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Assessment of Social, Dietary and Biochemical Correlates of Cardiometabolic Risk in
Pre-adolescent Hispanic Children

A dissertation

presented to

the faculty of Department of Biostatistics and Epidemiology

East Tennessee State University

In partial fulfillment

of the requirements for the degree

Doctor of Public Health with concentration in Epidemiology

by

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May 2017

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Keywords: cardiometabolic risk; overweight; elevated blood pressure; biomarker;

Hispanic children

ABSTRACT

Assessment of Social, Dietary and Biochemical Correlates of Cardiometabolic Risk in Pre-adolescent Hispanic Children

by

Abraham Basil Alhassan

Obesity, elevated blood pressure and dyslipidemia are highly prevalent in Hispanic children. Compared to their non-Hispanic White peers, Hispanic children experience higher prevalence of obesity and hypertension. The Hispanic population in Tennessee has been growing, with about a tenth of newborn babies being Hispanic. This study aimed to: 1. Examine the influence of sociodemographic factors on Hispanic children's cardiometabolic risk; 2. Assess the relationship between food group intake and cardiometabolic risk in Hispanic children; and 3. Evaluate the efficacy of non-traditional biomarkers for detecting cardiometabolic risk in Hispanic children. Data for the study came from a larger cross-sectional pilot study of metabolic syndrome in Hispanic children at a community health center in Johnson City, TN. Descriptive and multiple logistic regression analyses were used. The prevalence of overweight and elevated blood pressure were 40.7% and 31.0% respectively. Children of obese mothers were more likely than children of mothers with normal body mass index to engage in less than three days of at least 60 minutes of vigorous physical activity (PA) per week (*OR*: 6.47; 95% *CI*: 1.61-26.0). Children whose mothers did not engage in moderate PA were more likely to have elevated blood pressure (*OR*: 2.50, 95%*CI*: 1.02-4.53); and to engage in less than three days of at least 60 minutes of vigorous PA per week (*OR*:

2.92, 95% *CI*: 1.18-7.24), than children whose mothers engaged in moderate PA. Children generally exceeded fruit and legume intake recommendations, but did not meet vegetable, wholegrain, dairy and fiber recommendations. Higher legume (*OR*: 0.052, 95% *CI*: 0.04-0.64), dairy (*OR*: 0.61, 95% *CI*: 0.37-0.99) and fiber intake (*OR*: 0.88, 95% *CI*: 0.81-0.96) were protective against elevated blood pressure, but only fruit intake was protective against overweight (*OR*: 0.93, 95% *CI*: 0.87-0.99). Leptin, C-peptide and TNF- α showed significant positive correlations with cardiometabolic risk factors. The optimal cut-offs for detecting three or more cardiometabolic risk factors were: leptin, 5.95 ng/ml, C-peptide, 0.73 ng/; and TNF-alpha, 4.28 pg/ml.

Helping mothers to achieve and maintain a healthy BMI and promoting children's consumption of more vegetables, fruits, dairy and fiber could help reduce cardiometabolic risk in Hispanic children.

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ACRONYMS AND ABBREVIATIONS

AI – Adequate Intake
AUC – Area under the Curve
BP – Blood Pressure
BKFS – Block Kids Food Screener
CE – Cup Equivalents
OZE – Ounce Equivalents
C-peptide – Connecting peptide
DBP – Diastolic Blood Pressure
DGA – Dietary Guidelines for Americans
HDL-C – High Density Lipoprotein cholesterol
JCCHC – Johnson City Community Health Center
PAG – Physical Activity Guidelines for Americans
RDI – Recommended Daily Intake
SBP – Systolic Blood Pressure
TC – Total Cholesterol
TG – Triglycerides
TNF- α – Tumor necrosis factor alpha
U.S. – Unites States

CHAPTER 1

INTRODUCTION

Cardiometabolic diseases such as coronary artery disease, stroke and diabetes are rare in childhood (McGill, McMahan, & Gidding, 2008; Napoli et al., 2006); however, the underlying cardiometabolic risk factors such as low high density lipoprotein cholesterol (HDL-C), elevated triglycerides, high low density lipoprotein cholesterol (LDL-C), elevated blood pressure (BP), obesity, insulin resistance, and the early stages of atherosclerosis, often start in childhood and track into adulthood (McGill et al., 2008; Napoli et al., 2006).

Genetic, biological and behavioral factors such as age, sex, family history, diet, physical inactivity, smoking; and the social and physical characteristics of neighborhoods influence the development of cardiometabolic risk in childhood (Kelly, Pothoulakis, & LaMont, 1994; Mente, De Koning, Shannon, & Anand, 2009; Rao, 2016). Over time, exposure to cardiometabolic risk leads to advanced and irreversible atherosclerosis. Atherosclerotic events and effects such as arterial occlusion and rupture with embolism and thrombosis, mediate the development of cardiovascular disease (McGill et al., 2008).

The management of cardiometabolic risk combines lifestyle modification with pharmacotherapy. The American Heart Association (American Heart Association, 2013) and the National Heart, Lung and Blood Institute (National Heart, Lung, 2011), recommend a variety of policy, social and individualized measures for improving

cardiometabolic health-related behavior in the community. The Food and Drug Administration has approved many cholesterol lowering (U.S. Food and Drug Administration, 2010), anti-hypertensive (Falkner et al., 2004) and anti-diabetic medications (American Diabetes Association, 2016) for control of abnormal cholesterol, blood pressure and sugar levels, respectively.

Significance

Cardiometabolic diseases account for the highest morbidity and mortality in the U.S. Heart disease, stroke, and diabetes currently rank as first, fifth and seventh leading causes of death in the U.S (Mozaffarian et al., 2016; National Center for Health Statistics, 2016). Every year, about 735,000 adults experience a new or repeat heart attack; 795, 000 have a new or repeat stroke; and about 1.7 million are diagnosed with diabetes (Mozaffarian et al., 2016; National Center for Health Statistics, 2016). Using 2012 as baseline, 43.9% of all Americans are projected to have a form of cardiovascular disease by 2030 (Mozaffarian et al., 2016). Diseases of the cardiovascular system are the costliest in the U.S. In 2011-2012, direct and indirect cost estimates attributable to cardiovascular diseases totaled \$396 billion and \$183 billion respectively. (Mozaffarian et al., 2016). By 2030, direct and indirect costs of all cardiovascular diseases are projected to increase to 918 billion and 290 billion 2012 dollars respectively (Mozaffarian et al., 2016).

Cardiometabolic health of Hispanic children is an important public health issue in U.S and increasingly, in Tennessee. Hispanics are the largest minority ethnic group and

the fastest growing population in the U.S. By 2030, about a third of U.S children will be Hispanic (Murphey, Guzman, & Torres, 2014). Tennessee has experienced the third highest migration of Hispanics in the U.S, with one out of eight migrants being Hispanic (Nagle, Gustafson, & Burd, 2012). About a tenth of new born babies in Tennessee are Hispanic (Nagle et al., 2012). Compared to their non-Hispanic peers, Hispanic children experience higher prevalence of obesity and insulin resistance (Falkner & Cossrow, 2014); are more likely to experience obesity at an early age (2-to-5-year-olds) (Mozaffarian et al., 2016); are more likely to be severely obese (Skinner & Skelton, 2014); and higher prevalence of low HDL-C and hypertension.

Many multi-ethnic, nationally representative studies have examined the association between lifestyle, socio-demographic, environmental and biological factors and cardiometabolic risk in children (Daniels & Greer, 2008a; Kit et al., 2015; Ma, Zhang, & Xi, 2016; Ogden, Carroll, Kit, & Flegal, 2014; Taveras, Matthes, & Kleinman, 2010; Yeh, Viladrich, Bruning, & Roye, 2009). However, few studies have specifically examined cardiometabolic risk in Hispanic children, and even fewer have examined cardiometabolic risk in pre-pubertal Hispanic children.

Based on a comprehensive literature review, this study aims to examine three inter-related objectives and research questions to examine cardiometabolic risk in Hispanic children.

Study Objectives, Research Questions & Hypotheses

Objective 1

To assess the influence of socio-demographic and neighborhood factors on cardiometabolic risk in Hispanic children.

Research question 1. What is the prevalence of cardiometabolic risk factors in Hispanic children in Northeast Tennessee?

Hypothesis: The sample prevalence of hypertension and overweight are similar to national prevalence estimates for Hispanic children.

Research question 2. How do maternal obesity and physical activity influence Hispanic children's cardiometabolic risk?

Hypothesis: Children whose mothers are obese and less physically active are more likely to be overweight, less physically active and have elevated blood pressure than children whose mothers have a healthy body mass index and are physically active.

Research question 3. How do maternal perception of neighborhood safety, availability of physical activity amenities and rating of neighborhoods influence cardiometabolic risk in Hispanic children?

Hypothesis: Children of mothers who perceive their neighborhoods as unsafe, deprived of amenities and less desirable as places to bring up children will have higher cardiometabolic risk than children whose mothers perceive their

neighborhoods as safe, have amenities and more desirable as places to raise children.

Objective 2

To assess the influence of food group intake on cardiometabolic risk in Hispanic children.

Research question 1. How do mean food group intake in Hispanic children compare with recommended daily reference intake levels?

Hypothesis: Hispanic children meet recommendations for fruits, but not legumes, vegetables, wholegrain, dairy and fiber.

Research question 2. How do the sample proportions that do not meet food group recommendations compare with national proportions?

Hypothesis: Higher sample gender-age group proportions meet fruit recommendations, but similar proportions meet vegetable, fiber, legume, wholegrain and dairy recommendations compared with corresponding proportions of national (NHANES) gender-age groups.

Research question. What is the association between food group intake and cardiometabolic risk in Hispanic children?

Hypothesis: Higher fruit, vegetable, fiber, wholegrain, dairy and legume intake are protective against cardiometabolic risk in Hispanic children.

Objective 3

To evaluate the efficacy of non-traditional biomarkers for detection of cardiometabolic risk in Hispanic children.

Research question 1. What is the relationship between leptin, ghrelin, adiponectin, C-peptide, TNF- α , resistin, and IL-6 and cardiometabolic risk in Hispanic children?

Hypothesis: Leptin, C-peptide, TNF- α , and IL-6 levels are positively correlated with cardiometabolic risk factors; but adiponectin and ghrelin levels are negatively correlated with cardiometabolic risk factors.

Research question 2. How efficacious are non-traditional biomarkers in detecting cardiometabolic risk in Hispanic children?

Hypothesis: non-traditional biomarkers have at least moderate efficacy for detecting cardiometabolic risk in Hispanic children.

Research Purpose

The first purpose of our study is to contribute to the scant literature on how socio-demographic, neighborhood and dietary factors influence cardiometabolic health in pre-adolescent Hispanic children. This study also sought to specifically test the efficacy of non-traditional biomarkers for detection of cardiometabolic risk in pre-adolescent Hispanic children. Another purpose of our study is to identify leverage points for cardiometabolic risk prevention and control among Hispanic children in Northeast

Tennessee. Finally, our study aims to provide a baseline of cardiometabolic risk measures among Hispanic children in Northeast Tennessee for future reference.

Theoretical Framework

This study is grounded in the socio-ecological model (SEM) of health, the central idea of which is that cardiometabolic health-related behavior is the result of multiple interacting levels of influences (Glanz, Rimer, & Viswanath, 2008). Direction, and proximity of the multiple influences on behavior is an important idea of SEM. In order, from most proximal to distal, are intrapersonal (biological & psychological), interpersonal (social & cultural), organizational, community, physical environment and policy levels. Direction of influence on cardiometabolic health-related behavior runs from the most distal to the most proximal level of influence.

The consideration of environmental influences of behavior distinguishes SEM from behavioral models and theories which emphasize intrapersonal characteristics and proximal sociocultural influences (Glanz et al., 2008). The SEM is thus a more suitable framework for examining the complex factors underlying cardiometabolic health in Hispanic children. In this study, we conceptualize cardiometabolic risk in Hispanic children as the result of multiple interacting levels of influences, including the child's biology and behavior; the influence of the child's parents; and factors in the child's neighborhood (Figure 1.1). Per the SEM, Hispanic children who live in safe neighborhoods, where they have access to parks and recreational facilities, and have healthy parents who model physical activity are more likely to have superior

cardiometabolic health than Hispanic children who live in less safe neighborhoods, have less access to physical activity amenities and whose parents are obese and less physically active. Understanding the ecology of cardiometabolic risk among Hispanic children can inform efforts on improving the cardiometabolic health of the growing demographic in the region, Tennessee and U.S.

