

	Black girls		White girls		Black vs White p	All girls	
	n	Mean $\pm$ SD, median	n	Mean $\pm$ SD, median		n	Mean $\pm$ SD, median
Adiponectin (mg/L)	232	10.8 $\pm$ 4.9, 10.2	216	12.1 $\pm$ 4.8, 11.6	.0020 *	448	11.4 $\pm$ 4.9, 10.9
Age (yrs)	232	16.1 $\pm$ 0.5, 16.0	216	16.0 $\pm$ 0.5, 16.0	.13	448	16.0 $\pm$ 0.5, 15.9
BMI (kg/m ²)	232	25.0 $\pm$ 6.3, 23.3	216	22.3 $\pm$ 4.1, 21.3	<.0001 *	448	23.7 $\pm$ 5.5, 22.2
Waist circumference (cm)	232	74.9 $\pm$ 12.6, 70.5	216	70.7 $\pm$ 8.4, 68.4	.0007 *	448	72.8 $\pm$ 11.0, 69.9
Hip circumference (cm)	232	98.7 $\pm$ 12.0, 95.5	215	95.2 $\pm$ 8.4, 93.4	.0041 *	447	97.0 $\pm$ 10.6, 94.5
Waist / Hip	232	0.76 $\pm$ 0.048, 0.75	215	0.74 $\pm$ 0.041, 0.64	.0013 *	447	0.75 $\pm$ 0.05, 0.74
Triglyceride (mg/dl)	232	70 $\pm$ 28, 63	216	97 $\pm$ 56, 84	<.0001 *	448	83 $\pm$ 46, 72
HDL cholesterol (mg/dl)	231	55 $\pm$ 11, 54	216	51 $\pm$ 10, 50	<.0001 *	447	53 $\pm$ 11, 52
LDL cholesterol (mg/dl)	231	92 $\pm$ 27, 89	215	96 $\pm$ 29, 95	.16	446	94 $\pm$ 28, 92
Insulin (uU/ml)	216	17.7 $\pm$ 16.0, 12.9	208	12.2 $\pm$ 8.7, 10.8	<.0001 *	424	15.0 $\pm$ 13.2, 11.6
Systolic BP (mmHg)	232	111 $\pm$ 8, 110	216	111 $\pm$ 8, 110	.62	448	111 $\pm$ 8, 110
Diastolic BP (mmHg)	232	69 $\pm$ 9, 70	216	71 $\pm$ 8, 72	.029 *	448	70 $\pm$ 9, 71
Apolipoprotein A1 (mg/dl)	230	176 $\pm$ 27, 176	215	172 $\pm$ 24, 170	.055	445	174 $\pm$ 26, 173

* significant using Hochberg-Benjamini correction for false discovery rate ($p=.05$) for 13 comparisons between two race groups.

Table 2

Mean $\pm$ SD, and median adiponectin, and cardiovascular disease risk variables in 133 obese girls at mean age 16, and adiponectin—cardiovascular disease risk variable correlations

	Adiponectin 11.9 mg/L		Adiponectin >11.9 mg/L		p	Spearman correlation with adiponectin		
	n	Mean ± SD, median	n	Mean ± SD, median		n	r	p
Adiponectin (mg/L)	95	7.6 ± 2.5, 7.6	38	16.5± 3.8, 15.4				
Age (yrs)	95	16.1 ± 0.5, 16.0	38	16.1 ± 0.6, 16.1	.92	133	0.017	.85
BMI (kg/m ²)	95	30.5± 5.2, 28.5	38	29.9 ± 6.0, 27.7	.19	133	-0.15	.092
Waist circumference (cm)	95	86.5 ±10.7, 84.1	38	84.1 ± 12.0, 82.1	.17	133	-0.17	.057
Hip circumference (cm)	94	109.4 ±9.7, 106.9	38	109.8± 11.4, 104.9	.90	132	-0.038	.66
Waist / Hip	94	0.79 ±0.05, 0.78	38	0.76 ±0.05, 0.77	.036	132	-0.26	.0022 *
Triglyceride (mg/dl)	95	102 ± 71, 83	38	84 ± 40, 68	.14	133	-0.19	.026
HDL cholesterol (mg/dl)	95	48 ± 10, 46	38	55 ± 11, 54	.0007 *	133	0.27	.0014 *
LDL cholesterol (mg/dl)	94	102 ± 32, 95	38	94 ± 35, 98	.42	132	-0.095	.28
Insulin (uU/ml)	88	24.1 ±19.7, 20.1	38	14.2±6.3, 13.6	.0006 *	126	-0.38	<.0001 *
Systolic BP (mmHg)	95	115 ± 9, 115	38	114 ± 8, 115	.69	133	-0.028	.75
Diastolic BP (mmHg)	95	70 ±12, 71	38	74 ± 7, 74	.084	133	0.047	.59
Apolipoprotein A1 (mg/dl)	95	164 ± 25, 164	38	178±28, 181	.011 *	133	0.14	.088

* significant using Hochberg-Benjamini correction for false discovery rate ($p=.05$) for 12 comparisons between two groups; for 12 significance tests of correlations.

Table 3

Stepwise regression in 133 obese girls who had BMI ≥ 24.6 kg/m² by age 16 (43 white, 90 black).

Dependent variable	Significant explanatory variables	sign	Partial R ²	p
HDL (mg/dl) n=123 (38 white, 85 black)	Adiponectin category (>median 11.9 as 1, ≤ 11.9 as 0)	+	8.4%	.0011
	Race (W=1, B=2)	+	7.8%	.0011
Apo-A1 n=123 (38 white, 85 black)	Adiponectin category (>median 11.9 as 1, ≤ 11.9 as 0)	+	4.1%	.025

Dependent variable	Significant explanatory variables	sign	Partial R ²	p
Insulin (uU/ml) n=123 (38 white, 85 black)	Waist (cm)	+	8.0%	.0015
	Adiponectin category (>median 11.9 as 1, ≤ 11.9 as 0)	–	5.4%	.0074
	Smoke (Yes=1, No=0)	+	2.9%	.046

Forward-stepwise selection with significance level to enter (SLE)=0.15, and significance level to stay (SLS)=0.05.

Explanatory variables included adiponectin category (>11.9 , ≤ 11.9 mg/L), race, age, BMI, waist circumference, hip circumference, waist/hip ratio, insulin, cigarette smoking and maturation stage.

Forward-stepwise selection with significance level to enter (SLE)=0.15, and significance level to stay (SLS)=0.05.

Explanatory variables included adiponectin category (>11.9 , ≤ 11.9 mg/L), race, age, BMI, waist circumference, hip circumference, waist/hip ratio, cigarette smoking and maturation stage.

Table 4

Stepwise logistic regression in 133 obese girls who had BMI $\geq 24.6 \text{ kg/m}^2$ by age 16 (43 white, 90 black).

Dependent variable	Significant explanatory variables	sign	p	OR (95% CI)
metabolic syndrome (18 Yes, 106 no) 124 observations used (39 white, 85 black) AUC=0.766	Race (W=1, B=2)	–	.0008	0.15 (0.049 -0.45)
	Adiponectin category (>median 11.9 as 1, 11.9 as 0)	–	.043	0.20 (0.040-0.95)

Forward-stepwise selection with significance level to enter (SLE)=0.15, and significance level to stay (SLS)=0.05.

Explanatory variables included adiponectin category, race, age, insulin, cigarette smoking and maturation stage.