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Association of Puberty Stage and Weight Status with Cardiometabolic Risk in Children and Adolescents Living on the Texas-Mexico Border

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Abstract

Background: This retrospective cohort study aimed to examine the interaction effect between puberty stage and weight status on individual and clustering of cardiometabolic risk factors (CMRFs) among Mexican American children and adolescents. A total of 333 children and adolescents (aged 8–18 years) enrolled in the Cameron County Hispanic Cohort (CCHC) from 2014 to 2020 were included in the study.
Methods: CCHC is a longitudinal, randomly recruited cohort based on the United States Census tracts/blocks of Mexican Americans living on the Texas-Mexico border. Individual CMRFs, including high blood pressure, central obesity, hypertriglyceridemia, low high-density lipoprotein cholesterol, and insulin resistance (IR) were assessed. Clustering of CMRFs is defined as the presence of three or more individual CMRFs. Puberty stages were assessed using the Tanner criteria. Multivariable logistic regressions were conducted to assess the association of puberty, weight status, and the interaction of the two main exposures with individual and clustering of CMRFs.
Results: We observed that weight status had a dominant effect on all CMRF measures. The effect was especially prominent on central obesity and clustering of CMRFs. There were 95.4% of children with central obesity and 98.4% of those with clustering of CMRF were either overweight or obese. Entering puberty was associated with an increased risk of having IR [Tanner stage 2 vs. 1: odds ratio (OR) = 3.25, 95% confidence interval (95% CI) 1.28–8.27; Tanner stage 3 vs. 1: OR = 3.50, 95% CI 1.45–8.46] and hypertriglyceridemia (Tanner stage 2 vs. 1: OR = 2.67, 95% CI 1.11–6.45). However, the effects were not observed among those reaching the end of puberty (Tanner stage 4 and 5).
Conclusions: A significant interaction effect between weight status and puberty was not detected on any individual CMRF and in the clustering of CMRFs. Other factors positively associated with individual CMRFs, especially IR, were being female and having a family history of diabetes.

Keywords: puberty stage, weight status, cardiometabolic risk, children and adolescents

Introduction

According to the Center for Disease Control and Prevention (CDC), obesity affected 13.7 million (18.5%) of children aged 2–19 years in the United States in 2017–2018.[1] Childhood obesity is a public health concern associated with multiple cardiometabolic risk factors (CMRFs) that clusters in children and adolescents.[2] The CMRFs include central obesity, dyslipidemia [high triglycerides (TG), low high-density lipoprotein cholesterol (HDL-C)], high blood pressure (BP),

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and insulin resistance (IR). Without interventions, elevated CMRFs during childhood may lead to diabetes, early atherosclerosis, and cardiovascular diseases (CVDs) in adulthood,[2–5] resulting in premature mortality and physical morbidity.[6,7]

Puberty is another important predictor of cardiometabolic risk.[8–10] Puberty is a critical period that involves dramatic changes in body size, shape, fat composition, and metabolism. Literature findings suggest a potential interaction effect between puberty and obesity on individual CMRFs, such as IR. Moran et al. reported that IR increases during puberty and returns to normal in postpubertal period among normal weight adolescents.[11] However, Cardenas-Vargas et al. and Pilia et al. found that the increase in IR may be long-lasting in their obese counterparts and remain high after puberty.[12,13]

The interaction effect of puberty and obesity on CMRF has only been directly investigated in two studies.[14,15] Both Chan et al. and Ramírez-Vélez et al. found that the variance of CMRF explained by adding the interaction term between pubertal status and BMI is between 1% and 2%.[14,15] In these two studies, the outcome measure is the CMRF z-score, a sum of the z-scores for all individual CMRFs.[14,15] The interaction effect of puberty and obesity on individual CMRF is not examined. Given that puberty has a stronger impact on some individual CMRFs, such as IR, than others,[8,16] the interaction effect between obesity and puberty may also vary across individual CMRFs. The analysis based on the composite CMRF z-score may not be sensitive enough to detect the interaction effect of the two risk factors on a particular CMRF.