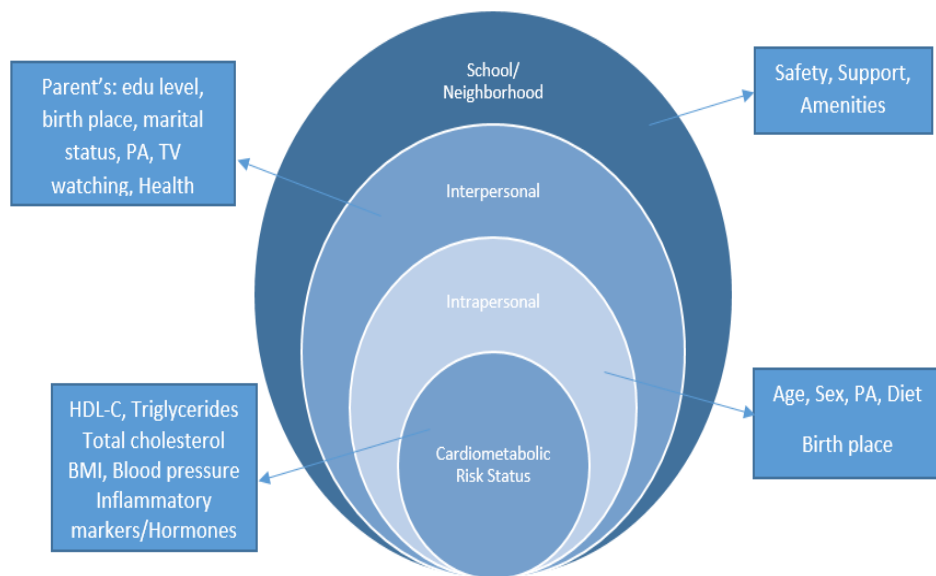


Figure 1.1. Socio-ecological model of cardiometabolic risk in Hispanic children.

Literature Review

Cardiometabolic Disease in the U.S.

A significant shift from infectious to chronic diseases as the leading cause of death in the U.S started at the dawn of the 20th century (Centers for Disease Control and Prevention, 1997, 1998). By 1997, over half (54.7%) of deaths in U.S were attributable to chronic diseases, namely heart disease and cancer, versus 4.5% attributable to infectious diseases, such as pneumonia, tuberculosis, diphtheria, diarrhea and enteritis. Since then, heart disease, stroke and diabetes have remained leading causes of death in the U.S, with more Americans dying from heart disease than any other disease (Centers for Disease Control and Prevention, 1997, 1998). In 2014, heart disease, stroke and diabetes, were the top, fifth and seventh leading causes of death respectively in the U.S; the age-adjusted mortality rate per 100,000 U.S population from heart disease, stroke and diabetes were 167.0, 36.5 and 20.9 respectively (National Center for Health Statistics, 2016). From 2000-2013, cardiovascular disease mortality decreased from a U.S age-standardized rate of 342.9 per 100,000 to 223.9 per 100,000. Despite the decrease, cardiovascular disease remains the leading cause of death in U.S (National Center for Health Statistics, 2016). This means that while some gains have been made in the levels of underlying risk factors, in general, there is still room for improvement in the cardiometabolic health of children and adults.

Cardiometabolic Risk in Children; Definitions and Epidemiology

The term cardiometabolic risk encompasses a wide range of risk factors, such as elevated triglycerides, high total cholesterol, high low density cholesterol (LDL), low high density cholesterol (HDL), hypertension, obesity, insulin resistance, overt diabetes, physical inactivity, smoking and markers of inflammation (Pérez et al., 2014), which independently increases one's likelihood of developing cardiovascular and metabolic diseases over the course of a lifetime. Cardiometabolic risk is related to the concept of the metabolic syndrome (Srikanthan, Feyh, Visweshwar, Shapiro, & Sodhi, 2016); however, the latter is more limited and emphasizes the idea of the clustering of select cardiometabolic risk-low HDL, high triglycerides, obesity, insulin resistance and hypertension- as more harmful to cardiometabolic health than individual risk factors.

Dyslipidemia. Dyslipidemia refers to abnormal levels of Low density lipoprotein cholesterol (LDL-C) high density lipoprotein cholesterol (HDL-C), triglycerides, total cholesterol (TC) and non-HDL cholesterol (non-HDL-C), associated with problems in lipid metabolism (Daniels et al., 2012). Dyslipidemia may be primarily genetic and run in families or secondary to specific health conditions such as endocrine, renal, metabolic diseases, and exogenous substances like alcohol and drugs; however, the most common form of dyslipidemia results from a combination of genetic, behavioral and environmental influences (Daniels et al., 2012). This type is commonly a combined dyslipidemia, with abnormalities in more than one type of cholesterol. The most common pattern is comorbid with obesity and consists of moderate to severe increase in triglycerides, normal to mild increase in LDL-C and low HDL-C (Daniels et al., 2012).

Post-mortem studies, such as the Pathobiological Determinants of Atherosclerosis in Youth (PBDAY) Study; studies of coronary artery calcium and carotid intima media; and prospective cohort studies, such as the Bogalusa Heart Study and the Young Finns Study (Berenson et al., 1998; Frontini et al., 2008; Juonala et al., 2008; McGill et al., 2000), have demonstrated that dyslipidemia is a risk factor for atherosclerosis and cardiovascular disease.

The National Cholesterol Education Program Expert Panel on cholesterol in children provides guidelines for classifying cholesterol levels in children (Lauer et al., 1992). Per 2011-2014 NHANES data, 22.3% of 6-to-19-year old Hispanic children had at least one of three dyslipidemias (high TC, low HDL-C or high non-HDL-C). Of all races, Hispanic children had the highest prevalence of low HDL-C and the second highest prevalence of non-HDL-C in 2011-2014. From 1988 to 2014, generally mean lipid levels and prevalence of dyslipidemia for all U.S children, 6-to-19 years of age, improved (Kit et al., 2012; Nguyen, Kit, & Carroll, 2015). Mean total cholesterol (TC) decreased significantly from 165mg/dl in 1988-1994 to 160 mg/dl in 2007/2010. This was associated with a significant decrease in prevalence of high TC from 11.3% in 1988-1994 to 7.4% in 2011-2014 (Kit et al., 2012; Nguyen, Kit, & Carroll, 2015). Similarly, mean HDL-C, mean non-HDL-C, mean triglycerides, prevalence of low HDL-C and prevalence of elevated triglycerides all improved significantly over the period (Kit et al., 2012; Nguyen, Kit, & Carroll, 2015). Similar trends were observed among Hispanic children, even though Hispanic children had higher prevalence of low HDL-C and high non-HDL-C compared to their non-Hispanic White and Black peers (Kit et al.,

2012; Nguyen, Kit, & Carroll, 2015). Despite the declining trends, there is much room for improvement: about a quarter of children, 6-19 years of age, still either have poor or intermediate lipid health on the AHA's total cholesterol metric of cardiovascular health (Mozaffarian et al., 2016).

Hypertension. Hypertension in children is defined as average systolic (SBP) and or diastolic (DBP) blood pressure higher than or equal to the 95th percentile for sex, age and height on three or more repeated measurements (Falkner et al., 2004).

Prehypertension, also referred to as high normal hypertension, is defined as average SBP or DBP higher than or equal to the 90th percentile, but less than the 95th percentile; SBP and DBP blood < 90th percentile is normal blood pressure (Falkner et al., 2004).

NHANES data show that between 1999-2000 and 2013-2014, the prevalence of hypertension among children 8-17 years of age, decreased significantly from 3.0% to 1.1%, while the prevalence of prehypertension levelled off (7.6% to 6.5%). A significant decrease in blood pressure occurred for both boys and girls—54.3% and 74.1% respectively over the period (Kit et al., 2015; Ma et al., 2016). Despite these gains, there is still room for improvement. About eighteen percent (17.7%) of children 12-to-19 years old have either poor or intermediate scores on the AHA's blood pressure metric of cardiovascular health (Mozaffarian et al., 2016). Blood pressure measurement during health visits is recommended for all children three years or older. Blood pressure is measured by auscultation using a stethoscope and a standard clinical sphygmomanometer. Accurate measurement requires a 5-minute rest and a cuff size that covers about 40% of the child's mid-arm (Falkner et al., 2004).

Racial disparities exist in the prevalence of childhood hypertension. Hispanic and non-Hispanic Black children experience higher prevalence of both hypertension and prehypertension. Childhood hypertension is an established risk factor for cardiovascular disease in adulthood (Mozaffarian et al., 2016).

Obesity. Obesity refers to excessive and unhealthy accumulation of fat in the body (Barlow & Committee, 2007). Body mass index (BMI), derived from the weight and height of a person, is a recommended and commonly used non-invasive screening method for detecting obesity in adults in primary care settings (Barlow & Committee, 2007). However, normal growth and development in childhood differs by sex and therefore influences BMI. To better accurately measure body fat in children, BMI is adjusted for age and sex. The Centers for Disease Control and Prevention (CDC), provides guidelines for classifying age and sex adjusted BMI percentiles in children into categories; < 5th percentile is considered underweight; \geq 5th-to-< 85th percentile is normal weight; 85th-to-< 95th percentile is overweight; and \leq 95th percentile is considered obese (Barlow & Committee, 2007).

Childhood overweight and obesity prevalence rates are high across all racial groups; however, Hispanic children are more likely to be overweight and obese compared to their non-Hispanic Black and White peers. Per 2011-2012 NHANES data, the national prevalence of overweight was 38.9% in 2-to-19-year-old Hispanic children, compared to 35.2% and 28.5% in non-Hispanic Black and non-Hispanic White children respectively. Additionally, Hispanic children experience higher prevalence of severe obesity and early childhood (2-5 years) obesity than their non-Hispanic Black and White

peers (Ogden, Carroll, Kit, & Flegal, 2014). From 1999 to 2012, the prevalence of obesity increased significantly for all racial and age groups in U.S (Figures 1.2 and 1.3).

Among 2-to-5-year children (Figure 1.2), obesity increased from 13.1% to 18% for Hispanic boys; and 12.2% to 15.2% for Hispanic girls (Ogden, Carroll, Curtin, Lamb, & Flegal, 2010; Ogden, Carroll, & Kit, 2012; Ogden et al., 2014). Hispanic boys almost consistently had highest prevalence of obesity over the period, with non-Hispanic White girls having the lowest prevalence of obesity (Figure 1.2 and 1.3). Similarly, among children 6-11 years old, minority groups experienced higher prevalence of obesity compared with their non-Hispanic White peers (Figure 1.2 and 1.3).

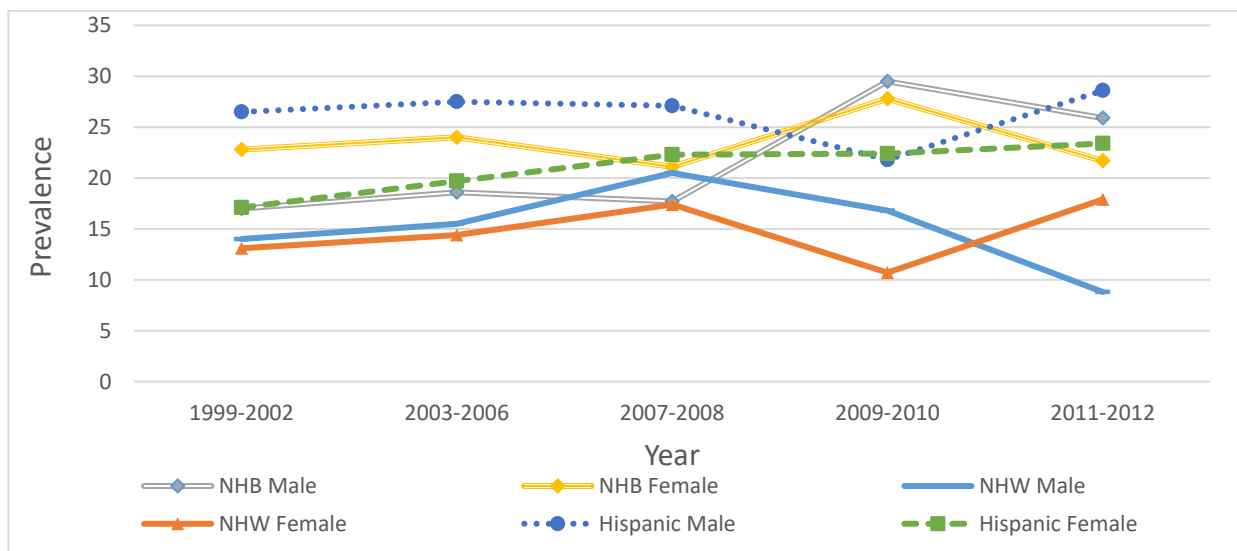


Figure 1.3. Prevalence of obesity among children, ages 6-11, 1999 — 2012

(Data source: NHANES 1971-1974 to 2011-2012)

