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High prevalence of cardiometabolic risk factors in Hispanic adolescents: Correlations with adipocytokines and markers of inflammation

Cynthia M. Pérez[1], **Ana P. Ortiz**[1,2], **Enrique Fuentes-Mattei**[3], **Guermarie Velázquez-Torres**[3,4,5], **Damarys Santiago**[2], **Katya Giovannetti**[6], **Raúl Bernabe**[2], **Mong-Hong Lee**[3,4,5], and **Sai-Ching J. Yeung**[7,8]

[1]Department of Biostatistics and Epidemiology, Graduate School of Public Health, Medical Sciences Campus, University of Puerto Rico, San Juan, Puerto Rico

[2]University of Puerto Rico Comprehensive Cancer Center, San Juan, Puerto Rico

[3]Department of Molecular and Cellular Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX

[4]The University of Texas Graduate School of Biomedical Sciences at Houston, Houston, TX

[5]The University of Texas MD Anderson Cancer Center, Program in Cancer Biology, Houston, TX

[6]Puerto Rico Clinical and Translational Research Consortium, University of Puerto Rico Medical Sciences Campus

[7]Department of Emergency Medicine, The University of Texas MD Anderson Cancer Center, Houston, TX

[8]Department of Endocrine Neoplasia and Hormonal Disorders, The University of Texas MD Anderson Cancer Center, Houston, TX

Abstract

Background—This study assessed the associations of cardiometabolic risk factors with systemic inflammation, insulin resistance, and adypocytokines in a Hispanic adolescent subgroup.

Methods—A clinic-based sample of 101 Puerto Rican adolescents, 48 of whom were overweight or obese based on BMI percentiles for age and sex, was recruited during 2010. Data were collected through interviews, blood pressure and anthropometric measurements, and blood drawing.

Results—Overall prevalence of the metabolic syndrome was 16.8% and increased to 37.5% among overweight/obese youth. The overweight/obese group exhibited significantly ($p<0.05$) higher values for abdominal obesity measures, systolic blood pressure, triglycerides, insulin resistance, C peptide, hs-CRP, fibrinogen, leptin, and IL-6 and lower levels of HDL-C, adiponectin, and IGF-1. Total adiponectin significantly correlated with most cardiovascular risk factors independent of sex, Tanner stage, and adiposity.

Address all correspondence and requests for reprints to: Cynthia M. Pérez, PhD, Department of Biostatistics and Epidemiology, Graduate School of Public Health, Medical Sciences Campus, University of Puerto Rico, P.O. Box 365067, San Juan, Puerto Rico 00936-5067; Phone: 787-758-2525 ext. 1454; Fax: 787-764-5831; cynthia.perez1@upr.edu.

Discussion—Altered cardiometabolic and adipocytokine profiles were present in this Hispanic subgroup, reinforcing the need to strengthen strategies addressing childhood obesity.

Keywords

Cardiometabolic risk; Adipocytokines; Inflammation; Hispanics; Adolescents

Introduction

In recent years, there has been an increased emphasis on comprehensive approaches to prevent childhood obesity and related cardiovascular disease risk factors (1–2). The prevalence of obesity has tripled among individuals aged 2 to 19 years over the past three decades and it continues to be higher among Hispanic and non-Hispanic Black youth (3). Particularly alarming are reports that document a two- to three-fold increase in the prevalence of cardiometabolic abnormalities and type 2 diabetes mellitus (DM) among youth worldwide (4,5). In the U.S. an estimated 8.6% of adolescents aged 12–19 years have the metabolic syndrome, with Hispanic males having the highest prevalence (11.2%) (6).