Moreover, the two studies examining the interaction between puberty and obesity on CMRFs do not include important risk factors such as family history of diabetes and children's mental health status.[14,15] Family history can influence a child's health through genetic inheritance, family lifestyle and other environmental factors. Studies show that a family history of diabetes is related to cardiometabolic risk in offspring.[17–20] The American Heart Association position paper stated that major depressive disorder predisposes youth to accelerated atherosclerosis and early CVD.[21]

Findings of previous studies show that adults of Hispanic decent have a higher risk of diabetes than other racial/ethnic groups in the United States (50% vs. 40%).[22] The prevalence of high BP, obesity, and dyslipidemia are also significantly higher in the Hispanic population than non-Hispanic, leading to an increased risk of CVD.[23,24]

Mexican Americans make up 65% of the Hispanic population in the United States. Many live in the southern states along the U.S.-Mexico border. Cameron County Hispanic Cohort (CCHC) is a longitudinal, randomly recruited cohort based on the U.S. Census tracts/blocks of Mexican Americans living on the Texas-Mexico border since 2004.[25,26] Studies on the adult participants of the CCHC found that the population had poor metabolic health.[26] The prevalence of diabetes, hypertension, and hypercholesterolemia in the cohort were 30.7%, 30.5%, and 48.2%, respectively, which was higher than the prevalence rates in the U.S. population and with much earlier age of onset.[26]

To advance the understanding of diabetes and CVD development in Mexican Americans, we examined the interplay of obesity and puberty on individual and the clustering of CMRFs after controlling for family history of diabetes and mental health status among pediatric participants of the CCHC.

Materials and Methods

Study sample

The CCHC is a randomly selected, community recruited cohort by U.S. Census Bureau blocks according to dwelling unit density, stratified into socioeconomic status quartiles in Cameron and Webb Counties in Texas starting in 2004. CCHC aims to examine the prevalence of chronic diseases among Mexican Americans residing in Texas-Mexico border towns, and the biological, environmental, social, lifestyle, and genetic risk factors affecting the development of the chronic diseases.[26] In 2014, the CCHC was expanded to include children and adolescents from 8 to 18 years old residing in households of CCHC adult participants.

CCHC pediatric data collected from 2014 to April 2020 were used in this analysis. The sample included 374 children and adolescents between 8 and 18 years old who have completed the baseline survey interview and physical examination. Participants who were underweight ($n=10$), with incomplete responses to the puberty development scale (PDS; $n=30$) or had a diagnosis of diabetes ($n=1$) were excluded. The final analytic sample included 333 pediatric participants.

Ethics statement

The Committee for the Protection of Human Subjects at the UTHealth Science Center in Houston reviewed and approved the protocol and informed consent forms, including permission to collect and store deidentified data and specimens for studies. The informed consent from parents/guardians and assent from children and adolescent participants were obtained.

Data collection

Measurement of anthropometric and laboratory parameters. Pediatric participants were invited to the School of Public Health Clinical Research Unit for physical examination, in-person interview, and blood-taking. The physical examination and in-person interviews were performed by bilingual research officers trained in good clinical practice at the School of Public Health Clinical Research Units. Weight and height were measured using standard procedures.[27] Central obesity was determined by measuring waist circumference (WC). WC was measured at the highest point of the iliac crest.[28,29] The WC percentile for Mexican American children was determined using Fernández et al.' methods derived from the National Health and Nutrition Examination Survey (NHANES).[30] Age- and sex-specific body mass index (BMI) percentile was calculated based on the CDC growth charts.[31] Sitting BP was measured on the right arm after the subject had rested quietly for 5 min.

Three readings for BP were obtained using the Welch Allyn vital signs machine, and the average was recorded.[32] BP for children was converted to BP percentile based on the table by the AAP.[33] The study participants provided 22 mL fasting (overnight) blood specimens by venipuncture during the visit. The fasting blood glucose and lipid profiles (total

cholesterol, HDL-C, TG, and calculated LDL) were analyzed at the Clinical Laboratory Improvement Amendments certified laboratory in Valley Baptist Hospital Central laboratory and measured using colorimetric assays in a Siemens Vista. The insulin level was analyzed in the UTHealth School of Public Health, Brownsville campus laboratory, and measured using the Mercodia Insulin ELISA kit (Mercodia AB, Uppsala, Sweden).

TG and HDL-C levels were converted to percentile based on the table by Daniels and Greer.[34]

Outcome measures

Cardiometabolic risk factors. There is not a universal definition for CMRF in children and adolescents. In this study, we used the modified criteria from AAP,[35] International Diabetes Federation,[36] Stavnsbo et al.,[37] and Cruz et al.[38] to determine whether the CCHC pediatric participants had any of the CMRF when they entered the study cohort, that is, central obesity, hypertriglyceridemia, low HDL-C, high BP, and IR.