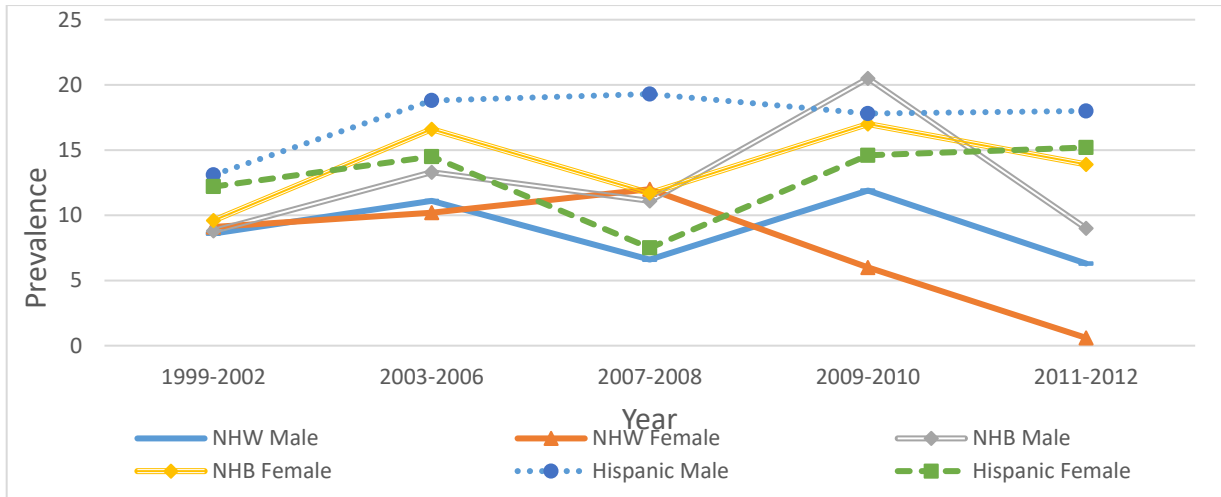


Figure 1.2. Prevalence of obesity among children, ages 2-5 years, 1999 — 2012

(Data source: NHANES 1999-2002 to 2011-2012)

Novel Biomarkers of Cardiometabolic Risk

Leptin. Leptin is a pro-inflammatory cytokine produced mainly by adipocytes (fat cells) and thus its other name, adipokine (Ghantous, Azrak, Hanache, Abou-Kheir & Zeidan, 2015). The levels of leptin therefore directly correlate with total body fat. Physiologically, it causes a net-negative energy balance by reducing appetite while increasing energy expenditure through an increase in sympathetic activity and glucose use (Ghantous et al., 2015). Leptin receptors are expressed in a wide-range of target organs, including the heart and endothelium. Leptin has been found to be associated with cardiometabolic risk, especially obesity (Ghantous et al., 2015).

Adiponectin. Adiponectin is an anti-inflammatory cytokine produced solely by adipocytes. It is produced in low, middle and high molecular weight forms, with the high

molecular weight (HMW) form being the most anti-inflammatory (Ghantous et al., 2015; Szmítko et al., 2007). Its functions include facilitating target organ response to insulin and inhibiting the formation of atheroma (Ghantous et al., 2015; Szmítko et al., 2007). Circulating levels of adiponectin are inversely related to cardiometabolic risk, but directly related to HDL-C. Losing weight increases adiponectin levels. Sex differences exist in adiponectin levels, with females having higher levels than males (Ghantous et al., 2015; Szmítko et al., 2007).

Leptin: adiponectin ratio. Some studies suggest that a leptin-adiponectin ratio (LAR) may be a more powerful marker for cardiometabolic risk than either leptin or adiponectin alone (Falahi, Khalkhali Rad, & Roosta, 2013). One downside of LAR is that because females have higher levels of adiponectin than males, LAR is more strongly correlated with cardiometabolic risk in males than females; an upside of LAR is that it may be better suited to assessing cardiometabolic risk in the non-fasting state (Finucane et al., 2009).

Ghrelin. Ghrelin is a hormone produced mainly in the stomach. It stimulates appetite and inhibits atherosclerosis (Tesauro et al., 2009; Varela et al., 2011). Circulating levels are inversely correlated with cardiometabolic risk, particularly obesity and insulin resistance; with the strength of correlation increasing as the number of risk factors increase. Sex differences exist, with females having higher ghrelin levels than males (Pulkkinen, Ukkola, Kolehmainen, & Uusitupa, 2010).

Interleukin-6 (IL-6). IL-6 is a pro-inflammatory cytokine which is produced by macrophages during the normal inflammatory response to infection and injury (Aroor, McKarns, Demarco, Jia, & Sowers, 2013). The mechanism of increased IL-6 secretion in cardiometabolic risk is related to an increased number of macrophages in fat tissue in response to fat cell dysfunction. IL-6 has been shown to have a direct positive correlation with cardiometabolic risk (Indulekha, Surendar, & Mohan, 2011).

Tumor necrosis factor-alpha (TNF- α). TNF- α is a pro-inflammatory cytokine produced by the fat surrounding organs, such as the stomach. It is directly correlated with cardiometabolic syndrome, particularly insulin resistance and hypertriglyceridemia (Indulekha et al., 2011; Musialik, 2012).

Diet and Cardiometabolic Risk in Children

Child nutrition and dietary patterns. Unhealthy dietary patterns contribute to the development of cardiovascular disease, yet, a significant proportion of American children do not eat a healthy diet. The 2015-2020 Dietary Guidelines for Americans (DGA) (U.S. Department of Agriculture, 2015) recommends that Americans eat a variety of nutrient dense foods, including vegetables, fruits, grains, fat-free or low-fat dairy, protein foods and oils, every day. The DGA and the National Cholesterol Education Program Expert Panel on Blood Cholesterol Levels in Children and Adolescents (Lauer et al., 1992) recommends limiting dietary saturated fat to less than 10% of daily calories, cholesterol to < 300mg/day, added sugar to less than 10% of daily calories, sodium to less than 2,300mg per day and alcohol, if consumed up to 1 drink and up to 2 drinks a

day for women and men of legal drinking age, respectively (Lauer et al., 1992; U.S. Department of Agriculture, 2015).

There is substantial evidence that adherence to dietary guidelines leads to better cardiometabolic health and vice versa. For example, in the Special Turku Coronary Risk Factor Intervention Project for Babies (Lapinleimu et al., 1995), 7-month old Finnish infants were randomized into either a group whose parents received counseling from a nutritionist for a low total fat, low saturated fat, low protein, low cholesterol and high carbohydrate diet or a group whose parents received basic health education and no instructions on the use of fats (Lapinleimu et al., 1995). After 14 years of follow-up, dietary assessments showed that children in the intervention arm ate significantly less total and saturated fat. These changes were associated with significantly lower risk of adverse TC, LDL-C, insulin levels, and obesity in intervention than control when assessed at various points during the study (Hakanen et al., 2006). In a randomized controlled trial (RCT) among 6-11-year-old children with heterozygous familial hyperlipidemia, one year of a low fat and cholesterol diet reduced TC and LDL-C levels by 4.4% and 5.5% respectively (Tonstad et al., 1996).

Meta-analyses of prospective cohort studies show that consumption of Legumes, nuts, fish, whole grain, fruits and vegetables, is associated with lower risk of cardiovascular disease (Afshin, Micha, Khatibzadeh, & Mozaffarian, 2014). For example, in a meta-analysis which included 91, 379 men and 129, 701 women, Dauchet, Amouyel, Hercberg and Dallongeville (2006) found that the risk of coronary heart disease decreased by 4% [RR (95%CI): 0.96(0.93-0.99), P=0.0027] for each

additional portion per day of fruit and vegetable intake and by 7% [RR (95%CI): 0.93(0.89-0.96), P=0.0001]] for fruit intake (Dauchet et al., 2006). In contrast, almost all observational studies have found that an increased intake of sodium increases cardiovascular risk and events such as stroke (Kalogeropoulos et al., 2015).

U.S children not meeting recommended food group intake. The healthy eating index (HEI) is a measure of conformance to dietary recommendations. Data from NHANES 1999 to 2010 show that the HEI of Americans, 2 years and older, increased from 49.1 to 57.8 (U.S. Department of Agriculture, 2015). However, there is still room for improvement: three quarters of Americans, including children and adolescents, have a diet which is low in vegetables, fruits, dairy and oils, and most Americans exceed the recommended limits for added sugars, saturated fats, and sodium (U.S. Department of Agriculture, 2015); in addition, the AHA scores about two thirds of Americans (63.4%) poorly on its healthy diet metric of cardiovascular health (Mozaffarian et al., 2016). Sex, and age differences exist in children's dietary patterns. Males eat more total protein, unprocessed red meats, sugar-sweetened beverage and salt than females. As children grow, average consumption of unprocessed meat, and sugar sweetened beverages increases (Rehm, Peñalvo, Afshin, & Mozaffarian, 2016).

Physical Activity

Physical activity (PA) refers to movement of the body which increases metabolism above the basal rate. Important dimensions of PA are: mode, that is whether physical activity is aerobic, muscle or bone strengthening; frequency; duration

and intensity (U.S. Department of Health and Human Services, 2008). The most common forms of PA applicable to children are leisure time, school and outdoor. The 2008 federal PA guidelines (PAG) recommends that children have at least 60 minutes of PA every day, including vigorous intensity PA, muscle and bone strengthening on three or more days (U.S. Department of Health and Human Services, 2008).

Despite evidence of the cardiovascular benefits of adequate physical activity and the detrimental effects of a sedentary lifestyle, a significant number of U.S children and adolescents do not meet recommendations. Per the 2013 Youth Risk Behavior Survey (YRBS) (Kann et al., 2014), 15.2% of high school students nationwide did not meet the PAG guideline of at least 60 minutes of PA in the past week; 41.3% spent three or more hours playing computer or video games un-related to school work; and 32.5% spent three or more hours watching television per day. Only 27.1% of high school students nationwide met the PAG guidelines. Of students in kindergarten through the 12th grade nationwide, only 29.4% attended structured daily physical education classes in school (Kann et al., 2012).

In general, high school students' engagement in PA has remained stable whereas their sedentary behavior has increased in the last decade. The proportion of students that play video or computer games for three or more hours on a typical school day, unrelated to school work, increased from 22.1% in 2003 to 41.3% in 2013. (Kann et al., 2012; Gahche, Fakhouri & Carroll et al., 2014).

Age, sex and ethnic differences exist in physical activity and sedentary lifestyle among children. Physical activity decreases from 9th to 12th grade; and boys are more likely than girls to meet PAG. For example, in the 2013 YRBS, about twice as many boys as girls met PA recommendations (36.6% versus 17.7%); and fewer girls than boys met muscle strengthening PA recommendations (61.8% versus 41.6%) (Kann et al., 2012). Non-Hispanic Black and Hispanic children spend more time on the screen than their non-Hispanic White peers. In the 2013 YRBS, 51.9% of non-Hispanic Black boys, 46.6% of non-Hispanic Black girls, 44.8% of Hispanic girls and 42.0% of Hispanic boys, versus 39.1% of non-Hispanic White girls and 35.6% of non-Hispanic White boys spent three or more hours per day on the computer. Similarly, watching television for three or more hours per day is more prevalent among non-Hispanic Black and Hispanic children than their non-Hispanic White peers (Kann et al., 2012).

Physical activity and cardiometabolic risk. There is strong evidence regarding the cardiometabolic benefits of physical activity. Because cardiovascular disease outcomes are rare in childhood, most studies examining incidence of cardiometabolic disease have occurred in adults. However, a few studies in children support the cardiometabolic benefits of PA. In a study of 4-to-7-year-old Finnish children participating in the STRIP study described previously, Saakslanti et al. (2004) found a statistically significant inverse correlation between reported PA and total cholesterol and a positive correlation between reported PA and HDL-C. Meyer, Kundt, Lenschow, Schuff-Werner and Kienast (2006) found PA to be effective in improving carotid intima-media thickness, and flow mediated vasodilation in a randomized controlled study of six adolescent.

Socioecological Factors, Culture and Cardiometabolic Risk

Family members and peers have a strong influence on the dietary patterns and physical activity behaviors of children and adolescents (Wardle & Cooke, 2008). Family and peers influence children's dietary and physical activity behaviors through several mechanisms including social norms, culture, role modelling and observational learning (Wardle & Cooke, 2008). Cultural differences in traditional cuisine, nurturing, communication, role modelling, beliefs and perceptions of body size and image have been noted to contribute to obesity (Wardle & Cooke, 2008).