Overweight Hispanic youth with the metabolic syndrome experience early deterioration in pancreatic beta-cell function and are significantly more insulin resistant than Caucasian youth, independent of body composition (7–10). Moreover, Hispanic children with type 2 DM have lower adiponectin levels compared to normoglycemic children (11,12), thus, suggesting that hypoadiponectinemia may partly contribute to the greater risk of type 2 DM among Hispanics (13,14). Numerous studies suggest that cardiometabolic risks as well as various obesity-related disorders, are mediated through adipocytokines associated with obesity (15–18). However, markers such as adiponectin, leptin, and C-reactive protein (CRP) have received more attention in studies of adolescents. Studies assessing systemic inflammation, insulin resistance and adypocytokines in subgroups of Hispanic adolescents and on their potential associations with various cardiometabolic alterations are more limited (12–15,18). Puerto Ricans, an admixed population of African, European, and Native American ancestries, have the highest age-adjusted prevalence and incidence of DM among all U.S. states and territories (19). This study examined the associations of cardiometabolic risk factors with adipocytokines and inflammatory markers, independent of sex, self-rated Tanner stage, and adiposity measures in a sample of Puerto Rican adolescents.

Methods

Study Population

A cross-sectional study of 101 consecutive adolescents aged 12 to 18 years attending the University of Puerto Rico Pediatric Clinics during 2009–2010 was carried out. A priori exclusion criteria included those who had a pre-existing diagnosis of type 2 DM, cardiovascular disease or genetic syndromes, subjects on medications known to affect glucose metabolism or abdominal fat distribution, and pregnant females. The University of Puerto Rico Medical Sciences Campus institutional review board approved the study, and written consent and assent were obtained from parents and adolescents, respectively.

Study Procedures

Anthropometric data—Weight, height, and body circumferences at defined sites were measured in duplicate following the NHANES III Anthropometric Video Procedures, and the average of the two measurements was used. Weight was measured to the nearest 0.1 kg by using a calibrated scale, whereas height was measured to the nearest 1 mm by using a wall-mounted stadiometer with the participant's shoes removed and head held in the Frankfurt horizontal plane. Body mass index (BMI) was classified according to the 2000 CDC Growth Charts for the U.S.: overweight and obesity were defined as having a BMI ≥ 85th percentile for age and sex, and normal weight was defined as a BMI between the 5th and 85th percentile for age and sex. Each BMI value was converted to a z score in groups defined by age and sex, using the 2000 CDC Growth Charts for the U.S. Waist circumference was measured to the nearest 1 mm at the high point of the iliac crest, at minimal respiration, when the participant was in a standing position. Hip circumference was measured at the level of greater trochanters and pubic symphysis to the nearest 1 mm. Waist to height ratio was also calculated.

Blood pressure—Blood pressure was measured using a sphygmomanometer and appropriate cuff size after a five-minute rest with the participant in the sitting position. Three blood pressure measurements were taken, and the average measurements were converted to percentiles using the age- and height-specific blood pressure tables provided by the Fourth Task Force Report on High Blood Pressure in children and adolescents (20).

Interview—Adolescents were interviewed regarding demographic characteristics and lifestyle behaviors including physical activity (engagement in moderate-intensity physical activities for at least 60 minutes for five or more days of the week), daily intake of fruits and vegetables, and lifetime tobacco use and alcohol consumption. Pubertal stage for sexual maturity was assessed by self-report from line drawings for development of testicle volume in boys and breast development in girls. The legal guardian of each adolescent was also interviewed to collect information on social characteristics, parental height and weight, and family and adolescent past medical histories.

Metabolic syndrome—Adolescents were classified as having the metabolic syndrome (6,21) if they met at least three of the following criteria: (1) diastolic or systolic blood pressure that exceeds the 90th percentile for age, sex and height, (2) fasting glucose ≥100 mg/dL, (3) triglycerides ≥110 mg/dL, (4) high density lipoprotein cholesterol (HDL-C) <40 mg/dL, and (5) waist circumference that exceeds the 90th percentile for age and sex (22).

Laboratory Assays—Blood was drawn from an antecubital vein in the morning after a 10-hour overnight fasting. Fasting plasma glucose (FPG in mg/dL) levels were determined using a commercial enzymatic colorimetric kit (Bayer Diagnostics, Tarrytown, NY). Fasting plasma insulin (FPI in μU/I) levels were measured using a commercial radioimmunoassay kit (Padebas Pharmacia, Piscataway, NJ). The homeostasis model assessment of insulin resistance (HOMA-IR) [(FPG x FPI)/405] was determined as described by Keskin et al. (23). Total cholesterol, triglycerides, and HDL-C were measured by enzymatic methods using the Abbot VP instrument (Abbott Laboratories, Chicago).

