HHS Public Access

Author manuscript

J Pediatr Endocrinol Metab. Author manuscript; available in PMC 2017 June 20.

Published in final edited form as:

J Pediatr Endocrinol Metab. 2011 ; 24(1-2): 29–33.

Vitamin D deficiency and insulin resistance in obese African-American adolescents

Gail Nunlee-Bland[1], **Kanwal Gambhir**[1], **Cynthia Abrams**[2], **Mustapha Abdul**[1], **Marjan Vahedi**[1], and **Wolali Odonkor**[1]

[1]Division of Endocrinology, Howard University, Washington, DC, USA

[2]Department of Biochemistry and Molecular Biology, Howard University, Washington, DC, USA

Abstract

Objective—The study aim determined if low 25-hydroxy vitamin D levels correlated with low levels of adiponectin and insulin resistance in African American adolescents with body mass index ≥85th%.

Patients and methods—Fasting blood levels of adiponectin, 25-hydroxy vitamin D, insulin, glucose, lipid, leptin and glycosylated hemoglobin were measured in a total of 34 (19 study and 15 control) African American adolescents between the ages of 10 and 20 years. Nutritional vitamin D intake and body composition measurements were assessed. Insulin resistance was calculated using the homeostasis model assessment.

Results—Adiponectin, fasting insulin, glucose, leptin, triglycerides, HDL, and 25-hydroxy vitamin D levels all reached statistical significance in the group with body mass index ≥85th percentile when compared to the control population. There was no difference in vitamin D intake between the two groups.

Conclusions—Low vitamin D levels correlated with low adiponectin levels and obesity and insulin resistance.

Keywords

African-American; adiponectin; adolescents; insulin resistance; obesity; vitamin D

Introduction

Rates of obesity have reached epidemic proportions in the United States affecting all ages and ethnic groups. More alarming is the rise in obesity in children. Obesity in the pediatric population is defined as a body mass index (BMI) ≥ 95th percentile for age and correlates with adiposity. Obese children may be as vulnerable as adults to the obesity-related cardiovascular and metabolic morbidity (1). Children with BMI ≥ 85th percentile are at risk for becoming obese and intervention is recommended at this stage. Minority children

Financial disclosure

Dr. Gail Nunlee-Bland received grant support from Baltimore DC Health Disparity Project 2P20MD30198-06.

None of the authors have any financial relationship relevant to this article to disclose.

between the ages of 12 and 18 years are particularly affected by obesity with over 20 % of African-American (AA) children having BMI of ≥ 95th percentile (2). Adipose tissue once thought to be just storage for energy is now known to secrete a variety of peptides known as adipokines that can contribute to insulin resistance (IR), hyperglycemia, dyslipidemia, hypertension, prothrombotic, and proinflammatory states. Adiponectin is one of the adipokines that is inversely related to obesity. Low levels of adiponectin are associated with IR and inflammatory states (3). Adiponectin levels change with age, sex and pubertal status, but generally stabilize between 13 and 16 years of age (4, 5).

In addition to the adipokines, recent literature suggests that low vitamin D levels are also associated with obesity and insulin resistance. Studies in adults associate low vitamin D levels with more insulin resistance and possible increased cardiovascular risk (6). Studies in children have also shown a correlation of low vitamin D with IR (7). Serum 25-hydroxyvitamin D [25(OH)D] is the best marker for vitamin D levels in the body. Vitamin D deficiency is generally defined as a 25(OH)D level of less than 50 nmol/L (20 ng/mL) and vitamin D insufficiency defined as a level of less than 75 nmol/L (30 ng/mL). Vitamin D deficiency is prevalent in minority children with several studies describing rates of deficiency in over 50% of AA adolescents (8, 9).