Socioeconomic status. Low household income levels, food insecurity, and inadequate or complete lack of health insurance are linked to higher cardiovascular morbidity and mortality (Braveman, Cubbin, Egerter, Williams, & Pamuk, 2010; Kaplan & Keil, 2016). Per data from the United States Department of Agriculture, in 2015, 6.4 million children were food insecure (U.S. Department of Agriculture, 2016). Out of that number, 541,000 children experienced reduced food intake. More Hispanics and non-Hispanic Black (NHB) households (19.1% and 21.5% respectively) were food insecure compared with non-Hispanic White (NHW) households (14.0%). Similarly, Hispanic households and NHB households were more likely to experience very low food security than NHW households (U.S. Department of Agriculture, 2016). In 2010, fewer Hispanic adults (60.9%) 25 years or older than their NHW (90.4) and NHB (81.4%) peers had obtained at least a high school diploma (Ryan & Siebens, 2012). Employment rates among Hispanics (66.4%) and NHW (64.0%) are similar; however, because Hispanics generally have lower educational attainment than NHW and face language and

documentation difficulties, a disproportionate fraction of Hispanics work in low paying jobs (U.S. Department of Agriculture, 2016). In 2015 the median income in Hispanic (\$45,148) and NHB (\$36,898) households was lower than the national median household income (\$56,516) and the median income in NHW households (\$62,950) (U.S. Department of Agriculture, 2016). Going together with low income levels is low insurance coverage. In 2011, Hispanics represented 30.1% of the US uninsured population compared with 11.1% in NHWs and 19.5% in NHBs (Bishaw & Semega, 2008).

Disparities research demonstrates socio-economic disparities in several health conditions and health related behaviors in children and adults (Braveman et al., 2010; Kaplan & Keil, 2016). When incomes are stretched thin, households may focus more on the quantity rather than the quality of food for instance; similarly, structured after-school physical activity programs may be viewed as dispensable. Socioeconomic disparities exist in the prevalence of obesity in children and is reported to be widening: while the prevalence of obesity is declining among children of mothers with a college education or higher, among children whose mothers only have a high school degree or less, it is increasing (Datar & Chung, 2015; Frederick, Snellman, & Putnam, 2014; Ogden, Lamb, Carroll, & Flegal, 2010). Socio-economic status (SES) is inversely associated with prevalence of obesity in NHW children (Ogden, Lamb, et al., 2010). In the study by Ogden et al. (2010), 2-to-19-year-old NHW boys and girls from households with income at or above 350% of the poverty level had a significantly lower prevalence of obesity than their peers from households with income below 130% of the poverty level.

However, among Hispanic children, findings on the association between SES and risk of obesity were inconsistent: Girls from households at or above 150% of the poverty level had a 4.8% higher prevalence of obesity than girls from households below 130% of the poverty level (Ogden et al., 2010). Other studies have found either a weak inverse relationship between parental education and child obesity or no association at all (Balistreri & Van Hook, 2009; Goldman, Kimbro, Turra, & Pebley, 2006). Studies on socioeconomic disparities in the risk of hypertension are few. In one large prospective study of more than 3,000 5-to-6-year-old Dutch children, Van Den Berg, Van Eijdsden, Galindo-Garre, Vrijkotte and Gemke (2013) found a 2.2 mmHg (95% CI: 1.4-3.0) higher systolic blood pressure and a 1.7 mmHg (95% CI: 1.1-2.4) higher diastolic blood pressure in children of low-educated women (no education, or primary school or lower vocational secondary or technical secondary education) compared with children of highly educated women (higher vocational or university education). Further, children of mothers with mid-level education (higher vocational secondary, or intermediate vocational education) (OR: 1.5, 95% CI: 1.18-1.92) or low education (OR: 1.80, 95% CI: 1.35-2.42) were more likely to have prehypertension compared with children of highly educated mothers.

Culture. The U.S Census Bureau uses the term Hispanic to refer to individuals of any race, ethnicity or ancestry who have origins in Mexico, Cuba, the Caribbean, Central America, South America, or other Spanish-speaking countries (Waterston, 2006). Hispanic households are generally larger, consisting of 3.4 people on average, compared with 2.5 people in NHW households (U.S. Census Bureau, 2010). About

one in four Hispanic parents speak Spanish only; generally, recent Hispanic immigrants or older foreign-born Hispanics are monolingual Spanish speakers (Dubard & Gizlice, 2008). Preference for Spanish language may negatively influence perceived health status, as well as health knowledge. (Dubard & Gizlice, 2008). Language barrier remains an obstacle for many Latino parents when they use the healthcare and public health systems, and affects their use of health services (Dubard & Gizlice, 2008).

Neighborhood factors and cardiometabolic risk. Neighborhood level factors such as safety, walkability, availability of recreational facilities, supermarkets, and transportation, influence health related behaviors. Several studies demonstrate that access to recreational and transportation facilities, such as sidewalks and paths for bicycling increases physical activity among children (Durand, Andalib, Dunton, Wolch, & Pentz, 2011). In a national study of 17000 adolescents, Gordon-Larsen, Nelson, Page and Popkin (2006) found greater access to recreational facilities to be associated with higher odds of participation in frequent PA. Despite clear evidence linking access to PA facilities with increased PA, studies which have examined the effect of access to PA facilities on health-related conditions such as obesity, have reported inconsistent findings. For example, Durand, Andalib, Dunton, Wolch and Pentz (2011) did not find any association, whereas Sallis et al. (2009) found lower risk of overweight in more walkable neighborhoods.

The School Environment and Cardiometabolic Risk

Children and adolescents spend a significant fraction of their time in the school environment: at least 6 hours a day for half of the year, for up to 13 years. That is more than time spent in all other settings except the home environment (Fox, Dodd, Wilson, & Gleason, 2009). Students may get as much as half of their daily calories from school (Story, 2009). Schools are therefore uniquely placed to help children meet PGA and DGA recommendations. The Association for Supervision and Curriculum Development and the CDC put together the Whole School, Whole Community, Whole Child (WSCC) model for promoting health and academic performance in U.S schools in 2014 (Association for Supervision and Curriculum Development, 2014). WSCC expanded the original eight components of the Coordinated School Health Program to ten: physical education and physical activity; nutrition environment and services; health services; counseling, psychological, and social services; social and emotional climate; physical environment; employee wellness; family engagement; and community involvement (Association for Supervision and curriculum Development, 2014). The underlying principle of the WSCC model is to care for the complete child and to provide guidance for the interdependent relationship between academic performance and health (Association for Supervision and curriculum Development, 2014).

School health education. The Centers for Disease Control and Prevention (CDC) recommends that students in grades K-12 have daily physical education (Centers for Disease Control and Prevention, 2011). School health education begins from pre-K and runs through grade 12. Instructions cover a host of topics including healthy eating,

physical activity, and tobacco use. Among other things, health education seeks to equip students with the information and skills they need to make healthful decisions and adopt healthy eating patterns and physical activity behaviors. Nationwide, there is room for improvement in school health education (Centers for Disease Control and Prevention, 2015b). In 2014, 74.1% of schools required students to receive instruction on nutrition and dietary behavior; an even lower 67.2% required students to receive instruction on PA. As students advance in grade, required PA and nutrition instruction decreases; in 2014, it increased from 30.5% among kindergarteners, peaked at 40.3% in 5th graders and then decreased to a minimum of 5.0% in 12th graders (Centers for Disease Control and Prevention, 2015b).

School physical activity. One of the objectives of Healthy People 2020 is to increase the proportion of adolescents who meet current physical activity recommendations (Office of Disease Prevention and Health Promotion, 2010). Schools can help meet this objective by adopting the Comprehensive School Physical Activity Program (CSPAP) (Centers for Disease Control and Prevention, 2011). CSPAP addresses physical education and physical activity in schools; and the involvement of school staff and families in children's PA (Centers for Disease Control and Prevention, 2013). School physical activity opportunities include recess and PA done in class. Furthermore, schools can work with students, their families and communities to provide opportunities for physical activity before and after school. Examples of before-and after-school physical activities include walking and biking to school programs, physical activity clubs, intramural, informal play on school grounds, and interscholastic sports

(Centers for Disease Control and Prevention, 2013). Schools can encourage physical activity before and after school by allowing students, families, and others in the community to use school facilities such as the track, gym, or fields. In addition, other organizations can establish joint use agreements with schools to allow them to use school facilities for physical fitness (Berkeley, 2010). The physical location of schools then becomes very important. Schools located within residential areas facilitate shared use (Berkeley, 2010).

School nutrition environment. The school nutrition environment provides students with opportunities to learn about and practice healthy eating through available foods and beverages, nutrition education, and messages about food in the cafeteria and throughout the school (Centers for Disease Control and Prevention, 2011). The quality of school food varies, depending on the source (Centers for Disease Control and Prevention, 2011). School breakfast and lunch which is reimbursed by the United States Department of Agriculture must meet dietary recommendations, but competitive foods sold at the school cafeteria, store and vending machines are not required to meet dietary guidelines (Story, 2009; U.S. Department of Agriculture, 2015).

In general, the quality of the school food environment has been headed in the right direction since 2000 (Centers for Disease Control and Prevention, 2015b): the proportion of schools that provided low-fat salad dressing increased from 66% in 2000 to 80.1% in 2014; the proportions of schools with 1 or more vending machines decreased from 47.8% in 2000 to 28.1% in 2014; while the percentage of school with a store, canteen or snack bar from which students can purchase foods and beverages

decreased from 35.7% in 2000 to 19.1% in 2014. Yet, there is still room for improvement. In 2014, 55% of schools offered a la carte lunch items to students; 35.4% of schools offered a la carte breakfast item to students; and 74.1% of schools sold soft drinks to students (Centers for Disease Control and Prevention, 2015b). Studies have demonstrated that the presence of competitive food reduces children's intake of fruits and vegetables, non-starchy vegetables, and milk, while increasing intake of total and saturated fat and sugar sweetened beverages (Templeton, Marlette, & Panemangalore, 2005). There is evidence that improving nutrition standards can improve children's eating patterns (Katz et al., 2005) and reduce overweight among students (Gortmaker et al., 1999).

Policy Environment and Cardiometabolic Risk

The literature review above demonstrates that a wide range of factors, including demographic and socioeconomic, influence children's health-related behaviors. The goal of population health is to change the context of behavior to facilitate healthy decision making by individuals (Pearson, 2011). Population health approaches use federal, state and local policy to achieve better health outcomes for communities. Policies can be approached from a socioeconomic, legal or regulatory perspective (Pearson, 2011). In general, cardiometabolic policy for communities is aimed at improving eating patterns and physical activity; reducing smoking and exposure to second-hand tobacco; improving compliance with screening and diagnosis of dyslipidemia and hypertension; improving adherence to treatment of hypertension and

dyslipidemia; and improving early detection and management of cardiovascular disease (Pearson, 2011). Effective policy interventions to reduce sedentary behavior in children are related to physical activity in school, leisure-time physical activity, outdoor play and local transportation (National Heart, Lung, and Blood Institute, 2011; Pearson et al., 2013). Policies can encourage children to use physically active means to travel to and from school by providing walking and bicycle paths. Bicycle and pedestrian trails are particularly cost-effective strategies to encourage physical activity (Wang, Macera, Scudder-soucie, & Schmid, 2004). Legal policies, such as shared use agreements can remove prohibitions on the use of school facilities by the community after school hours (Berkeley, 2010). Other legal and regulatory policy approaches can change the built environment, such as transportation plans, construction of parks, and green spaces.

Management of Cardiometabolic Risk

Prevention and control of cardiometabolic risk. Prevention and control of cardiometabolic risk in children takes two approaches. One approach aims to move the entire community distribution of cardiometabolic risk to a lower level through community-wide changes in risk behaviors (Pearson, 2011). In contrast, a clinical approach seeks to treat those with severe risk, with or without associated disease (Pearson, 2011). Both approaches are important for cardiometabolic risk prevention and control in children.

Effective cardiometabolic risk prevention is a multifaceted approach that targets: risk behaviors, the communities in which behaviors occur, and the public health

infrastructure and services (Pearson, 2011). Risk behavior modification interventions include promoting compliance with dietary recommendations (example, low saturated fat and sodium); regular physical activity; smoking cessation; and school health education (National Heart, Lung, 2011; Pearson, 2011). As noted previously, because children spend a lot of time in school, the school system provides a unique opportunity to help children cultivate healthy lifestyles. The Whole School, Whole Community, Whole Child (WSCC) model was put together by the Association for Supervision and Curriculum Development and the CDC in 2014 for U.S schools (Association for Supervision and curriculum Development, 2014) and serves as a guide for schools to integrate student health and academic work.

Clinical management of hyperlipidemias. The 1992 NCEP Pediatric Panel (Lauer et al., 1992) and the AHA (McCrindle et al., 2007) recommend a combination of lifestyle and drug-based management of LDL-C abnormalities. Drug-based management with a statin or a bile acid sequestrant is recommended only in children at least ten years old after a 6 -12 month trial of lifestyle/dietary modification has failed (McCrindle et al., 2007; Miller, Wright, & Browne, 2015). The lipid threshold for initiation of pharmacotherapy is an isolated LDL-C level equal to or higher than 190 mg/dL or an LDL of at least 160 mg/dL, together with either a positive family history of premature cardiovascular disease or the presence of two or more other cardiovascular disease risk factors. (McCrindle et al., 2007).