A two-site immunoassay for measuring fibrinogen in plasma was used (DiaPharma Group Inc., West Chester, OH). High-sensitivity C reactive protein (hs-CRP) was measured using an ultrasensitive commercial assay kit (Kamiya Biomedical, Seattle, WA). Total adiponectin was measured using a commercially available quantitative sandwich enzyme-linked immunoassay kit (Human Adiponectin/Acrp30 Quantikine ELISA; R&D Systems, Minneapolis, MN). Plasma levels of insulin-like growth factor 1 (IGF-I) and insulin-like growth factor binding protein-3 (IGFBP-3) were assayed by corresponding enzyme-linked immunosorbent assays with reagents from Diagnostic Systems Laboratory (Webster, TX). Plasma cytokines [IL-6, TNF-α, monocyte chemoattractant protein 1 (MCP-1)] and gut hormones [glucagon, C peptide, glucose insulinotropic peptide (GIP), glucagon like peptide 1 (GLP-1), total amylin, ghrelin, pancreatic polypeptide (PP), peptide YY (PYY)] were determined in duplicate by using Multiplex Immunoassay kits (Milliplex MAP Human Metabolic Hormone Magnetic Bead Panel HMHMAG-34K; EMD Millipore, Billerica, MA).

Statistical Analysis—Due to the skewness of the raw data, log-transformed values of selected adipocytokines were used. Differences between lean and overweight/obese adolescents were assessed using Student's t-test, Wilcoxon-Mann-Whitney test for medians, and Chi-square test for independence or Fisher's exact test, when appropriate. Partial Spearman's correlations were performed to determine the associations of cardiometabolic risk factors with adipocytokines and inflammatory markers, while adjusting for sex and Tanner stage. Additional adjustment for age did not alter the strength or significance of these correlations.

Multivariable stepwise linear regression analysis with forward selection was performed to assess which variables contributed significantly to the variation of the individual cardiometabolic risk factors after adjusting for sex, Tanner stage and adiposity. The significant ($p<0.05$) positive correlations of BMI z score with central adiposity measures ($r=0.82$ for waist circumference, $r=0.83$ for waist-to-height ratio, and $r=0.69$ for waist-to-hip ratio) precluded inclusion of these measures in a single model. Therefore, all models were adjusted separately for BMI z score, waist circumference, waist-to-hip ratio and waist-to-height ratio. Standardized β-estimate was used to determine which variable had the strongest effect on individual cardiometabolic risk factors. Analyses were performed using Stata version 11 (StataCorp LP, College Station, TX).

Results

Of 101 adolescents recruited into the study, nearly half were either overweight (21.8%) or obese (25.7%). Overweight and obese adolescents were similar to lean adolescents in the distribution of age, sex, Tanner stage, parental BMI and selected lifestyles (Table 1). Application of the definition used for metabolic syndrome produced an overall prevalence of 16.8%, increasing to 37.5% among those who were overweight or obese. The overweight or obese group exhibited significantly ($p<0.05$) higher values for waist circumference, waist-to-hip ratio, waist-to-height ratio, systolic blood pressure, total cholesterol, and triglycerides, and lower levels of HDL-C (Table 1). Prevalence of the metabolic syndrome was marginally ($p=0.068$) higher in males (22.8%) than in females (9.1%), with males having significantly

(p<0.05) higher prevalence of elevated blood pressure and reduced HDL-C (data not shown). Despite glucose levels were not significantly different in both groups, overweight and obese youth had significantly (p<0.001) higher levels of fasting insulin and HOMA-IR than normal weight youth (Table 1). Insulin resistance, defined as a HOMA cutoff point ≥3.16 (32), was significantly higher among overweight/obese adolescents than among the lean group (81.3% vs. 35.6%, p<0.001), with an overall median value of 3.5, which was above the selected cutoff point (3.16). This group also had significantly (p<0.01) lower levels of IGF-1 and adiponectin but higher concentrations of C peptide, hs-CRP, fibrinogen, leptin, and IL-6 compared with lean adolescents.