We considered central obesity as WC ≥90th percentile adjusted for age, sex, and height,[36] hypertriglyceridemia as TG ≥90th percentile adjusted for age and sex,[38] low HDL-C as HDL-C ≤10th percentile adjusted for age and sex,[38] high BP as either systolic or diastolic BP ≥90th percentile adjusted for height, age, and sex,[38] and IR as homeostasis model assessment of insulin resistance (HOMA-IR) ≥2.6.[39,40] HOMA-IR is a validated surrogate measure used to assess IR for large epidemiologic studies. It is highly correlated with the hyperinsulinemic-euglycemic clamp, the gold standard technique used in assessing IR.[41] The HOMA-IR value is calculated by dividing the product of insulin (microunits per milliliter) and glucose (mg/dL) by 22.5.[41] We defined clustering of CMRFs as the presence of three or more individual CMRF in the participants.

Main exposure measures

Overweight/obesity. All the study participants' height (cm) and weight (kg) were measured. The age- and sex-specific percentiles of BMI were calculated based on the CDC growth charts for children and adolescents.[42] The BMI-for-age percentile was further classified as overweight/obese (BMI ≥85th percentile) or normal weight (5th percentile ≤ BMI <85th percentile).

Puberty stages. The puberty stage was assessed using the self-assessed PDS questionnaire.[43] The PDS was used to determine the puberty status for both boys and girls. It comprised two sets of five self-reported questionnaires related to growth in height, body hair, skin changes, pubertal development of breast and genitalia stage, as well as sex-specific line drawings and figures.

Females were asked to report breast development, pubertal development of pubic hair, and age of menarche. Males were asked to report voice changes, growth of facial hair, and pubertal development of pubic hair and genitalia. The response options included not yet started (1 point), barely started (2 points), definitely started (3 points), seems complete (4 points), or I don't know (missing). For females, an answer of yes on the menstruation item was 4 points while no was 1 point. The point values were then averaged, and the final PDS score was converted to the Tanner Scale's five stages of development.

The staging was determined based on the category score calculated from the criteria set by Carskadon and Acebon.[44] The five staging categories for girls included Tanner stage 1 (≤3 points), Tanner stage 2 (3 points and no menarche), Tanner stage 3 (4 points and no menarche), Tanner stage 4 (≤7 points and menarche), and Tanner stage 5 (8 points and menarche). The categories for boys included Tanner stage 1 (3 points), Tanner stage 2 (4 or 5 points), Tanner stage 3 (6–8 points), Tanner stage 4 (9–11 points), and Tanner stage 5 (12 points).

Covariates

Depression/anxiety. Children and adolescents were screened for depression and anxiety using the Center for Epidemiological Studies–Depression (CES-D) form[45] and Zung's Self-rating Anxiety Scale (SAS).[46] CES-D is a validated questionnaire consisting of 20-item on a 4-point scale that measures nine different depressive symptoms groups as defined by the *American Psychiatric Association Diagnostic Manual, Fifth Edition* DSM-V (*Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition*).[45] The symptoms evaluated included sadness, loss of interest, appetite, sleep, thinking/concentration, guilt, tiredness, movement, and suicidal ideation.[45] Individuals were categorized as having depression if their total CES-D score was ≥16.[45,47]

SAS is a questionnaire consisting of 20-items on a 4-point scale that measures anxiety levels. The raw score is summed and converted to the Anxiety Status Index (ASI) based on Zung's conversion table.[46] An ASI from 20 to 44 is considered normal, 45 to 59 is considered as having minimal to moderate anxiety, 60 to 74 is considered severe anxiety, and 75 and over is considered most extreme anxiety. In this study, children and adolescents were categorized as having depression/anxiety if either CES-D ≥16 or ASI ≥45.[46]

Family history of diabetes. The CCHC pediatric data were further linked to the adult CCHC data using the household identification number to obtain the family history of diabetes among the participants. A child was considered to have a family history of diabetes if first-degree family members (father, mother, and siblings) had diagnosed or undiagnosed diabetes (taking any diabetes medication or fasting blood glucose ≥126 mg/dL or A1c ≥6.5%).

Demographics variables. Participant demographics, including age, sex, and race were obtained during the in-person interview.