Clinical management of hypertension. Routine measurement of BP during health care visits is recommended for children three or more years old (Chobanian et al., 2003;

National Heart, Lung, 2011). As with dyslipidemia, lifestyle approaches are usually the first line of treatment when obesity is present. Indications for use of pharmacologic agents include, symptomatic hypertension, secondary hypertension, established hypertensive target-organ damage, and failure of lifestyle modification to control blood pressure. Angiotensin converting enzyme inhibitors (ACE-inhibitors), angiotensin receptor blockers (ARBs), alpha and beta blockers, and calcium channel blockers are pharmacologic options for treatment of hypertension in children (Chobanian et al., 2003; Rao, 2016)

Clinical management of overweight and obesity. Combined weight loss programs that include behavior change counseling, reduced dietary caloric intake, and increased physical activity, are effective in reducing obesity in children older than six years, but not in younger children (Barlow & Committee, 2007). The drug Orlistat (under the trade name Xenical) has been approved by the FDA for weight loss in obese children at least twelve years old, in conjunction with a reduced caloric intake children (Barlow & Committee, 2007). Orlistat may cause severe liver injury children (Barlow & Committee, 2007). Adolescents with BMI greater than 35 kg/m² and associated comorbidities may benefit from bariatric surgery on research protocol, in conjunction with a multicomponent weight loss program (Barlow & Committee, 2007).

CHAPTER 2

SOCIODEMOGRAPHIC, NEIGHBORHOOD FACTORS AND CARDIOMETABOLIC RISK IN HISPANIC CHILDREN

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Abstract

Objective: Socio-demographic factors, such as maternal physical activity, body mass index, and perception of the neighborhoods in which their children live, have been associated with children's cardiometabolic risk; however, few studies have examined this relationship in pre-adolescent Hispanic children. This study aims to assess how mother's physical activity, body mass index, and perception of the neighborhoods in which their children live, influence Hispanic children's cardiometabolic risk.

Methods: Data (N=118) came from a cross-sectional pilot study of metabolic syndrome in Hispanic children receiving well-child care at a community health center in Johnson City, TN, from June 2015 to September 2016. Mothers reported their body mass index (BMI), physical activity, perception of the safety and availability of physical activity (PA) amenities where their children live, and rated their satisfaction with their children's neighborhoods as a place to bring up children. Mothers also reported their children's PA and screen time. Children's height, weight, and blood pressure were measured. Multiple logistic regression was used to examine the relationship between maternal factors and children's PA, blood pressure and BMI status, adjusting for mother's education and the child's sex and age.

Results: One hundred and eighteen (118) mother-child dyads were studied. The mean age of children was 6.36 years ($SD=2.75$). About a third (31.4%) of children had elevated blood pressure and 40.7% were overweight. Children of obese mothers were more likely than children of mothers with normal BMI to engage in less than three days

of at least 60 minutes of vigorous physical activity per week (*OR*: 6.47; 95% *CI*: 1.61-26.0); children whose mothers did not engage in moderate physical activity were more likely to engage in less than three days of at least 60 minutes of vigorous physical activity per week (*OR*: 2.92, *CI*: 1.18-7.24); and have elevated blood pressure (*OR*: 2.50, 95% *CI*: 1.02-4.53) than children whose mothers engaged in moderate PA.

Conclusions: A high proportion of Hispanic children were overweight and had elevated blood pressure. Interventions to help Hispanic mothers achieve and maintain healthy weight and model physical activity could be important for cardiometabolic risk reduction in Hispanic children.

Keywords: mother's body mass index; mother's physical activity; mother's neighborhood perceptions; children's cardiometabolic risk; Hispanic children

Introduction

Cardiometabolic risk is used to refer to a wide-range of risk factors, such as elevated blood pressure and obesity, which increase the risk of developing cardiometabolic diseases including heart disease and diabetes. Compared to their non-Hispanic White peers, Hispanic children experience higher prevalence of obesity (Falkner & Cossrow, 2014); are more likely to experience obesity at an early age; be severely obese (Mozaffarian et al., 2016); and have higher prevalence of hypertension (Kit et al., 2015; Nguyen et al., 2015). For example, the prevalence of obesity among 2-to-18-year-olds in 2011-2014 was 14.7% for non-Hispanic White children versus 21.9% for Hispanic children (Ogden, Carroll, Fryar, & Flegal, 2015); the prevalence of elevated blood pressure among 8-to-17-year-olds in 2011-2012 was 9.4% for non-Hispanic White children versus 11.5% for Hispanic children (B. K. Kit et al., 2015); and among 2-to-5-year-olds, in 2011-2012, the prevalence of obesity was 3.5% for non-Hispanic White children versus 16.7 for Hispanic children (Ogden, Carroll, Kit, & Flegal, 2014). Obesity and hypertension are important public health issues because of their association with heart disease, stroke and diabetes, which rank as the top, fifth and seventh leading causes of death among U.S adults, respectively.

A positive energy balance resulting from a complex set of risk factors including poor diet, physical inactivity, genes, aging and ethnicity underlie the development of overweight and obesity (Rao, 2016). A similar set of complex risk factors including obesity, high dietary salt intake, being male, older age, and ethnicity drive the development of hypertension in children (Rao, 2016). How these risk factors interact to

cause obesity and hypertension is complicated; however, many studies are shedding light on how socioeconomic, neighborhood factors and parental physical activity influence obesity and hypertension in children (Durand et al., 2011; Gordon-Larsen et al., 2006; Rosendranz & Dzewaltowski, 2011; Sallis, Bowles, et al., 2009; Sallis, Saelens, et al., 2009; Van Den Berg et al., 2013). These studies are very important in identifying leverage points in the fight to improve children's cardiovascular health.

Socioeconomic disparities in obesity among children in general is widening: while the prevalence of obesity is declining among children of mothers with a college education or higher, it is increasing among children whose mothers only have a high school degree or less (Datar & Chung, 2015; Frederick et al., 2014; Ogden, Lamb, et al., 2010). Data from the National Health and Nutrition Examination Survey 2005-2008 showed the prevalence of obesity in 2-to-19-year-old NHW boys and girls from households with income at or above 350% of the poverty level to be significantly lower than the prevalence of obesity in children from households with income below 130% of the poverty level (Ogden, Lamb, et al., 2010). However, among Hispanic children, the association between household income and the prevalence of obesity was not only insignificant, but also inconsistent: Girls from households at or above 150% of the poverty level had a 4.8% higher prevalence of obesity than girls from households below 130% of the poverty level (Ogden, Lamb, et al., 2010). Other studies have found either a weak inverse relationship between parental education and BMI or no association at all (Balistreri & Van Hook, 2009; Goldman et al., 2006).

Disparities studies on pediatric hypertension are few. In a large prospective study of more than 3,000 5-to-6-year-old Dutch children, Van Den Berg et al. (2013) found a 2.2 mmHg (95% CI: 1.4-3.0) higher systolic blood pressure and a 1.7 mmHg (95% CI: 1.1-2.4) higher diastolic blood pressure in children of low-educated women (no education, or primary school or lower vocational secondary or technical secondary education) compared with children of highly educated women (higher vocational or university education). Further, children of mothers with mid-level education (higher vocational secondary, or intermediate vocational education) (OR: 1.5, 95% CI: 1.18-1.92) or low education (OR: 1.80, 95% CI: 1.35-2.42) were more likely to have prehypertension compared with children of highly educated mothers. In another large study of young adults in the National Longitudinal study of Adolescent Health, household income was found to have a significant inverse association with systolic blood pressure: each \$50, 000 increase in household income was found to decrease systolic blood pressure by about 0.6 mmHg (Brummett et al., 2011).

The built environment is used in part to refer to the social characteristics of the man-made environment which shapes opportunities for children's physical activity and eating patterns (Miranda, Edwards, Anthopoulos, Dolinsky, & Kemper, 2012). Parental perceptions of the neighborhood context, such as safety, availability of playgrounds, and parks have an important effect on the BMI of children (Bacha et al., 2010; O Connor et al., 2014). Neighborhoods which are less safe and lack amenities for physical activity are associated with overweight (Bacha et al., 2010; Mendoza, McLeod, Chen, Nicklas, & Baranowski, 2014; Miranda et al., 2012; Singh, Kogan, Van Dyck, & Siahpush, 2008;

Taveras et al., 2010). In a large multi-ethnic study of 2-to-18-year-old children in Durham, North Carolina, Miranda et al. (2012) found that independent of age, sex, race and health insurance status, higher levels of violent crime, total crime, and nuisance in a child's residential area were associated with a significantly higher risk of overweight. Singh, Siahpush and Kogan (2010) found that children living in neighborhoods which were unsafe and had no sidewalks, parks and recreational facilities had 20%-60% higher odds of being obese than their peers from more favorable neighborhoods.

Like maternal perception of the safety of the neighborhoods in which children live, some studies have identified maternal physical activity and obesity as risk factors for obesity in children (Fuemmeler, Anderson, & Mâsse, 2011; Ruiz, Gesell, Buchowski, Lambert, & Barkin, 2011; Whitaker, Wright, Pepe, Seidel, & Dietz, 1997). O Connor et al. (2014) found that Hispanic mothers' perception of the social characteristics of their environments explained up to 33% of the variance of different types of physical activity related parenting behaviors such as engagement, promoting inactivity and registering their children for sports; Mendoza et al. (2014) found that Hispanic mothers' perception of their neighborhoods as disorderly was associated with higher BMI z-scores in their children; and in a retrospective cohort study, Whitaker et al.(1997) found maternal obesity to be the primary predictor of children less than three years of age developing obesity in adulthood.

To the best of our knowledge, no study has examined the effect of maternal BMI, maternal physical activity and maternal perception of the neighborhoods on the blood pressure and BMI of pre-adolescent Hispanic children as young as two years old.

Because obesity often clusters with hypertension, it is reasonable to expect maternal to influence children's blood pressure and BMI. Despite the high prevalence of obesity and elevated blood pressure in Hispanic children in general, we do not know of any local (Northeast Tennessee) and state (Tennessee) estimates for pre-adolescent Hispanic children. Based on these and other knowledge gaps in previous studies presented above, this study tests three related hypotheses in pre-adolescent Hispanic children: First, we hypothesize that the prevalence of overweight and elevated blood pressure in our sample would be similar to national estimates for Hispanic children. Second, if mothers express satisfaction with the neighborhoods in which their children live as a place to bring up children and perceive those neighborhoods as safe and having amenities, then they are more likely to encourage more physical activity for their children; their children will have less screen time (TV or video), more physical activity and over time, a lower prevalence of overweight and elevated blood pressure. Third, mothers who engage in less physical activity and are obese are less likely to model physical activity; and their children will be less physically active, have more screen time and over time, have higher prevalence of overweight and elevated blood pressure.

Methods

Data Source and Participants

Data for this project came from the Study of Metabolic Syndrome in Hispanic Children, a cross-sectional study of Hispanic children ages 2-10 years, and their mothers at the Johnson City Community Health Center (JCCHC); the study was conducted by an interdisciplinary group of researchers from East Tennessee State University. Funding was provided by the Tennessee Board of Regents. The study collected a wide range of survey, anthropometric and laboratory data on the cardiometabolic health of participants. It sought to establish baseline measures of metabolic syndrome in Hispanic children in Northeast Tennessee and to follow-up the initial study participants as a cohort. The study was reviewed and approved by the Institutional Review Board at East Tennessee State University.

Participants were mothers and their children who came to the JCCHC for a well-child visit. Inclusion criteria for child participants included: being 2-10 years of age; Hispanic, as defined by the U.S. Census Bureau; not having diabetes, or any serious illnesses such as cancer or cognitive problems. A total of 150 mother-child dyads were recruited in the study, beginning from June 2015 and ending in September 2016. Of the 150 children 21 of a set of 21 pairs of siblings and 4 of two sets of three siblings were randomly eliminated from the analytic set. Two children with BMI < the 5th percentile, were also excluded from the analytic set because the study is interested in only normal, overweight and obese children. An additional five children had incomplete blood

pressure, anthropometric or socio-demographic data and were therefore excluded. The final analytic sample comprised 118 mother-child dyads.

Data Collection Methods

Mothers of potentially eligible children were approached by a trained research assistant about participating in the study. Informed consent was obtained from interested mothers in either Spanish or English Language and a child assent from children seven years and older in English language. The trained research assistant working with a pediatric nurse practitioner and a laboratory technician collected survey, anthropometric, blood pressure and laboratory data of children, but only survey data of mothers. Surveys were administered in English or Spanish language and the mother was the respondent.

Measurement of child body weight and height was based on standard protocol (Centres for Disease Control and Prevention, 2007). A standard scale which was tested and calibrated daily for accuracy was used to measure weight to the nearest 0.2 pounds. A stadiometer was used to measure height to the nearest one-eighth of an inch. Height and weight for mothers were self-reported. Auscultation with a stethoscope and a standard clinical mercury sphygmomanometer was used to measure child blood pressure. Mothers self-reported their height and weight in the parent questionnaire.