The objective of this study was to evaluate the relationship of 25(OH)D to adiponectin and insulin resistance in a population of AA adolescents with BMI ≥ 85th% compared to normal weight AA adolescents between the ages of 10 and 19 with a family history of type 2 diabetes in either a first- or second-degree relative. The aim of this study was to determine if low 25(OH)D correlated with low adiponectin and was associated with more insulin resistance using the homeostasis model assessment (HOMA) model to assess insulin resistance in overweight, obese and normal weight AA adolescents (10).

Patients and methods

Patients and control subjects

The study population included a total of 19 AA adolescents between the ages of 10 and 20 years who had a BMI of greater than or equal to the 85th percentile and a control population of 15 AA adolescents within the same age range with a BMI of <85th percentile. All subjects had a family history of type 2 diabetes in either a parent or grandparent. Howard University Institutional Review Board approved the study. The subjects gave assent if under the age of 18 and subjects 18 years or older and guardians gave written informed consent. Study participants were excluded if they were pregnant or there was a known history of diabetes, heart, renal, liver and thyroid disease. Also, subjects were not on medication known to influence insulin, lipid and glucose metabolism. The study and control subjects had not indulged in competitive sports.

Nutritional and body composition measurements

These studies were performed in the General Clinical Research Centers at Howard University Hospital with two separate outpatient visits. The first visit was for nutritional and body composition assessment. Assessment of dietary vitamin D intake was conducted

through administration of the Youth Adolescent Questionnaire (YAQ), a tool developed and validated by Harvard University to determine nutrient intake (11). The questionnaire was self administered, but in order to ensure standardization of data collection, directions as provided by Harvard University were given orally, by the same investigator, to each subject. The completed forms were sent to the Channing Laboratory at Harvard University for quantitation of nutrient intake. Vitamin D intake was compared between groups based on intake level and intake as a percent of the dietary reference intake (DRI). Body composition measurements included calculation of the BMI using the formula [weight (kg)/height (m^2)]. The BMI percentile was determined using the CDC table for calculated BMI values for selected height and weight ages from 2 to 20 years. Percent body fat was determined using the Tanita TBF-300™ scale (TANITA American, Arlington Heights, IL, USA). This scale measures weights up to 400 pounds (181.4 kg) and uses the foot-to-foot bioimpedance analyzer (BIA) technology to determine fat mass, fat free-mass, fat percentage, and total body water. The computer processor imbedded in the scale determined the percentage of body fat based on age and gender using equations with dual energy X-ray absorptiometry as a reference. Subjects consumed no caffeinated products 4 h before the test, and emptied their bladders 30 min before the test. Subjects were measured in bare feet. Waist, abdomen and hip circumferences were measured, with a non-stretchable tape. The waist circumference was measured at the level of the umbilicus while the patient was in the supine position and the hip circumference was measured at the level of the pubic symphysis while the patient was in the supine position. Blood pressures (BP) were measured at three separate times at least 10 min apart and averaged. Pubertal development was assessed by physical examination according to the criteria of Tanner.

Blood analysis

The second visit was within a week and assessed metabolic parameters. Subjects were advised on a weight-maintaining stabilization diet that consisted of 55% carbohydrate, 30% fat and 15% protein in total energy content. Intense exercise activities were avoided. The oral glucose tolerance test was performed on all subjects with BMI ≥ 85th percentile to assess for impaired glucose tolerance and diabetes. Oral glucose (Glutol, Custom Laboratories, Baltimore, MD, USA) was administered in a dose of 1.75 g/kg body weight to a maximum of 75 g. Blood samples were drawn at −10 and 0 min before glucose was administered and blood samples were obtained at 30, 60, 90, and 120 min after glucose consumption was complete. Fasting blood samples for glucose, lipids, adiponectin, insulin, 25(OH)D, and leptin were obtained on all subjects. A 2-h plasma glucose of ≥ 7.8 mmol/L (140 mg/dL) was defined as impaired and a fasting plasma glucose of ≥ 7 mmol/L (126 mg/dL) and/or 2 h post-glucose load of ≥ 11.1 mmol/L (200 mg/dL) was defined as diabetes. Insulin resistance using the HOMA model was calculated as fasting insulin (μU/mL) × fasting glucose (mmol/L)/22.5.