Statistical analysis

Descriptive statistics were used to describe the sample characteristics. Mean and standard deviations were used to describe continuous variables, whereas frequency and percentage were used to describe categorical variables. In addition, the unadjusted associations between the main risk factors (puberty stage and weight status) and individual CMRF (central obesity, hypertriglyceridemia, low HDL-C, high BP, and IR) as well as clustering of CMRFs (presence of three or more CMRF) were assessed using chi-squared test.

Multivariable logistic regressions were applied to examine the relationship of weight status, Tanner stage, the interaction of weight status and Tanner age with individual

CMRFs and clustering of CMRFs after adjusting for age, sex, family history of diabetes, and the presence of depression/anxiety.

All analyses were conducted using SAS 9.4 statistical software (SAS Institute, Inc., Cary, NC). An alpha level of $P < 0.05$ was considered statistically significant.

Results

Cohort characteristics

Table 1 presents the characteristics of the CCHC children and adolescents included in this study. The study sample included a comparable number of children in the age groups of 8 to 12 years (49.3%) and 13 to 18 years (50.8%). The average age [mean (SD)] was 9.46 (1.25) years for Tanner stage 1, 10.9 (1.72) years for Tanner stage 2, 13.2 (2.4) years for Tanner stage 3, 13.9 (2.1) years for Tanner stage 4, and 15.5 (1.6) years for Tanner stage 5. Almost all participants were white (99.7%), and 97% belong to Mexican American ethnicity (Table 1).

Table 1. Cohort Characteristics of the Cameron County Hispanic Cohort Children and Adolescents

Variables	*All* (n = *333*), n (%)
Age, years	
8–12	164 (49.3)
13–18	169 (50.8)
Gender	
Female	164 (49.3)
Male	169 (50.8)
Race	
White	332 (99.7)
Black/African American	1 (0.3)
Hispanic	
Mexican American	323 (97.0)
Not Hispanic	9 (2.7)
Puerto Rican	1 (0.3)
Tanner stage	
Stage 1	74 (22.2)
Stage 2	40 (12.0)
Stage 3	72 (21.6)
Stage 4	116 (34.8)
Stage 5	31 (9.3)
Weight category	
Normal	162 (48.7)
Overweight/obesity	171 (51.4)
CMRFs	
High blood pressure	32 (9.6)
Central obesity	87 (26.1)
Hypertriglyceridemia	114 (34.2)
Low HDL-C	70 (21.0)
Insulin resistance	130 (39.0)
Children with ≥3 CMRFs	64 (19.2)
Anxiety/depression	
Yes	36 (10.8)
No	297 (89.2)
Family history of diabetes	
Yes	122 (36.6)
No	211 (63.4)

CMRFs, cardiometabolic risk factors; HDL-C, high-density lipoprotein cholesterol.

Of the 333 pediatric participants, 39% (39.0%) had IR (HOMA-IR above 2.6), one-third (34.2%) had hypertriglyceridemia, one-quarter (26.1%) had central obesity, and 64 (19.2%) had clustering of CMRFs. Supplementary Table S1 presents the comparisons of patient characteristics between those with and without individual and clustering of CMRFs.

Unadjusted analysis of the association between puberty stage/weight status and individual CMRF/clustering of CMRFs

Table 2 presents the bivariate analysis results of the association between weight status and CMRF measures, and between puberty stage and CMRF measures. Being overweight/obese, compared to being normal weight, was associated with central obesity ($P < 0.05$), hypertriglyceridemia ($P = 0.04$), low HDL-C ($P < 0.05$), IR ($P = 0.04$), and clustering of CMRFs ($P < 0.05$), Tanner stage was significantly associated with hypertriglyceridemia ($P < 0.05$), IR ($P = 0.03$), and clustering of CMRFs ($P = 0.02$) but not associated with high BP, central obesity, and low HDL-C.

Multivariable logistic regression of the association between puberty stage/weight status and individual CMRFs

Nearly all children in the study cohort with central obesity were overweight or obese (95.4%) indicating the nonexistence of an interaction effect between puberty stage and weight status on central obesity. The interaction effects between puberty stage and weight status were assessed on other individual CMRFs, including hypertriglyceridemia, low HDL-C, high BP, and IR. A significant interaction effect was not detected on any of these four individual CMRFs.