Outcome Measures

Child systolic and diastolic blood pressure percentiles were obtained from CDC blood pressure charts and categorized as: 1. normal blood pressure (systolic or diastolic blood pressure <90th percentile) and 2. elevated blood pressure (systolic or diastolic blood pressure ≥90th percentile) (Falkner et al., 2004). Child BMI percentiles were calculated using the 2000 CDC growth charts (CDC, Age-based Pediatric Growth Reference Charts, 2000). Participants were grouped as: 1. underweight (less than the 5th percentile), 2. Healthy weight (5th-84th percentiles), 3. Overweight (≥85th-94th percentiles), and 4. obese (≥95th percentile) (CDC, Age-based Pediatric Growth Reference Charts, 2000). Two children who were underweight were removed from the analytic sample because of the study's focus on normal weight and overweight children. The remaining three BMI categories were collapsed into two categories: 1. normal weight children (5th through 84th percentile) and 2. Overweight and obese children which included children with BMI from 85th percentile and above, for age and sex.

Child physical activity was assessed by the question: "during the past 7 days, on how many days was your child physically active for a total of at least 60 minutes per day? Add up all the time he/she spent in any kind of physical activity that increased his/her heart rate and made him/her breathe hard some of the time" (National Center for Health Statistics, 2013). The responses ranged from zero to 7 days. We preferred to categorize the number of days of children's PA in a week using recommended guidelines (U.S. Department of Health and Human Services, 2008), however, because

of the small sample size and distribution of responses, the variable was categorized as:
1. < 3 days of vigorous PA per week and 2. \geq 3 days of vigorous PA per week.

Child screen time (TV and video) was assessed by the question: "over the past 30 days, on average how many hours per day did your child sit and watch TV or videos" (National Center for Health Statistics, 2013). The responses ranged from zero to 8. Based on the American Academy of Pediatrics' recommendation, the variable was categorized as: 1. \leq 2 hours per day and 2. > 2 hours per day (American Academy of Pediatrics, 2010).

Sociodemographic Measures

Child age was computed as completed years from reported date of birth. Child sex was reported as either male or female. Age was categorized as: 1. 2-5 and 2. 6-10 years to reflect developmental, biological and social differences by age. Mothers reported their age in completed years. Educational attainment has been used as a proxy for socioeconomic status (Hendrie, Sohonpal, Lange, & Golley, 2013) because income levels increase with higher educational attainment. Mother's education was used as a proxy for mother's socioeconomic status and categorized as: 1. less than 9th grade 2. 9th-11th grade 3. High school graduate/GED or equivalent and 4. Some college, AA degree or above. Birth place of child was categorized as: 1. Tennessee, 2. elsewhere in the U.S outside Tennessee and 3. Outside the U.S. Hispanic origin of child was categorized as: 1. Mexican-American and 2. Other, including Puerto-Rican, Argentine, Columbian, Guatemalan, Argentine, Ecuadorian and El-Salvadorian.

Neighborhood Safety and Amenities Measures

Mother's perception of neighborhood safety combined responses to the following statements: 1. it is safe for children to play outside during the day and 2. It is safe to walk alone in this neighborhood (town or village) after dark (Statistics Canada, 2009b). Cronbach's alpha for each item on the scale in the Canadian National Longitudinal Survey of Children and Youth, September 2008 to July 2009 (Statistics Canada, 2009a) was greater than 0.7 for children 2-15 years old. The response categories to both questions were: 1. completely agree, 2. Agree, 3. Disagree and 4. Completely disagree. No respondent chose '4. Completely disagree'. Neighborhood safety¹ was computed as follows: 1. completely safe, if responses to both safety items were 1 (completely safe); 2. Safe, if responses were 1 and 2 or 2 and 2; and 3. Unsafe, if response to either safety question included 3.

Mothers rated their satisfaction with the neighborhoods in which their children live as a place to bring up children as follows: 1. Excellent, 2. Somewhat good, 3. Average, 4. Somewhat bad and 5. Very bad (Statistics Canada, 2009b). There were no responses for categories 4-5, Somewhat bad and Very bad. Because of the small number of responses in category 3, it was combined with category 2 to create two response categories: 1. Excellent and 2. Somewhat good or average.

Perceived availability of amenities in the neighborhood was assessed by the statement: there are enough parks, playgrounds and green spaces in your neighborhood (Statistics Canada, 2009b). Valid responses were: 1. Yes or 2. No.

Mother's BMI and Physical Activity

Mothers reported their own weight and height. Mother's BMI was calculated and categorized as: healthy ($18.5 \text{ kg/m}^2 \leq \text{BMI} \leq 24.9 \text{ kg/m}^2$) 2. Overweight ($25 \text{ kg/m}^2 \leq \text{BMI} \leq 29.9 \text{ kg/m}^2$) and 3. Obese ($\text{BMI} \geq 30 \text{ kg/m}^2$) (Centers for Disease Control and Prevention, 2015a).

Mother's physical activity was assessed by the question: in a typical week, do you do any moderate-intensity sports, fitness, or recreational activities which cause a small increase in breathing or heart rate such as brisk walking, bicycling, swimming, or golf for at least 10 minutes continuously? (National Center for Health Statistics, 2013). The responses were: 1. Yes or 2. No.

Statistical Analyses

Chi-squared and Fisher's exact tests were used to examine differences in the prevalence of elevated blood pressure and overweight by sociodemographic subgroups, and the relationship between mother's BMI status, physical activity, perceptions of the neighborhood and children's PA, blood pressure and BMI. Chi-squared and Fisher's exact tests were also used to examine bivariate association children's PA, blood pressure, BMI and TV watching. Univariate associations with an alpha less than 0.2 were adjusted for mother's education, age and marital status in multiple logistic regression models based with either child BMI category or blood pressure category as the dependent variable. Alpha less than 0.05 was set as the threshold for statistically

significant associations. Data analysis was performed in statistical analyst system (version 9.4, SAS Inc., Cary, NC, USA).

Results

The mean age of the children was 6.36 years ($SD=2.75$); about 6 out of 10 (61%) were 6-to-10-years-old; and half were girls (Table 2.1). Regarding Hispanic origin, about three quarters (76.3%) identified as Mexican-American; and nearly one-quarter remaining (23.7%) identified as other Hispanic origin (Puerto Rican, Guatemalan, Ecuadorian and Columbian). Most participants (89.8%) were born in the U.S (consisting of 69.5% born in Tennessee and 20.3% born in other states) (Table 2.1). The mean age of mothers was 32.7 years ($SD=5.69$) and 88.9% reported no education beyond high school or equivalent the equivalent of high school (not shown in tables).

About a third (31.4%) of children had elevated blood pressure, and about 4 out of 10 (40.7) were overweight. About a fifth (22.0%) of children watched TV or videos for two or more hours on a typical day, and about a third (31.0%) engaged in less than three days of sixty or more minutes of vigorous physical activity per week (Table 2.1).

Two-to-five-year-old children had 23.5% higher prevalence of elevated blood pressure compared to 6-to-10-year-olds (45.7% vs. 22.2%, $p=0.007$) (Table 2.1). Children whose mothers did not engage in moderate physical activity had 15.5% higher prevalence of elevated blood pressure (38.7% vs. 23.2%, $p=0.07$) (Table 2.2); and 14.5% higher prevalence of engaging in less than three days of at least 60 minutes of vigorous physical activity per week, (33.9% vs. 19.4%, $p=0.072$) (Table 2.2), than

children whose mothers engaged in moderate physical activity. Children whose mothers did not engage in moderate physical activity had 12.9 % higher prevalence of overweight than children whose mothers engaged in moderate physical activity, (46.8% vs. 33.9%, $p=0.08$) (Table 2.2).

Table 2.3 shows bivariate associations between children's physical activity, TV watching, blood pressure and BMI. Children's BMI and BP were associated ($p=0.046$) (Table 2.1).

In multiple logistic regression, children of obese mothers were 6.47 times more likely than children of mothers with normal BMI to engage in less than three days of at least 60 minutes of vigorous physical activity per week (95% *CI*: 1.61-26.0) (Table 2.4). Children whose mothers did not engage in moderate physical activity were 2.92 times more likely to engage in less than three days of at least 60 minutes of vigorous physical activity per week (*OR*: 2.92, *CI*: 1.18-7.24); and 2.5 times more likely to have elevated blood pressure (*OR*: 2.50, 95% *CI*: 1.02-4.53) than children whose mothers engaged in moderate PA (Table 2.4).

There was a trend for children from neighborhoods perceived as least safe to be more likely to engage in less than three days of at least 60 minutes of vigorous physical activity per week than their peers from neighborhoods perceived as most safe (*OR*: 2.93: 95% *CI*: 0.95-9.01); and for children whose mothers rated their neighborhoods less highly as places to bring up children to be more likely to be overweight or obese,

than children whose mothers rated their neighborhoods more highly as places to bring up children (*OR*: 2.07; 95% *CI*: 0.96-4.44) (Table 2.4)

Table 2.1. Sociodemographic characteristics of children by cardiometabolic risk factor (N=118) ^a

Characteristic	Total n (%)	Elevated BP n (%) p-value ^b	Overweight n (%) p-value ^b	>2hrs TV/day n (%) p-value ^b	<3 Days PA/Wk n (%) p-value ^b
Total sample, n(%)	118(100.0)	37(31.4)	48(40.7)	26(22)	31(26.3)
Sex, n(%)		0.17	0.45	0.66	0.83
Male	59(50.0)	22(37.3)	26(44.1)	14(23.7)	16(27.1)
Female	59(50.0)	15(25.4)	22(37.3)	12(20.3)	15(25.4)
Age group, n(%)		0.007	0.47	0.33	0.70
2-5 years	46(39.0)	21(45.7)	18(39.1)	8(17.4)	13(28.3)
6-10 years	72(61.0)	16(22.2)	30(41.7)	18(25)	18(25)
Parent's education, n(%)		0.95	0.93	0.10	0.27
<9th grade	53(44.9)	18(34.0)	23(43.4)	12(22.6)	14(26.4)
9-11th	20(16.9)	6(30.0)	7(35.0)	4(20)	2(10.0)
High school/GED	32(27.1)	9(28.1)	13(40.6)	4(12.5)	11(34.4)
>=Some college	13(11.0)	4(30.0)	5(38.5)	6(46.2)	4(30.8)
Hispanic Origin, n(%)		0.57	0.86	0.67	0.19
Mexican-American	90(76.3)	27(30.0)	37(41.1)	19(21.1)	21(23.3)
Other ^c	28(23.7)	10(35.7)	11(39.3)	7(25)	10(35.7)
Birth Place, n(%)		0.085	0.94	0.018	0.37
Tennessee	82(69.5)	31(37.8)	34(41.5)	13(15.9)	19(23.2)
Elsewhere in U.S.	24(20.3)	4(16.7)	9(37.5)	7(29.2)	7(29.2)
Outside U.S.	12(10.2)	2(16.7)	5(41.7)	6(50)	5(41.7)

^a Data from study of metabolic syndrome in Hispanic children, at a community health center in Johnson City, TN, 2015-2016

^b p-value from chi-squared or Fisher's exact test

Abbreviations: BP=Blood Pressure; >2hrs TV/day=greater than an average of 2 hours of watching TV or videos in the past 30 days; < 3Days PA/Wk=Less than 3 days of physical activity for at least 60 minutes per day in the past 7 days

^c Other Hispanic origin (Puerto-Rican, Argentine, Columbian, Guatemalan, Argentine, Ecuadorian and El-Salvadorian)

Table 2.2. Association between maternal neighborhood perception, BMI, physical activity and children's cardiometabolic risk (N=118) ^a

Characteristic	n(%) of Total	Elevated BP n(%)	p-value ^b	Overweight n(%)	p-value ^b	>2hrs TV/day n(%)	p-value ^b	<3 Days PA/Wk n(%)	p-value ^b
Neighborhood rating, n(%)			0.46		0.052		0.845		0.213
Excellent	57(48.3)	16(28.1)		18(31.6)		13(22.8)		12(21.1)	
Somewhat good/average	61(51.7)	21(34.4)		30(49.2)		13(21.3)		19(31.1)	
Neighborhood safety ^c , n(%)			0.73	19(39.6)	0.98		0.73		0.179
Completely agree	48(40.7)	17(35.4)		17(41.5)		12(25.0)		9(18.8)	
Agree	41(34.7)	12(29.3)		12(41.4)		9(22.0)		11(26.8)	
Disagree	29(24.6)	8(27.6)				5(17.2)		11(37.9)	
Moderate PA by mother, n(%)			0.07		0.08		0.551		0.072
Yes	62(52.5)	13(23.2)		19(33.9)		11(19.6)		12(19.4)	
No	56(47.5)	24(38.7)		29(46.8)		15(24.2)		19(33.9)	
Mother's BMI, n(%)			0.15		0.25		0.31		0.003
Normal	25(21.2)	10(40.0)		9(36.0)		7(28.0)		3(12.0)	
Overweight	47(39.8)	10(21.3)		16(34.0)		7(14.9)		8(17.0)	
Obese	46(39.0)	17(37.0)		23(50.0)		12(26.1)		20(43.5)	
Enough PA amenities ^d , n(%)			0.88		0.20		0.23		0.916
Yes	106(89.8)	33(31.1)		41(38.7)		25(23.6)		28(26.4)	
No	12(10.2)	4(33.3)		7(58.3)		1(8.3)		3(25.0)	

^a Data from study of metabolic syndrome in Hispanic children at a community health center in Johnson City, TN, 2015-2016

^b p-value from chi-squared or Fisher's exact test

Abbreviations: BP=Blood Pressure; >2hrs TV/day=Greater than an average of 2 hours of watching TV or videos in the past 30 days; < 3Days PA/Wk =Less than 3 days of physical activity for at least 60 minutes per day in the past 7 days

^c Neighborhood safety combined responses to: 1. it is safe for children to play outside during the day and 2. It is safe to walk alone in this neighborhood (town or village) after dark.