Partial's Spearman's correlations showed that systolic blood pressure was positively (p<0.05) associated to all four adiposity measures, insulin, HOMA-IR, C peptide, hs-CRP, fibrinogen, and leptin, whereas it was negatively associated to adiponectin (Table 2). Diastolic blood pressure was positively associated to BMI z score, waist circumference, waist-to-height ratio, insulin, HOMA-IR, and C peptide, but negatively associated to adiponectin. HDL-C was inversely (p<0.05) correlated to all four adiposity measures, insulin, HOMA-IR, hs-CRP, and leptin, and positively correlated with IGF-1 and adiponectin. In contrast, triglycerides only correlated positively with insulin, HOMA-IR, C peptide, fibrinogen and leptin, but inversely with adiponectin. Glucose correlated positively with insulin and HOMA-IR, but inversely with glucagon and MCP-1. Finally, HOMA-IR correlated positively with BMI z score, waist circumference, waist-to-height ratio, hs-CRP, fibrinogen, leptin, IL-6, and amylin, whereas an inverse correlation was observed for adiponectin.

Multivariable stepwise linear regression models were run for each of the cardiometabolic risk factors adjusting for sex and self-rated Tanner stage (Table 3). Both adiponectin (p=0.001) and HOMA-IR (p<0.001) remained significantly associated to systolic blood pressure, together accounting for 42% of its variation. Additional adjustment for BMI z score and waist circumference, but not waist-to-hip ratio, attenuated the regression coefficients but statistical significance was retained. Adiponectin (p=0.027) was the only variable that remained independently associated to diastolic blood pressure, explaining only 7% of its variance. This result remained unaltered after adjustment for waist-to-hip ratio but attenuated considerably to non-significance after controlling for either BMI z score or waist circumference. IGF-1 (p=0.001) and adiponectin (p=0.002) were significantly associated to HDL-C, accounting for 22% of its variation. Adjustment for waist-to-hip ratio did not alter these results; however, adjustment for waist circumference attenuated both regression coefficients despite retaining statistical significance, whereas adjustment for BMI z score attenuated the significance level for adiponectin (p=0.082). Adiponectin (p=0.026) was significantly associated only to triglycerides, and additional adjustment for BMI z score attenuated to marginal significance (p=0.062), but remained unaltered after adjustment for waist circumference or waist-to-hip ratio. Although adjustment for waist circumference did not alter the marginal association between fibrinogen and triglycerides (p=0.072), BMI z score and waist-to-hip ratio attenuated this association to non-significance.

GIP (p=0.001) and insulin (p=0.007) were independently associated to glucose levels, explaining 19% of glucose variation, and the aforementioned associations remained

unaltered when adding BMI z score, waist circumference or waist-to-hip ratio. Leptin ($p<0.001$), total amylin ($p=0.003$), adiponectin ($p=0.006$) and pancreatic polypeptide ($p=0.025$) independently influenced insulin resistance, as determined by HOMA-IR, accounting for 45% of its total variation. Repeating this analysis after adjusting for waist-to-hip ratio yielded similar results, although the regression coefficients attenuated after additional adjustment for BMI z score or waist circumference. When the regression models for cardiometabolic risk factors were adjusted for waist-to-height ratio, estimated coefficients and significance levels were similar to those for waist circumference (data not shown).

Discussion

Our findings provide evidence for the first time of the presence of an adverse cardiometabolic risk profile (elevated systolic blood pressure, atherogenic dyslipidemia, insulin resistance and metabolic syndrome) in this group of overweight and obese Puerto Rican adolescents. Nearly two-thirds of adolescents exhibited at least one cardiometabolic abnormality, and 16.8% met the definition of the metabolic syndrome used in this study. This prevalence was marginally higher in males, and it nearly doubled among those who were overweight or obese (35.4%). The most common metabolic syndrome abnormalities were atherogenic dyslipidemia, elevated blood pressure and abdominal obesity, findings that are consistent with the most prominent features of the metabolic syndrome among Hispanic youth in the U.S. (6).