Biochemical measurements

Fasting lipid profile, glycosylated hemoglobin (HbA_{1c}), and chemistry panel were measured in the Howard University Hospital core laboratory on the autoanalyzers Beckman LX-20 and Beckman BXC. Adiponectin, leptin, insulin and 25(OH)D were measured in the molecular endocrinology laboratory at Howard University Hospital using commercially available

radioimmunoassay kits. Insulin, adiponectin, and leptin measurements were from the Millipore kits (formerly Linco Research, Inc., 6 Research Park, MO, USA). The 25(OH) D was measured using the kit from Immunodiagnostic Systems Limited (Fountain Hills, AZ, USA). All plasma glucose samples were collected in heparinized tubes and centrifuged (Refrigerated Beckman CPR) at 2000 × *g* 20 min at 4°C for 20 min. All plasma samples were stored at −70°C until analyzed.

Adiponectin, insulin, leptin and 25(OH)D were measured by radioimmunoassay protocols provided by the manufacturer. The adiponectin kit used ^{125}I–labeled murine adiponectin and a multispecies adiponectin antiserum to determine the levels of adiponectin in plasma samples by double antibody /PEG technique. The adiponectin standards were prepared using recombinant human adiponectin. The assay was extremely sensitive and required ×500 dilution with assay buffer. The final results were adjusted for appropriate dilution. The values from reference curve read in nM were converted to ng/mL by multiplying by 0.4. This assay kit had a precision of 5.3%–6.1% CV intra-assay and 7.3%–8.2% inter-assay.

The radioimmunoassay kit of insulin uses ^{125}I-labeled human insulin and human insulin antiserum to determine the level of insulin in the plasma samples by double antibody/PEG technique. A standard curve was set up with increasing concentrations of unlabeled standard insulin and from the curve the amount insulin was calculated. Acceptance criteria of the run were similar to adiponectin procedure as described above. The limit of sensitivity for the human insulin assay was 2 μU/mL. Limit of linearity for this assay was 200 μU/mL. All the obese subjects' samples were diluted ×5 because of high insulin values.

Leptin concentrations in plasma samples were assayed by RIA kit as described for adiponectin. The limit of sensitivity for the assay was 0.5 ng/L. The precision of the assay was 3.4%–8.3% (within) and 3.0%–6.2% in between assay.

Fifty micro-liters plasma samples, calibrators, and quality control samples were extracted for 25(OH)D with reagents supplied in the kit. Assay tubes containing extracted samples, non-specific binding, calibrators and controls in duplicate, ^{125}I-labeled 25(OH)D were reacted with specific antibody against 25(OH)D. The bound 25(OH) D was precipitated with reagent Sac-cel ^{R} supplied in the kit. The rest of the RIA protocol was similar to the other hormones described above. The assay kit had a precision of 5.3%–6.1% CV intra-assay and 7.3%–8.2% inter-assay.

Statistical analysis

Analysis of the data was performed using SAS version (9.1) (SAS Institute, Cary, NC, USA). Wilcoxin Score and Kruskal-Wallis test and Pearson's correlation coefficient were used to assess statistical differences, with p-values of <0.05 as statistically significant. Means±standard deviation was used for descriptive data.

Results

Table 1 shows the clinical characteristics of the study subjects. All subjects had a Tanner stage of 2 or greater. Laboratory data is summarized in Table 2. Adiponectin levels were