Table 3 presents the multivariable logistic regression results for the association of puberty stage and weight status with individual CMRFs. After controlling the covariates, we found that weight status was significantly associated with hypertriglyceridemia, low HDL-C, and IR. Compared to children with normal weight, being overweight/obese was associated with 7.68 times higher odds of having low-HDL-C [odds ratio (OR) = 7.68, 95% confidence interval (95% CI) 3.78–15.58], 4.85 times higher odds of having hypertriglyceridemia (OR = 4.85, 95% CI 2.80–8.39), and 6.22 times higher odds of having IR (OR = 6.22, 95% CI 3.66–10.57).

Tanner stage was associated with hypertriglyceridemia and IR. Specifically, Tanner stage 2 was associated with 3.25 times higher odds of IR (OR = 3.25, 95% CI 1.28–8.27) and 2.67 times higher odds of having hypertriglyceridemia (OR = 2.67, 95% CI 1.11–6.45) compared to Tanner stage 1. Tanner stage 3 was associated with 3.50 times higher odds of IR than Tanner stage 1 (OR = 3.50, 95% CI 1.45–8.46). In overweight/obese children, those in Tanner stage 2 have 3.17 times (OR = 3.17, 95% CI 0.99–10.19) higher odds of having central obesity than those in Tanner stage 1. Tanner stages 4 and 5 were not associated with any individual CMRFs.

Table 2. Unadjusted Analysis of the Association Between Pubertal Stage, Weight Status, and Individual Cardiometabolic Risk Factor and Clustering of Cardiometabolic Risk Factors

Variables	*High blood pressure* (n=*32*), n *(%)*	*No high blood pressure* (n=*301*), n *(%)*	P	*Central obesity* (n=*87*), n *(%)*	*No central obesity* (n=*246*), n *(%)*	P	*Hypertriglyceridemia* (n=*114*), *n (%)*	*No hypertriglyceridemia* (n=*219*), n *(%)*	P
Age, years			0.23			0.30			<0.05*
8–12	19 (59.4)	145 (48.2)		47 (54.0)	117 (47.6)		70 (61.4)	94 (42.9)	
13–18	13 (40.6)	156 (51.8)		40 (46.0)	129 (52.4)		44 (38.6)	125 (57.1)	
Sex			<0.05*			0.83			<0.05*
Male	24 (75.0)	140 (46.5)		42 (48.3)	122 (49.6)		73 (64.0)	91 (41.6)	
Female	8 (25.0)	161 (53.5)		45 (51.7)	124 (50.4)		41 (36.0)	128 (58.5)	
Tanner stage			0.19			0.17			<0.05*
1	8 (25.0)	66 (21.9)		17 (19.5)	57 (23.2)		31 (27.2)	43 (19.6)	
2	5 (15.6)	35 (11.6)		17 (19.5)	23 (9.4)		26 (22.8)	14 (6.4)	
3	11 (34.4)	61 (20.3)		17 (19.5)	55 (22.5)		22 (19.3)	50 (22.8)	
4	7 (21.9)	109 (36.2)		29 (33.3)	87 (35.4)		28 (24.6)	88 (40.2)	
5	1 (3.1)	30 (10.0)		7 (8.1)	24 (9.8)		7 (6.1)	24 (11.0)	
Weight category			0.19			<0.05*			0.04*
Normal	12 (37.5)	150 (49.8)		4 (4.6)	158 (64.2)		30 (26.3)	132 (60.3)	
Overweight/obesity	20 (62.5)	151 (50.2)		83 (95.4)	88 (35.8)		84 (73.7)	87 (39.7)	
Anxiety/depression			0.36			0.87			0.17
No	27 (84.4)	270 (89.7)		78 (89.7)	219 (89.0)		98 (86.0)	199 (90.9)	
Yes	5 (15.6)	31 (10.3)		9 (10.3)	27 (11.0)		16 (14.0)	20 (9.1)	
Family history of diabetes			0.26			0.29			0.96
No	18 (56.3)	193 (64.1)		51 (58.6)	160 (65.0)		72 (63.2)	139 (63.5)	
Yes	14 (43.8)	108 (35.9)		36 (41.4)	86 (35.0)		42 (36.8)	80 (36.5)	