The epidemic of adolescent obesity is ongoing. There have been significant increases in waist circumference and blood glucose documented in U.S. adolescents from 1999 to 2008, with Mexican-American adolescents having larger waist values and Mexican-American female adolescents experiencing a significant increase in cardiometabolic risk factor clustering score (24). Although it is unknown whether these trends are also occurring in Puerto Rico due to the lack of population-based data on obesity and cardiometabolic risk factors, a handful of studies have documented the high prevalence of obesity in Puerto Rican children and adolescents (25–29). Despite our findings are in agreement with previous investigations that have evidenced clustering of cardiometabolic biomarkers in childhood and adolescence, and that a high percentage of overweight and obese youth in the U.S. exhibit the metabolic syndrome (6,7,21,24), the prevalence of the metabolic syndrome (16.8%) in this sample of Puerto Rican adolescents was 1.5 times higher than that for Hispanic youth in the U.S. (11.2%) (6). Although our findings cannot be generalized to the population of adolescents in Puerto Rico due to the nature of the sample, these findings are worrisome since cardiometabolic risk factors track from childhood into adulthood and are predictive of premature cardiovascular disease and type 2 DM (30).

Insulin resistance is the most common metabolic alteration related to obesity, and it represents an important link between obesity and other cardiometabolic complications including the metabolic syndrome and type 2 DM (7,8,10,12,30). Cumulative evidence indicates that adipose tissue seems to play a key role in the pathogenesis of insulin resistance through dysregulated production of adipocytokines and increased local and systemic inflammation (11,12,14,15–18,21). Youth in this study exhibited a high prevalence of

insulin resistance (defined as HOMA-IR≥3.16) and an altered inflammatory and adipocytokine profile that included elevated levels of hs-CRP, fibrinogen, IL-6, and leptin and reduced levels of adiponectin. Thus, if these findings continue to hold true for the general population of adolescents, a future epidemic of premature cardiovascular disease and type 2 DM in the Puerto Rican population is yet to come.

In line with previous investigations (13,30–33), adiponectin and HOMA-IR were significant contributors of both systolic and diastolic blood pressures, after controlling for sex, self-rated Tanner stage, and adiposity measures (BMI, waist circumference and waist-to-hip ratio). Several studies that have shown significant associations between lipid parameters and total adiponectin support the notion that adiponectin may represent the missing link between adiposity, insulin resistance and lipid metabolism (12–14,30,33–35). Our findings are consistent with these studies showing that the positive association of total adiponectin with plasma HDL-C concentrations and the negative association with triglycerides were still significant after controlling for adiposity measures. With regard to the positive relationship between HDL-C and plasma IGF-1, previous data have demonstrated a positive relationship of IGF-I with HDL-C, suggesting a regulatory role of IGF-1 on plasma lipid concentration (35,36). Since glucose homeostasis is regulated by the interaction of insulin, glucagon, amylin and incretin hormones, it was not surprising that both GIP and fasting insulin turned out to be the significant contributors to glucose variation (37). Of interest, glucose was the only metabolic syndrome component that was not related to adiponectin, a finding consistent with other studies in children and adolescents (12,17). The majority (98%) of youth in this study had normal glucose values (<100 mg/dL); this observation is consistent with the three-stage model for the development of type 2 DM proposed by Beck-Nielsen and Groop (38), the stage 1 of which has fasting hyperinsulinemia with normal or slightly increased blood glucose. In accordance with previous studies, significant correlations of leptin, amylin, adiponectin, and pancreatic polypeptide with HOMA-IR were found. The potential role of leptin and adiponectin in glucose metabolism and insulin sensitivity has been suggested in previous studies (11,13,16,17). In keeping with previous observations that amylin is increased under conditions associated with insulin resistance (39), we found that total amylin was positively correlated to HOMA-IR variation in the multivariable model. On the other hand, we found that pancreatic peptide levels were negatively correlated with insulin resistance in the multivariable regression model, a finding consistent with amelioration of insulin resistance after repeated administration of this gut hormone in mice (40). In contrast with studies in other populations, we did not observe significant associations with hs-CRP, fibrinogen, and IL-6 in the multivariable model for HOMA-IR, although levels of these biomarkers were markedly increased in overweight/obese youth and correlated positively and significantly with HOMA-IR in the bivariate analysis.