^d There are enough parks, playgrounds and green spaces in your neighborhood

^e empty cell (zero)

Table 2.3. Bivariate associations between children’s physical activity, TV watching, blood pressure and BMI categories (N=118) ^a

Characteristic	Elevated BP	Overweight	>2 Hrs TV/day	<3 Days PA/WK
	n(%)	n(%)	n(%)	n(%)
			p-value	p-value
				p-value
Characteristic				
Blood pressure				0.30
Normal	//	//	//	19(23.5)
Elevated	//	//	//	12(32.4)
Child BMI	0.046			0.87
Normal	17(24.3)	//	//	18(25.7)
Overweight	20(41.7)	//	//	13(27.1)
TV watching	0.17	0.85	0.93	
> 2 hours	26(28.3)	11(42.3)	7(22.6)	//
< 2 hours	11(42.3)	37(40.2)	19(21.8)	//

^a Data from study of metabolic syndrome in Hispanic children at a community health center in Johnson City, TN, 2015-2016
 //: Bivariate association is either not of interest or already test on a different row in this same table

Table 2.4. Odds ratios and 95% confidence intervals for maternal neighborhood perception, BMI and physical activity and overweight and elevated blood pressure in children (N=118) ^a

	<3 days of PA/WK OR (95% CI) ^b	Overweight or Obese OR (95% CI) ^b	Elevated BP OR (95% CI) ^c
Age group			
2-5 vs 6-10 years	0.24(0.04-1.33)	0.90(0.40-2.02)	4.45(1.68-11.78)
Mal vs Female			
	0.70(0.27-1.84)	1.32(0.61-2.87)	2.06(0.82-5.21)
Education			
< 9 th grade (ref)			
9-11 th grade	0.24(0.04-1.33)	0.74(0.24-2.25)	0.75(0.21-2.68)
High school/GED	2.44(0.77-7.79)	0.83(0.33-2.13)	0.548(0.17-1.68)
>= Some college	1.02(0.21-5.01)	0.83(0.223-1.13)	1.14(0.25-5.20)
Neighborhood safety			
completely agree(ref)			
agree	1.55(0.54-4.37)	na	na
disagree	2.93(0.95-9.01)	na	na
Moderate PA by mother			
yes(ref)			
No	2.92(1.18-7.24) **	1.77(0.82-3.83)	2.50(1.02-4.53) **
Mother's BMI			
Normal(ref)			
Overweight	1.20(0.28-5.27)	na	0.41(0.13-1.27)
Obese	6.47(1.61-26.0) ***	na	0.70(0.24-2.02)
Neighborhood Rating			
excellent(ref)			
somewhat good/average	na	2.07(0.96-4.44)	na

^a Data from study of metabolic syndrome in Hispanic children at a community health center in Johnson City, TN, 2015-2016

^b adjusted for mother's education, child's age, sex,

^c Adjusted for mother's education, child's sex, age, BMI, and TV watching

Abbreviations: BP=Blood Pressure; >2hrs TV/day=Greater than an average of 2 hours of watching TV or videos in the past 30 days; < 3Days PA/Wk=Less than 3 days of physical activity for at least 60 minutes per day in the past 7 days; na=not tested in multiple logistic regression because alpha of univariate association between variables was >= 0.2

** p-value < 0.05, *** p-value < 0.01

Discussion

In this study of socio-demographic correlates of cardiometabolic risk in pre-adolescent Hispanic children of mostly Mexican-American origin, we found that about 4 out of every 10 children were overweight or obese (40.7%), and about three out of every ten had elevated blood pressure (31.4%). Two-to-five-year-old children had significantly higher prevalence of elevated blood pressure than 6-to-10-year-olds.

The prevalence of overweight in 2-to-5-year-olds (39.1%) in this study is 9.3% higher than overweight estimates for 2-to-5-year-old Hispanic children in the National Health and Nutrition Examination Survey (NHANES), 2011-2012 (Ogden et al., 2014); In contrast, the prevalence of overweight in 6-to-10-year-olds (41.7%) is similar to estimates for 6-to-11-year-old Hispanic children (46.2%) in NHANES 2011-2012 (Ogden et al., 2014).

Estimates of the prevalence of elevated blood pressure in children are few: in a large cohort study of 3-to-18-year-old children presenting for well-child care, Hansen, Gunn and Kaelbar (2007) determined the prevalence of elevated blood pressure to be 7.0%; a study by Ma, Zhang and Xi (2016) using NHANES 2013-2014 data reported the prevalence of elevated blood pressure in 8-to-17-year-olds to be 7.0%; and Kit et al. (2015) also using NHANES data estimated the prevalence of elevated blood pressure in 8-to-17-year-old children to be 11.0% in 2011-2012. The prevalence of elevated blood pressure in this study exceeds estimates from these previous studies. Overweight is a risk factor for elevated blood pressure (Ewald & Haldeman, 2016). The higher prevalence of overweight in the sample compared to national estimates could therefore partly explain the high prevalence of elevated blood pressure. Another explanation is

the low socioeconomic status of participants: about 85% of mothers reported a household income less than the 2017 federal poverty level for a household of four (\$24,600); and 89% of mothers had only a high school education or less. Low socioeconomic status is associated with significantly higher obesity and hypertension (Brummett et al., 2011; Van Den Berg et al., 2013).

This study also found that children of obese mothers were 6.47 times more likely than children of mothers with normal BMI to engage in less than three days of at least 60 minutes of vigorous physical activity per week; and children whose mothers did not engage in moderate PA were 2.92 times more likely to engage in less than three days of at least sixty minutes of vigorous physical activity than children whose mothers engaged in moderate PA. Our findings comport with previous studies which have found strong mother-child correlations in physical activity and a strong association between maternal obesity and child physical activity. In a study of 3-to-5-year-old Hispanic children and their mothers at a local community center in Nashville, TN, Ruiz, Gessel, Buchowski, Lambert and Barkin (2011) observed strong mother-child correlation in sedentary behavior and moderate physical activity; Fuemmeler, Anderson and Masse (2011) found a high correlation of moderate-to-vigorous physical activity (MVPA) between mothers and their children. Rosendranz and Dzewaltowski (2011) found that mother-child shared physical activity was negatively associated with child BMI percentile, and that maternal BMI was positively correlated with child BMI. The same study evaluated the effects of physical activity-related-parenting behaviors (PARPBs) such as encouragement, transporting the child for physical activity and watching the

child do physical activity. Of all PARPB, PA encouragement had the strongest correlation with child PA.

We found that children whose mothers did not engage in moderate PA were 2.5 times more likely to have elevated blood pressure than children whose mothers engaged in moderate PA. Physical inactivity and overweight are risk factors for elevated blood pressure in children (Ewald & Haldeman, 2016; Gopinath, Hardy, Kifley, Baur, & Mitchell, 2014; Leary et al., 2008). However, after controlling for child physical activity, and body mass index, children whose mothers did not engage in moderate physical activity remained significantly more likely to have elevated blood pressure than children whose mothers engaged in moderate physical activity. To the best of our knowledge, this is the first study to report a significant association between maternal physical activity and child blood pressure in pre-adolescent Hispanic children, independent of child's BMI and physical activity.

We did not find significant associations between mother's perception of neighborhood safety, and mother's rating of the neighborhood as a place to bring up children and children's physical activity, blood pressure or BMI; however, there was a trend with children from neighborhoods perceived as least safe being more likely to engage in less than three days of at least sixty minutes of vigorous physical activity per week than their peers from neighborhoods perceived as most safe; and children whose parents rated their neighborhoods less highly as places to bring up children more likely to be overweight or obese, than children whose mothers rated their neighborhoods more highly as places to bring up children. Previous studies have examined the association between mothers perceived neighborhood safety, neighborhood amenities

and their children's physical activity and body mass index, with mixed results. In a large multi-ethnic study of 2-to-8-year-old children in Durham, North Carolina, Miranda et al. (2012) found that higher levels of neighborhood crime and nuisance were associated with significantly higher risk of overweight in children; likewise, Singh et al. (2010) found that children living in neighborhoods which were unsafe and had no PA amenities had 20%-60% higher odds of being obese than their peers from more favorable neighborhoods; and Datar and colleagues Datar, Nicosia and Shier (2013) in their study found that more TV watching and less physical activity in children whose parents perceived their neighborhoods as less safe. In contrast, in a cross-sectional survey of more than 3,000 children in 20 large U.S cities, maternal perception of neighborhood safety was not found to be associated with their children's outdoor play time or risk for obesity (Burdette & Whitaker, 2005); and in the study by Datar et al. (2013) maternal perception of neighborhood safety was not associated with their children's obesity risk for obesity. In this study, we found a trend, with children from neighborhoods perceived as least safe being more likely to engage in less than three days of at least sixty minutes of vigorous physical activity per week than their peers from neighborhoods perceived as most safe. The finding of only a trend, is likely due to the small sample size of the study.

This study has some limitations. The sample size was small and we may therefore have missed significant associations. Second, being a convenient cross-sectional study of predominantly Mexican-Americans, our findings may not be generalizable to all Hispanic children and do not indicate causality. Third, our inability to control for diet may potentially confound our findings. However, these weaknesses

should be weighed against the strengths of this study. To the best of our knowledge, this is the first study which has assessed the prevalence and sociodemographic correlates of elevated blood pressure in pre-adolescent Hispanic children in Tennessee.

The prevalence of overweight and elevated blood pressure in the sample, especially in 2-to-5-year-olds were higher than expected and thus very concerning. Low maternal physical activity was associated with elevated blood pressure and lower physical activity in children; likewise, maternal obesity was associated with lower physical activity in children. Our findings suggest that public health interventions which encourage maternal modelling of physical activity and weight control could be important in preventing obesity and hypertension in Hispanic children.

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CHAPTER 3

FOOD GROUP INTAKE AND CARDIOMETABOLIC RISK IN HISPANIC CHILDREN

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Abstract

Background: Adequate intake of vegetables, fruits, legumes, fiber, wholegrains and dairy is protective against obesity, hypertension and dyslipidemia; however, U.S children do not meet recommendations for these food groups. The objectives of this study were to assess intake of these food groups and to examine their association with cardiometabolic risk factors in Hispanic children.

Methods: Data ($n=116$) came from a cross-sectional pilot study of metabolic syndrome in Hispanic children receiving well-child care at a community health center in Johnson City, TN. The last week version of the Block Kids Food Screener (BKFS) was used to collect children's food intake in the past week. Children's blood pressure, height, weight and lipids were measured. Binomial test of proportions was used to compare sample and Nation Health and Nutrition Examination Survey (NHANES) gender-age group proportions not meeting food group recommendations. Multiple logistic regression was used to examine the association between food group intake and cardiometabolic risk.

Results: The mean age of child participants was 6.25 years ($SD=2.79$). Intake of fruits and legumes in all gender-age groups of sample children exceeded the minimum recommendations. Significantly higher proportions of all gender-age groups (except 9-to-10-year-old girls) met legume recommendations; significantly higher proportion of 4-to-10-year-old girls met fiber and fruit recommendations; significantly higher proportion of 4-to-8-year-old boys met fiber recommendations, compared to corresponding NHANES gender-age group proportions. Apart from these differences, the sample proportions meeting vegetables, wholegrains, and fiber and dairy recommendations were not different from corresponding NHANES gender-age proportions. Children with

elevated blood pressure had less intake of fruits, vegetables, and legumes than children with normal blood pressure. Legume intake (*OR*: 0.052, 95% *CI*: 0.04-0.64), dairy intake (*OR*: 0.61, 95% *CI*: 0.37-0.99) and fiber intake (*OR*: 0.88, 95% *CI*: 0.81-0.96) were protective against elevated blood pressure, but only fruit intake was protective against overweight (*OR*: 0.93, 95% *CI*: 0.87-0.99).