significantly lower in the BMI ≥ 85th percentile adolescents (p<0.0001). The levels of insulin, fasting blood glucose, HOMA-IR, leptin, triglycerides and high density lipoprotein (HDL) were statistically significant between the overweight/obese adolescents compared to the normal weight adolescents. Adolescents with BMIs ≥ 85th percentile were more insulin resistant and had higher triglycerides, but lower HDL. Only one subject had an impaired OGTT and none had an OGTT consistent with diabetes. Also, overweight/obese adolescents had significantly lower 25(OH)D levels (p<0.001) when compared to the normal weight adolescents. Dietary vitamin D consumption, mean±SD in the (BMI ≥ 85th%) was 226±165.6 IU/day and in (controls) was 190±129.6 IU/day. Vitamin D intake as a percent of the DRI was 113±82.2% in (BMI ≥ 85th%) and 95±64.8% in control subjects. The percent of (BMI ≥ 85th%) subjects having a daily intake of vitamin D <75% of the DRI was 42% compared with 53% of the controls. No statistical difference in vitamin D intake was found between these groups either on the basis of daily intake (p=0.512) or intake as a percent of the DRI (p=0.513). The 25(OH)D level correlated with adiponectin (p<0.001) and both adiponectin and 25(OH) D levels correlated with IR using the HOMA at p-values of 0.018 and 0.042, respectively (Table 2).

Discussion

The results of our study indicated that adiponectin correlated with vitamin D levels and both correlated with IR. A population-based study conducted by Lee et al. demonstrated that obesity was the most important risk factor for IR that was independent of race, sex, or age (12). Also, in this study, pubertal status did not appear to affect IR values significantly in overweight and normal weight adolescents. As in Lee et al.'s study, we found that higher HOMA-IR correlated with obesity and low adiponectin levels. Several studies in the pediatric population have demonstrated an inverse relationship of adiponectin with obesity and IR (5, 13, 14). Adolescents with BMIs ≥ 85th percentile had much lower 25(OH)D and adiponectin levels when compared to normal weight controls. Even though there was no significant difference between the two groups in the intake of vitamin D, their plasma levels of 25-OH vitamin D were significantly different from each other (33.7±10 nmol/L in obese and 56.93±18.63 nmol/L in non-obese, p=004).

Vitamin D is crucial to the overall health and well-being of human beings. Vitamin D receptors are found throughout the body affecting the skeleton, muscles, pancreas, brain, prostate, breast, colon, immune cells, heart, and other organs (15). Several disorders have been associated with vitamin D deficiency including rickets, cancer, autoimmune disorders, and IR. Also, vitamin D deficiency has been linked to cardiovascular disease including hypertension, and coronary artery calcification (16). McGill et al. demonstrated a relationship of markers of type 2 diabetes (large waist and elevated HbA_{1c}) and low serum 25(OH)D in adults (17). Proposed mechanisms of low vitamin D and IR include impaired insulin action, and glucose metabolism in adipose tissue, although there is no consensus as to the level of 25(OH)D that is considered to be adequate. Levels of <50 nmol/L traditionally have been considered insufficient. However, recent data suggests 25(OH) D levels of >75 nmol/L may be optimal due to the fact that secondary hyperparathyroidism is less likely to occur when the serum levels of 25(OH)D exceed 75 nmol/L (18).

The prevalence of vitamin D deficiency among adolescents is quite high. Tangorra et al. studied 217 obese adolescents and found that 55.2% of the subjects were vitamin D deficient using a level of 25(OH)D of <50 nmol/L. The National Health and Nutrition Examination Survey (NHANES) study of US children and adolescents aged 1 to 21 years from 2001 to 2004 had an overall prevalence rate of 9% for 25(OH)D deficiency using less than 37.5 nmol/L as the cutoff and 61% were insufficient with 25(OH)D levels below 50 nmol/L (19). In the NHANES study, non-Hispanic blacks, girls, older age, obesity, and sedentary lifestyle were more likely to be associated with 25(OH)D deficiency. As in our study, these studies showed an association of increased BMI, systolic blood pressure and decreased HDL with low levels of 25(OH)D. Our study and other studies have also supported the observation that 25(OH)D insufficiency is found in over 50% of the adolescent population In our study, 17 out of the 19 obese subjects had 25(OH)D levels below 50 nmol/L and all had levels below 75 nmol/L. Even the lean controls (8 out of 15) had 25(OH)D levels at less than 50 nmol/L and only 2 had levels above 75 nmol/L. African American adolescents are particularly at risk for 25(OH)D deficiency due to skin pigmentation, lack of adequate sun exposure and inadequate vitamin D intake. The long-term effects of 25(OH)D deficiency in adolescents and the relationship to cardiovascular and metabolic health are not known.