Several limitations in this study should be noted. Inherent to the study design, the ability to draw inferences regarding causality between cardiometabolic risk factors and adipocytokines and inflammatory markers is hindered. Since a non-probability sampling was used to select the study group, we cannot directly generalize our findings to the adolescent population in Puerto Rico; however, measures of adiposity and lipids were fairly comparable to those reported in previous studies. Although clamp technology is the gold standard measure of insulin resistance, the index used for determining insulin resistance highly

correlates with the hyperinsulinemic euglycemic clamp measure among youth (23). Moreover, we did not measure high molecular weight adiponectin, which might be a better marker of insulin resistance than total adiponectin. Given our small sample size, additional studies are required to confirm these observations and explore the underlying mechanisms. These limitations must be balanced against the strengths of this study, which include precise methods used for assays and body composition measurements, extensive data from the face-to-face interview in both youth and parents and biological plausibility with most of the findings.

Our epidemiologic evidence show that this sample of youth exhibits altered cardiometabolic and adipocytokine profiles with high prevalence, reinforcing the need to monitor trends in childhood obesity and design evidence-based public health programs for its prevention.

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Table 1

Baseline characteristics* of 101 Hispanic adolescents according to BMI percentile

	Normal weight* (n=53)	Overweight & Obese* (n=48)	P value†
Age, years	15.3 (1.8)	14.9 (2.0)	0.28
Male gender	30 (56.6)	27 (56.3)	0.97
Tanner stage	4.0 (0.9)	3.7 (1.1)	0.11
Maternal BMI, kg/m^2	29.0 (7.6)	31.5 (8.5)	0.12
Paternal BMI, kg/m^2	28.5 (4.9)	29.3 (4.9)	0.41
Ever smoked	1 (1.9)	2 (4.2)	0.60
Ever consumed alcohol	30 (56.6)	19 (39.6)	0.09
Regular physical activity	14 (26.4)	9 (18.8)	0.36
Daily consumption of fruits and vegetables	24 (45.3)	17 (34.4)	0.31
Metabolic syndrome	0	17 (35.4)	<0.001
BMI, kg/m^2	19.6 (2.4)	30.7 (6.6)	<0.001
Waist circumference, cm	70.9 (5.4)	94.7 (16.2)	<0.001
Waist circumference>90th percentile for age and sex	0 (-)	23 (47.9)	<0.001
Waist-to-hip ratio	0.8 (0.05)	0.9 (0.09)	<0.001
Waist-to-height ratio	0.4 (0.03)	0.6 (0.09)	<0.001
Systolic blood pressure, mm Hg	106.9 (10.6)	116.0 (12.6)	<0.001
Diastolic blood pressure, mm Hg	56.9 (7.8)	58.5 (6.2)	0.25
Blood pressure >90th percentile for age, sex and height	8 (15.1)	17 (35.4)	0.018
Total cholesterol, mg/dl	140.0 (128.0, 157.0)	153.5 (134.5, 182.0)	0.011
Triglycerides, mg/dl	83.0 (60.0, 101.0)	94.0 (71.0, 130.5)	0.022
Triglycerides ≥110 mg/dL	10 (18.9)	20 (41.7)	0.012
HDL-C, mg/dl	49.0 (42.0, 59.0)	39.0 (32.0, 48.0)	<0.001
HDL-C<40 mg/dl	13 (24.5)	25 (52.1)	0.004
Glucose, mg/dl	85.4 (6.5)	86.4 (5.4)	0.40
Glucose ≥100 mg/dL	1 (1.9)	1 (1.9)	>0.99
Insulin, μU/ml	8.3 (6.4, 13.1)	18.5 (13.0, 26.6)	<0.001
HOMA-IR	1.8 (1.3, 2.8)	4.1 (2.9, 5.8)	<0.001
HOMA-IR≥3.16	19 (35.6)	39 (81.3)	<0.001
IGF-1, μg/l	272.1 (186.6, 384.0)	216.3 (166.5, 263.1)	0.004
IGF-BP3, μg/l	2573.3 (2271.8, 2925.8)	2503.5 (2102.5, 2843.2)	0.34
C peptide, pg/ml	1148.0 (889.0, 1474.0)	1785.0 (1398.5, 2214.5)	<0.001
Glucose insulinotropic peptide, pg/ml	13.4 (10.1, 19.5)	14.1 (11.4, 18.5)	0.89
Glucagon like peptide 1, pg/ml	41.1 (28.5, 63.7)	38.5 (25.6, 62.6)	0.37
Glucagon, pg/ml	0.0 (0.0, 7.7)	0.0 (0.0, 0.0)	0.46
hs-CRP, mg/L	0.3 (0.3, 0.3)	0.6 (0.3, 1.1)	<0.001
Fibrinogen, mg/dl	245.0 (216.2, 279.4)	294.3 (247.4, 342.1)	<0.001
Adiponectin, μg/ml	13.3 (9.7, 16.7)	8.0 (3.8, 11.9)	<0.001
Leptin, μg/ml	4.1 (1.5, 10.6)	24.9 (14.4, 41.6)	<0.001
Ghrelin, pg/ml	9.0 (6.1, 12.9)	7.6 (4.8, 12.9)	0.21