Variables	*Low HDL-C* (n=*70*), n *(%)*	*No Low HDL-C* (n=*263*), n *(%)*	P	*Insulin resistance* (n=*130*), n *(%)*	*No insulin resistance* (n=*203*), n *(%)*	P	*Clustering of CMRFs* (≥*3 CMRF*) (N=*64*), n *(%)*	*No clustering of CMRFs* (n=*269*), n *(%)*	P
Age, years			0.89			0.82			0.07
8–12	35 (50.0)	129 (49.1)		63 (48.5)	101 (49.8)		38 (59.4)	126 (46.8)	
13–18	35 (50.0)	134 (51.0)		67 (51.5)	102 (50.3)		26 (40.6)	143 (53.2)	
Gender			0.50			0.04*			0.49
Male	37 (52.9)	127 (48.3)		55 (42.3)	109 (53.7)		34 (53.1)	130 (48.3)	
Female	33 (47.1)	136 (51.7)		75 (57.7)	94 (46.3)		30 (46.9)	139 (51.7)	

(*continued*)

Table 2. Continued

Variables	*Low HDL-C* (n = *70*), n *(%)*	*No Low HDL-C* (n = *263*), n *(%)*	P	*Insulin resistance* (n = *130*), n *(%)*	*No insulin resistance* (n = *203*), n *(%)*	P	*Clustering of CMRFs* (*≥3 CMRF*) (N = *64*), n *(%)*	*No clustering of CMRFs* (n = *269*), n *(%)*	P
Tanner stage			0.40			0.03*			0.02*
1	13 (18.6)	61 (23.2)		17 (13.1)	57 (28.1)		11 (17.2)	63 (23.4)	
2	13 (18.6)	27 (10.3)		18 (13.9)	22 (10.8)		15 (23.4)	25 (9.3)	
3	15 (21.4)	57 (21.7)		32 (24.6)	40 (19.7)		16 (25.0)	45 (20.8)	
4	22 (31.4)	94 (35.7)		48 (36.9)	68 (33.5)		19 (30.0)	97 (36.1)	
5	7 (10.0)	24 (9.1)		15 (11.5)	16 (7.9)		3 (4.7)	28 (10.4)	
Weight category			<0.05*			<0.05*			<0.05*
Normal	11 (15.7)	151 (57.4)		31 (23.9)	131 (64.5)		1 (1.56)	161 (60.0)	
Overweight/obesity	59 (84.3)	112 (42.6)		99 (76.2)	72 (35.5)		63 (98.4)	108 (40.2)	
Anxiety/depression			0.85			0.73			0.35
No	62 (88.6)	235 (89.4)		115 (88.5)	182 (89.7)		55 (85.9)	242 (90.0)	
Yes	8 (11.4)	28 (10.7)		15 (11.5)	21 (10.3)		9 (14.1)	27 (10.0)	
Family history of diabetes			0.71			<0.05*			0.11
No	43 (61.4)	168 (63.9)		70 (53.9)	141 (69.5)		29 (45.3)	176 (65.4)	
Yes	27 (38.6)	95 (36.1)		60 (46.2)	62 (30.5)		35 (54.7)	93 (34.6)	

High blood pressure: Systolic or diastolic blood pressure ≥90th percentile adjusted for height, age, and gender.
Central obesity: WC ≥90th percentile for age.
Hypertriglyceridemia: Triglycerides ≥90th percentile adjusted for age and gender.
Low HDL-C: HDL-C ≤10th percentile adjusted for age and gender.
Insulin resistance: HOMA-IR ≥2.6.
*$P < 0.05$.
HOMA-IR, homeostasis model assessment of insulin resistance; WC, waist circumference.

Table 3. Multivariable Logistic Regression of the Association Between Pubertal Stage, Weight Status, and Cardiometabolic Risk Factor