Conclusion

The relationship of adiponectin to vitamin D level is not known. In our study, low adiponectin levels also correlated strongly with low 25(OH)D levels. The significance of this relationship is not clear and may be due to association or coincidental findings. However, Liu et al. also found a relationship in nondiabetic adults of low 25(OH)D with low adiponectin and low HDL, along with an inverse relationship to IR, thereby suggesting a relationship of 25(OH)D status and IR (20). Low levels of adiponectin in the pediatric population may be a marker for future adverse metabolic and cardiovascular outcomes and other hormones including vitamin D may modulate this. Though our numbers were small in this study, more studies are needed in the pediatric population to evaluate the relationship of low 25(OH)D, adiponectin and IR to metabolic and adverse cardiovascular outcomes.

References

1. Dietz WH, Robinson TN. Overweight children and adolescents. N Engl J Med. 2005; 352:2100–9. [PubMed: 15901863]
2. Ogden CL, Carroll MD, Curtin LR, McDowell MA, Tabak CJ, et al. Prevalence of overweight and obesity in the United States, 1999–2004. J Am Med Assoc. 2006; 295:1549–55.
3. Kershaw EE, Flier JS. Adipose tissue as an endocrine organ. J Clin Endocrinol Metab. 2004; 89:2548–56. [PubMed: 15181022]
4. Andersen KK, Frystyk J, Wolthers OD, Heuck C, Flyvbjerg A. Gender differences of oligomers and total adiponectin during puberty: a cross-sectional study of 859 Danish school children. J Clin Endocrinol Metab. 2007; 92:1857–62. [PubMed: 17284625]
5. Punthakee Z, Delvin EE, O'Loughlin J, Paradis G, Levy E, et al. Adiponectin, adiposity, and insulin resistance in children and adolescents. J Clin Endocrinol Metab. 2006; 91:2119–25. [PubMed: 16537675]
6. Chiu KC, Chu A, Go VL, Saad MF. Hypovitaminosis D is associated with insulin resistance and {beta} cell dysfunction. Am J Clin Nutr. 2004; 79:820–5. [PubMed: 15113720]