	Normal weight* (n=53)	Overweight & Obese* (n=48)	P value†
TNF-α, pg/ml	4.8 (3.7, 6.9)	4.9 (3.5, 6.9)	0.92
IL-6, pg/ml	1.0 (0.8, 2.1)	1.9 (1.4, 2.9)	<0.001
Total amylin, pg/ml	7.9 (5.8, 11.9)	10.6 (7.0, 14.4)	0.10
Monocyte chemoattractant protein 1, pg/ml	124.0 (104.0, 150.0)	122.0 (104.5, 146.5)	0.83
Pancreatic polypeptide, pg/ml	51.2 (25.6, 93.1)	32.5 (16.9, 85.2)	0.10
Peptide YY, pg/ml	92.5 (63.1, 130.0)	78.4 (42.5, 136.5)	0.20

*Data are expressed as mean (SD), median (25^{th} and 75^{th} percentiles) or frequency (percent).

†P value derived from two-independent samples t-test, two-independent samples Wilcoxon-Mann-Whitney test for medians, and Chi-square test for independence or Fisher's exact test when appropriate.

Table 2

Spearman's correlations between cardiometabolic risk factors and adiposity measures, metabolic parameters and adipocytokines in Hispanic adolescents (n=101)

Parameter	SBP	DBP	HDL-C	Triglycerides	Glucose	HOMA-IR
BMI z score	0.52*	0.24†	−0.39*	0.15	0.11	0.67*
Waist circumference	0.49*	0.23†	−0.46*	0.17	0.11	0.60*
Waist-to-hip ratio	0.45*	0.22†	−0.43*	0.20	0.06	0.62*
Waist-to-height ratio	0.12*	0.08	−0.16†	0.08	−0.02	0.18
Log(Insulin)	0.47*	0.20†	−0.24†	0.27†	0.22†	-
HOMA-IR	0.47*	0.21†	−0.25†	0.27†	0.31†	-
IGF-1	−0.17	−0.04	0.29†	−0.03	0.09	−0.01
IGF-BP3	−0.11	0.02	−0.01	0.10	−0.06	−0.09
C peptide	0.42*	0.28*	−0.19	0.24†	0.10	-
Log(Glucose insulinotropic peptide)	0.11	0.01	0.02	0.12	−0.14	0.22
Log(Glucagon like peptide 1)	0.05	0.02	−0.09	−0.03	−0.16	−0.05
Glucagon	−0.09	−0.08	0.01	−0.09	−0.29†	−0.10
Log(hs-CRP)	0.26†	0.06	−0.37*	0.09	0.08	0.41*
Fibrinogen	0.23†	0.16	−0.12	0.21†	0.07	0.38*
Adiponectin	−0.41*	−0.21†	0.31†	−0.23†	−0.07	−0.43*
Leptin	0.37*	0.15	−0.11†	0.20†	0.08	0.62*
Ghrelin	0.01	0.04	−0.10	0.02	−0.13	−0.07
Log(TNF-α)	−0.04	−0.07	−0.10	−0.01	−0.19	−0.05
Log(IL-6)	0.17	0.09	−0.20	0.11	−0.10	0.22†
Log(Amylin)	0.13	0.01	−0.11	0.11	−0.09	0.36*
Log(MCP-1)	−0.03	−0.10	−0.13	0.07	−0.34*	−0.18
Pancreatic polypeptide	0.11	0.04	−0.10	−0.004	−0.16	0.001
Peptide YY	0.05	0.02	−0.08	−0.004	−0.16	−0.08