	Type of CMRF											
	High blood pressure		*Central obesity*[a]		*Hypertriglyceridemia*		*Low HDL-C*		*Insulin resistance*		*Clustering of CMRFs*[a] *(≥3 CMRF)*	
Variables	*Odds ratio (95% CI)*	P	*Odds ratio (95% CI)*	P	*Odds ratio (95% CI)*	P	*Odds ratio (95% CI)*	P	*Odds ratio (95% CI)*	P	*Odds ratio (95% CI)*	P
Age, years												
8–12	Ref		Ref		Ref		Ref		Ref		Ref	
13–18	0.66 (0.24–1.76)	0.40	1.48 (0.48–3.19)	0.32	0.85 (0.43–1.69)	0.64	1.43 (0.67–3.05)	0.36	0.80 (0.41–1.55)	0.50	0.59 (0.29–1.21)	0.15
Sex												
Male	Ref		Ref		Ref		Ref		Ref		Ref	
Female	0.34 (0.13–0.90)	0.03*	2.26 (1.00–5.11)	0.05	0.49 (0.27–0.90)	0.02*	1.03 (0.51–2.07)	0.93	1.91 (1.04–3.49)	0.04*	1.03 (0.53–1.97)	0.94
Tanner stage												
1	Ref		Ref		Ref		Ref		Ref		Ref	
2	1.32 (0.30–4.53)	0.66	3.17 (0.99–10.19)	0.05*	2.67 (1.11–6.45)	0.03*	2.07 (0.78–5.41)	0.14	3.25 (1.28–8.27)	0.02*	4.26 (1.67–10.84)	<0.05*
3	2.01 (0.63–6.43)	0.24	0.73 (0.27–2.01)	0.55	0.56 (0.24–1.30)	0.18	0.93 (0.35–2.47)	0.88	3.50 (1.45–8.46)	0.01*	2.41 (0.93–6.26)	0.07
4	1.21 (0.30–4.89)	0.82	0.42 (0.13–1.33)	0.14	0.58 (0.23–1.46)	0.25	0.81 (0.28–2.35)	0.69	2.45 (0.96–6.24)	0.06	1.72 (0.61–4.82)	0.31
5	0.82 (0.07–9.45)	0.87	0.38 (0.08–1.88)	0.24	0.64 (0.18–2.36)	0.50	1.00 (0.25–4.19)	1	3.28 (0.94–11.45)	0.06	0.97 (0.20–4.76)	0.97
Weight category												
Normal	Ref				Ref		Ref		Ref			
Overweight/ obesity	1.43 (0.65–3.14)	0.37	—		4.85 (2.80–8.39)	<0.05*	7.68 (3.78–15.58)	<0.05*	6.22 (3.66–10.57)	<0.05*	—	
Anxiety/depression												
No	Ref		Ref		Ref		Ref		Ref		Ref	
Yes	1.96 (0.67–5.72)	0.22	1.22 (0.47–1.70)	0.71	2.15 (0.98–4.72)	0.06	2.15 (0.98–4.71)	0.06	1.52 (0.67–3.44)	0.32	1.75 (0.76–4.04)	0.19
Family history of diabetes												
No	Ref		Ref		Ref		Ref		Ref		Ref	
Yes	1.34 (0.63–2.88)	0.45	0.90 (0.47–1.70)	0.74	0.88 (0.52–1.49)	0.62	0.88 (0.52–1.49)	0.62	2.00 (1.19–3.35)	0.01*	1.75 (0.98–3.10)	0.06

[a]We only conducted the regression in the overweight/obese group as almost everyone with central adiposity or clustering of CMRF are overweight/obese.
*$P < 0.05$.
95% CI, 95% confidence interval.

In addition to weight status and Tanner stage, other factors associated with one or multiple individual CMRF were sex and family history of diabetes. Sex was associated with high BP, hypertriglyceridemia, and IR. Compared with boys, girls had 1.91 times higher odds of having IR (OR = 1.91, 95% CI 1.04–3.49), 66% less likely of having high BP (OR = 0.34, 95% CI 0.13–0.90), and 51% less likely of having hypertriglyceridemia (OR = 0.49, 95% CI 0.27–0.90) than boys. Family history of diabetes was associated with IR only. Children with family history of diabetes had two times higher odds of having IR (OR = 2.00, 95% CI 1.19–3.35) than children without.

Multivariable logistic regression of the association between puberty stage, weight status, and clustering of CMRFs

Similar to the findings on central obesity, almost all children having clustering of CMRFs were overweight or obese (98.4%). Therefore, the multivariable logistic regression analysis was conducted among overweight/obese individuals only to assess the association of puberty stage with clustering of CMRFs. The results showed that, within overweight/obese children, those in Tanner stage 2 had 4.26 higher odds of having clustering of CMRFs (OR = 4.26, 95% CI 1.67–10.84) than those in Tanner stage 1. Similar association was not observed among children in Tanner stages 3, 4, and 5.

Discussion

Consistent with published studies,[48,49] we observed that being overweight/obese is the most important risk factor associated with CMRFs. Our findings show that being overweight/obese is positively associated with all individual and clustering of CMRFs. The effect is especially prominent on central obesity and clustering of CMRFs. Among 87 children with central obesity, only 4 had normal weight. Of the 64 children who have clustering of CMRFs, nearly all ($n = 63$) were overweight/obese.