7. Alemzadeh R, Kichler J, Babar G, Calhoun M. Hypovitaminosis D in obese children and adolescents: relationship with adiposity, insulin sensitivity, ethnicity, and season. Metabolism. 2008; 57:183–91. [PubMed: 18191047]
8. Gordon CM, DePeter KC, Feldman HA, Grace E, Emans SJ. Prevalence of vitamin D deficiency among healthy adolescents. Arch Pediatr Adolesc Med. 2004; 158:531–7. [PubMed: 15184215]
9. Smotkin-Tangorra M, Purushothaman R, Gupta A, Nejati G, Anhalt H, et al. Prevalence of vitamin D insufficiency in obese children and adolescents. J Pediatr Endocrinol Metab. 2007; 20:817–23. [PubMed: 17849744]
10. Wallace TM, Levy JC, Matthews DR. Use and abuse of HOMAmodeling. Diabetes Care. 2004; 27:1487–95. [PubMed: 15161807]
11. Rockett HR. Validity and reliability of the Youth/Adolescent Questionnaire. J Am Diet Assoc. 2005; 105:1867–8. [PubMed: 16321589]
12. Lee JM, Okumura MJ, Davis MM, Herman WH, Gurney JG. Prevalence and determinants of insulin resistance among U.S. adolescents: a population-based study. Diabetes Care. 2006; 29:2427–32. [PubMed: 17065679]
13. Lee S, Bacha F, Gungor N, Arslanian S. Comparison of different definitions of pediatric metabolic syndrome: relation to abdominal adiposity, insulin resistance, adiponectin, and inflammatory biomarkers. J Pediatr. 2008; 152:177–84. [PubMed: 18206686]
14. Reinehr T, Roth C, Menke T, Andler W. Adiponectin before and after weight loss in obese children. J Clin Endocrinol Metab. 2004; 89:3790–4. [PubMed: 15292306]
15. Holick MF. Sunlight and vitamin D for bone health and prevention of autoimmune diseases, cancers, and cardiovascular disease. Am J Clin Nutr. 2004; 80(Suppl 6):1678S–88. [PubMed: 15585788]
16. Wang TJ, Pencina MJ, Booth SL, Jacques PF, Ingelsson E, et al. Vitamin D deficiency and risk of cardiovascular disease. Circulation. 2008; 117:503–11. [PubMed: 18180395]
17. McGill AT, Stewart J, Lithander F, Strik C, Poppitt S. Relationships of low serum vitamin D3 with anthropometry and markers of the metabolic syndrome and diabetes in overweight and obesity. Nutr J. 2008; 7:4. [PubMed: 18226257]
18. Holick MF. Vitamin D deficiency. N Engl J Med. 2007; 357:266–81. [PubMed: 17634462]
19. Kumar J, Muntner P, Kaskel FJ, Hailpern SM, Melamed ML. Prevalence and associations of 25-hydroxyvitamin D deficiency in US children: NHANES 2001–2004. Pediatrics. 2009; 124:e362–70. [PubMed: 19661054]
20. Liu E, Meigs JB, Pittas AG, McKeown NM, Economos CD, et al. Plasma 25-hydroxyvitamin D is associated with markers of the insulin resistant phenotype in nondiabetic adults. J Nutr. 2009; 139:329–34. [PubMed: 19106328]

Table 1

Study population clinical characteristics.

Characteristics	BMI ≥ 85th percentile n=19	BMI <85th percentile n=15	p-Value*
Age	13.00±2.56	15.20±3.74	0.068
M:F	8:11	6:9	
Height, cm	165.51±14.39	164.93±12.71	0.958
Height SDS	1.28±1.04	0.82±0.88	0.267
Weight, kg	03.72±31.79	59.14±12.71	<0.001
BMI, kg/m^2	37.07±6.68	21.33±2.16	<0.001
BMI percentile	98.84±0.5	64.80±19.25	<0.001
% Body fat	43.33±20.78	20.79±8.55	<0.001
Systolic blood pressure, mm Hg	125±14.35	113±10.48	0.012
Diastolic blood pressure, mm Hg	71.79±8.42	64.60±6.87	0.015
Waist, cm	110.24±15.92	75.36±6.04	<0.001

* p-Value of the characteristic parameter was <0.05, it was considered significantly different.

Table 2

The relationship of insulin resistance and vitamin D in obese and normal weight African-American adolescents.

Hormonal/metabolic parameters	BMI ≥ 85th percentile n=19	BMI <85th percentile n=15	p-Value*
Adiponectin, μg/mL	6.79±4.55	17.28±6.89	<0.0001
Fasting insulin, μU/mL	33.00±17.62	18.70±7.65	0.023
Fasting glucose, mg/dL	94.10±13.37	84.93±9.32	0.028
2-h post prandial glucose, mg/dL	113.68±28.54	*	
HOMA-IR	3.96±1.84	2.34±0.948	0.01
Leptin, ng/mL	44.01±13.22	12.00±13.25	<0.001
Triglycerides, mg/dL	105.89±81.84	62.60±38.38	0.03
HDL, mg/dL	36.26±10.94	51.27±19.54	0.004
LDL, mg/dL	105.48±37.53	98.87±29.53	0.6149
25-hydroxy vitamin D, nmol/L	33.7±9.95	51.93±18.63	0.004
$HgbA_{1c}$	5.44±0.48	5.22±0.37	0.33

* p-Values <0.05 were considered significantly different.