* P<0.001,

† P<0.05

Table 3

Stepwise multivariate linear regression models for cardiometabolic risk factors in Hispanic adolescents (n=101)

Dependent variable	Independent variable	Model 1* Standardized β coefficient	Model 2† Standardized β coefficient	Model 3‡ Standardized β coefficient	Model 4§ Standardized β coefficient
Systolic blood pressure	HOMA-IR	0.34 (p<0.001)	0.22 (p=0.018)	0.18 (p=0.046)	0.34 (p<0.001)
	Adiponectin	−0.29 (p=0.001)	−0.22 (p=0.014)	−0.23 (p=0.006)	−0.29 (p=0.001)
	Adjusted $R^{2\dagger}$	**0.42**	**0.46**	**0.48**	**0.41**
Diastolic blood pressure	Adiponectin	−0.23 (p=0.027)	−0.18 (p=0.10)	−0.18 (p=0.09)	−0.22 (p=0.036)
	Adjusted $R^{2\dagger}$	**0.07**	**0.07**	**0.07**	**0.07**
HDL-C	IGF-1	0.30 (p=0.001)	0.23 (p=0.017)	0.22 (p=0.027)	0.28 (p=0.004)
	Adiponectin	0.29 (p=0.002)	0.17 (p=0.082)	0.21 (p=0.032)	0.28 (p=0.004)
	Adjusted $R^{2\dagger}$	**0.22**	**0.27**	**0.25**	**0.22**
Triglycerides	Adiponectin	−0.23 (p=0.026)	−0.21 (p=0.062)	−0.23 (p=0.033)	−0.21 (p=0.04)
	Fibrinogen	0.18 (p=0.072)	0.17 (p=0.125)	0.19 (p=0.094)	0.16 (p=0.118)
	Adjusted $R^{2\dagger}$	**0.09**	**0.08**	**0.08**	**0.09**
Glucose	Log(Glucose insulinotropic peptide)	−0.32 (p=0.001)	−0.32 (p=0.001)	−0.33 (p<0.001)	−0.32 (p=0.001)
	Log(Insulin)	0.26 (p=0.007)	0.29 (p=0.025)	0.30 (p=0.004)	0.30 (p=0.017)
	Adjusted $R^{2\dagger}$	**0.19**	**0.18**	**0.19**	**0.18**
HOMA-IR	Leptin	0.50 (p<0.001)	0.43 (p<0.001)	0.40 (p=0.008)	0.51 (p<0.001)
	Log(Amylin)	0.29 (p=0.003)	0.27 (p=0.005)	0.28 (p=0.003)	0.29 (p=0.003)
	Adiponectin	−0.23 (p=0.006)	−0.21 (p=0.020)	−0.22 (p=0.011)	−0.23 (p=0.006)
	Pancreatic polypeptide	−0.20 (p=0.025)	−0.19 (p=0.043)	−0.19 (p=0.039)	−0.21 (p=0.024)
	Adjusted $R^{2\dagger}$	**0.45**	**0.45**	**0.44**	**0.44**

*Adjusted for sex and Tanner stage

†Adjusted for sex, Tanner stage and BMI z score

‡Adjusted for sex, Tanner stage and waist circumference

§Adjusted for sex, Tanner stage and waist-to-hip ratio