We also found that puberty was a significant factor associated with CMRFs. However, unlike children's weight status, puberty stage only affected some individual CMRFs (IR and hypertriglyceridemia) and clustering of CMRFs. For the CMRFs measures affected by puberty stage, the impacts were significant in Tanner stages 2 and/or 3, representing the time that children enter puberty, and the effects faded away in Tanner stages 4 and 5, indicating the effects of puberty on CMRF may be temporary.

The primary finding of our study is that a significant interaction effect was not observed between weight status and puberty on both individual and clustering of CMRFs. The finding implies that the impact of overweight/obesity and puberty stage on CMRFs are independent of each other. Given the temporary effect of puberty, and the similar prevalence of individual and clustering CMRFs among children (aged 8–12) and adolescents (aged 13–18) in the study cohort, addressing overweight/obesity in school-aged children may be critical to slow down the development of CMRF and to prevent its consequent diabetes and CVDs.

As an improvement over prior research examining the interaction effect of puberty and obesity on CMRF, our analysis included two additional CMRF risk factors: family history of diabetes and comorbid mental disorders. We found that family history of diabetes was associated with two times higher odds of having abnormal IR. The finding could be explained by the genetic disposition (Amerindian ancestral components),[50] which further worsens when children gain weight and enter puberty. The effect was especially significant among girls where the odds of having IR were almost two times higher than boys. This could be explained by the fact that visceral fats is inversely correlated with insulin sensitivity in girls but not boys.[51] Thus, girls are generally more prone to IR than boys.

These findings further suggest that, despite the dominant impact of children's weight status, the development of CMRF is also multifactorial. It is well understood that diabetes is more prevalent in Hispanic adults than in the general U.S. population.[52] In our study cohort of Mexican American children living on the U.S.-Mexico border, 20% had at least one first-degree family member with diabetes. The success of interventions aiming to address overweight and obesity in this special population depends not only on intervening early in the children's life, but also requires addressing the health behaviors of children's family, given that diabetes is often intergenerational.

Our data showed that children who were severely obese almost always had parents who are overweight/obese, and the family often shares unhealthy lifestyles and poor health behaviors. Family-based public health interventions such as the CATCH program in schools to educate both children and their parents on healthy lifestyles, which include diet and physical activity, may be necessary in the study population.

Strengths

Our study adds to the literature by assessing the interaction effect of overweight/obesity and puberty on both individual and clustering of CMRFs in a unique population of Mexican American children and adolescents living on the Texas-Mexico border.[53,54] The inclusion of important confounding factors missed in prior literature, such as family history of diabetes and children's mental health status was also an advantage.

Limitations

Despite its strengths, our study has limitations. CCHC pediatric cohort is a longitudinal cohort that aims to follow children from childhood to adulthood. However, the follow-up data for most pediatric participants is still insufficient for a longitudinal analysis examining the childhood risk factors' effect on the morbidities of young adults. The current study using only the baseline data of CCHC pediatric cohort is cross-sectional in nature. Future studies using longitudinal CCHC cohort data will be conducted to examine the dynamic change of CMRFs in the population and the long-term effects of CMRFs on the progression of CVD.

This study's sample size was relatively small compared to other epidemiologic studies targeting children of Hispanic descent.[55] A common concern of small samples is that it decreases the power of the study and increases the margin of error, and subsequently, fails to detect the existing difference. However, we believe our study sample, although relatively small, is sufficient to answer the research question given (1) the consistency between our findings and

published data and (2) the robustness of our main finding of no interaction effects between weight status and puberty stage on individual and clustering of CMRFs. We compared the variance explained by multivariable models with and without the interaction term. The difference between the two types of models in terms of the percentages of variance explained was negligible (<0.5%), which in turn confirmed our findings.

Conclusion

The risk of having individual and clustering of CMRFs in Mexican American children was associated with children's weight status, puberty stage, sex, and family history of diabetes. Significant interaction effects between weight status and puberty stages on individual and clustering of CMRFs were not observed.

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Authors' Contributions

Material preparation and analysis were performed by E.V.L. Laboratory result analysis was conducted by J.R. E.V.L. and H.C. jointly wrote the first draft. E.V.L., H.C., and M.L. had full access to the data and take the responsibility for the integrity of the data in the study and the accuracy of the analysis. All authors read, edited, and approved the final article.

Author Disclosure Statement

No conflicting financial interests exist.

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Supplementary Material

Supplementary Table S1

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