Conclusions: The overall sample generally under-consumed vegetables, wholegrains, dairy and fiber, with at-risk-children consuming even less. The study confirmed the protective effects of under-consumed food-groups. This suggests that increasing the consumption of these food groups could reduce cardiometabolic risk in Hispanic children.

Keywords: food groups; recommendation; elevated blood pressure; overweight; Hispanic children

Introduction

Hispanic children experience higher prevalence of obesity and insulin resistance (Falkner & Cossrow, 2014); early age onset obesity (Mozaffarian et al., 2016); severe obesity (Skinner & Skelton, 2014); low high density lipoprotein (HDL-C); and hypertension (Nguyen et al., 2015) compared to their non-Hispanic White peers.

A diet which is rich in a variety of nutrient dense foods including vegetables, fruits, grains, fat-free or low-fat dairy, proteins and oils, but limited in sodium, added sugar, saturated fat and cholesterol can improve children's cardiometabolic health (U.S. Department of Agriculture, 2015).

The U.S. Department of Agriculture (2015) in its 2015-2020 Dietary Guidelines for Americans (DGA) reported that U.S children fall short of recommendations for fruits, vegetables, dairy, wholegrains, legumes and fiber intake, but overconsume solid fats, refined grains, added sugar, and salt. The U.S Department of Agriculture recommends an increase in children's fruit, vegetables, dairy, wholegrain, legume and fiber intake, and a decrease in their intake of solid fat, added sugar and salt, to align with healthy eating patterns. The proportions of U.S children, by gender-age groups, who meet recommendations for the above under-consumed food groups is generally below 50% (National Cancer Institute, 2015). The proportions meeting vegetable, wholegrain and fiber consumption are the lowest (generally < 5%) of all the above under-consumed food groups (National Cancer Institute, 2015).

Extensive studies among multi-ethnic and Caucasian children provide evidence that a diet with reduced saturated fatty acids and trans-fat, high mono-unsaturated fatty

acids (MUFA) and poly-unsaturated fatty acids (PUFA) (Farvid et al., 2014), but rich in legumes, nuts, fish, whole grain, fruits and vegetables (Afshin et al., 2014), is associated with a superior lipid profile, healthier blood pressure, body mass index and lower incidence of cardiometabolic disease (Dauchet et al., 2006). However, there are limited studies which characterize food group intake and the relationship of food intake with cardiometabolic risk in Hispanic children (Kong et al., 2013; Nielsen, Rossen, Harris, & Odgen, 2014; Salvo, Frediani, Ziegler, & Cole, 2012). Because Hispanics have a unique culture, it is reasonable to expect unique eating patterns which could explain the high prevalence of cardiometabolic risk in this population. Among 2-to-5-year-old Hispanic children participating in the Special Supplemental Nutrition Program for Women, Infants and Children (WIC), the proportion who met the recommended intake for vegetables, fruits, dairy and whole grains ranged from 21.3% for whole grains to 66.3% for fruits population (Kong et al., 2013). Salvo, Frediani, Ziegler and Cole (2012) found that Hispanic children, aged 2.84 years (SD=1.12) consumed significantly more whole fruits and dairy, but a lower proportion of grains than their African-American peers.

Age, sex, and risk status are associated with dietary intake in children (Loprinzi & Davis, 2016; Nielsen et al., 2014). Generally, 2-to-5-year-old children consume more fruits than adolescents (Salvo et al., 2012). Boys eat more protein, unprocessed red meats, sugar-sweetened beverage and salt than females. As children grow, average consumption of unprocessed meat, and sugar sweetened beverages increases (Rehm et al., 2016). Compared to normal weight children, obese children have higher daily caloric intake (Butte, Puyau, Adolph, Vohra, & Zakeri, 2007).

Uncontrolled cardiometabolic risk in childhood can lead to diseases with high morbidity and cost, such as heart disease, stroke and diabetes (Mozaffarian et al., 2016) in adulthood. Because Hispanics are the largest minority and fastest growing ethnic group in the U.S (Murphey et al., 2014), the high prevalence of cardiometabolic risk in Hispanic children is an important public health issue. This study sought to characterize food intake among Hispanic children and to examine the association between food group intake and cardiometabolic risk. Findings are expected to help guide future lifestyle related interventions and policies directed at improving cardiometabolic health in Hispanic children.

Methods

Data Source and Participants

Data for this project came from a cross-sectional study of metabolic syndrome in 150 Hispanic children, ages 2-10 years at a community health center, from June 2015 to September 2016. The study was conducted by an interdisciplinary group of researchers from East Tennessee State University. Funding was provided by the Tennessee Board of Regents. The study was reviewed and approved by the Institutional Review Board at East Tennessee State University. Participants were mothers and their children who came to the community health center for a well-child visit. Inclusion criteria for children included: being 2-10 years of age: Hispanic, as defined by the U.S. Census Bureau; not having diabetes, or any serious illnesses such as cancer or cognitive problems.

Data Collection Methods

Mothers of potentially eligible children were approached by a trained research assistant about participating in the study. Informed consent was obtained from interested mothers in either Spanish or English Language and a child assent from children seven years and older. The trained research assistant working with a pediatric nurse practitioner and a laboratory technician collected survey, anthropometric, blood pressure and laboratory data of children, but only survey data of mothers. Surveys were administered in English or Spanish language and the mother was the respondent.

The last week version of the Block Kids Food Screener (BKFS) (Hunsberger, O'Malley, Block, & Norris, 2015) was used to collect child food intake data over the past week. Two sets of questions in the BKFS assessed children's intake of various food groups in the past week: 1. *how many days last week did your child eat or drink a food type?* And 2. *How much in one day?*

Measurement of child body weight and height was based on standard protocol (Centres for Disease Control and Prevention, 2007). A standard scale which was tested and calibrated daily for accuracy was used to measure weight to the nearest 0.2 pounds. A stadiometer was used to measure height to the nearest one-eighth of an inch. Auscultation with a stethoscope and a standard clinical mercury sphygmomanometer was used to measure child blood pressure.

Four milliliters (4mls) of blood was drawn from the ante-cubital fossa of each child into a serum separator tube (SST). The samples were then stored at -80°C and later analyzed for HDL-C and triglycerides.

Outcome Measures

Child systolic and diastolic blood pressure percentiles were obtained from CDC blood pressure charts and categorized as: 1. normal blood pressure (systolic or diastolic blood pressure < 90th percentile) and 2. Elevated blood pressure (systolic or diastolic blood pressure \geq 90th percentile) (Falkner et al., 2004). Child BMI percentiles were calculated using the 2000 CDC growth chart (CDC, Age-based Pediatric Growth Reference Charts, 2000). Participants were categorized as: 1. underweight (less than 5th percentile), 2. Healthy weight (5th -84th percentiles), 3. Overweight (\geq 85th -94th percentiles), and 4. obese (\geq 95th percentile) (Centers for Disease Control and Prevention, 2000). Two children who were underweight were removed from the analytic sample because of our focus on normal weight and overweight children. The remaining three BMI categories were collapsed into two categories: 1. normal weight (5th through 84th percentile) and 2. Overweight children (BMI from 85th percentile and above, for age and sex). The Lipid Research Clinics Program Prevalence Study results (Daniels & Greer, 2008a) was used to categorize child HDL-C and triglyceride levels: 1. normal triglyceride (< 95th percentile of triglycerides for age and sex) and 2. Elevated triglyceride levels (\geq 95th percentile of triglyceride for age and sex). HDL-C was categorized as: 1. normal HDL-C (> 5th percentile of HDL-C) and 2. Low HDL-C (\leq 5th percentile of HDL-C).

Food Measures

Completed food screeners (BKFS) were processed by Nutrition Quest LLC into quantitative food measures including: 1. total daily fruit intake in cup equivalents (CE),

2. Total daily vegetable intake excluding potatoes and legumes (CE), 3. Total daily whole grain intake in ounce equivalents (OZE), 4. Total daily fiber intake in grams, 5. Total daily dairy intake (CE), 6. Total daily legume intake (CE).

Food group data was used as either a continuous variable or categorized as: 1. Meeting recommendations or 2. Not meeting recommendations, by comparing mean daily intake of food groups with corresponding gender-age group DGA recommendations. Table 3.1 shows DGA food group intake recommendations for gender-age groups.

Table 3.1. Daily food group intake recommendations by gender-age group for children ^a

	Gender-Age Groups					
	Male			Female		
	1-3 years	4-8 years	9-10 years	1-3 years	4-8 years	9-10 years
Food Group						
Fruits(CE)	>=1	>=1	>=1.5	>=1	>=1	>=1.5
Vegetables(CE)	>=1	>=1.5	>=2	>=1	>=1.5	>=1.5
Dairy(CE)	>=2	>=2.5	>=2.75	>=2	>=2.5	>=2.75
Wholegrain(OZE)	>=1.5	>=2	>=2.5	>=1.5	>=2	>=2.5
Legumes(CE)	>=0.054	>=0.054	>=0.14	>=0.054	>=0.054	>=0.054
Fiber(grams)	>=14	>=19.6	>=25.2	>=14	>=16.8	>=22.4

Abbreviations: CE=cup equivalents; OZE=ounce equivalents
^aReferences from Dietary Guidelines for Americans, 2015-2020

Sociodemographic Measures

Child age was computed as completed years from reported date of birth and the date the child was recruited. Child sex was reported as either male or female. Child age was categorized as: 2-4 years, 5-7 years and 8-10 years, to reflect developmental, biological and social differences in children. Educational attainment has been used as a proxy for socioeconomic status (Hendrie et al., 2013) because income levels increase with higher educational attainment. Mother's education was used as a proxy for mother's socioeconomic status and categorized as: 1. Less than 9th grade 2. 9th – 11th grade 3. High school graduate/GED or equivalent and 4. Some college, AA degree or above.

Statistical Analyses

Binomial test of proportions was used to compare sample and NHANES gender-age group proportions not meeting recommendations. Independent samples *t*-test was used to assess mean differences in daily food group intake by risk category (HDL-category, triglyceride category, BMI-category and BP-category). Univariate, and then multiple logistic regression were used to examine the relationship between food group intake and cardiometabolic risk, adjusting for maternal education, and child age and sex. An alpha threshold of 0.2 was used to select food groups from bivariate analysis for multiple logistic regression analysis. All tests were two-sided; an alpha level of 0.05 was applied as the threshold for significance. All analysis was done in statistical analyst system (version 9.4, SAS Inc., Cary, NC, USA).

Results

Of 150 Hispanic children participants, 21 of a set of 21 pairs of siblings and 4 of a set of two sets of three siblings were randomly eliminated from the analytic set. Two children with BMI < 5th percentile, were also excluded from the analytic set because of the study's focus on children who had normal BMI or were overweight. An additional seven children did not have data for body mass index and blood pressure and 24 children did not have lipid data. The final analytic set comprised 116 children with complete dietary, BMI and blood pressure data and a sub-analytic set of 99 children with complete dietary, BMI, blood pressure and lipid data. Demographic characteristics of the two samples are similar and summarized in Table 3.2. In the larger sample ($N=116$), the mean age was 6.25 years ($SD=2.79$), girls formed half (50%) the sample and 46.6% of mothers of children in the larger sample ($n=116$) had less than 9th grade education.

Mean daily intake of fruits and legumes for all sample gender-age groups exceeded minimum recommendations (Table 3.3 and Table 3.4). Sample daily intake of fruits ranged from mean \pm SD=1.80 \pm 0.78 CE in 2-to-3-year-old boys to 2.61 \pm 1.11 CE in 9-10-year-old girls (Table 3.3); daily intake of legumes ranged from mean \pm SD=0.13 \pm 0.09 CE in two-to-three-year-old boys to 0.31 \pm 0.34 CE in 9-to-10-year-old girls (Table 3.4). However, mean daily intake of vegetables (without potato), wholegrains, fiber and dairy were below the minimum recommendations for all sample gender-age groups (except for dairy intake among 2-to-3-year-olds) (Table 3.3 and Table 3.4). Mean daily intake of vegetables ranged from mean \pm SD=0.26 \pm 0.17 CE in 2-to-3-year-old boys to 0.89 \pm 0.61 CE in 9-to-10-year-old girls (Table 3.3); mean daily

intake of dairy ranged from mean \pm SD=1.54 \pm 0.92 in 2-to-3-year-old boys to 2.43 \pm 0.87 in 4-to-8-year-old boys (Table 3.3); mean daily intake of wholegrains ranged from mean \pm SD=0.24 \pm 0.15 OZE in 2-to-3-year-old boys to 0.85 \pm 0.15 OZE in 9-to-10-year-old girls (Table 3.4); and mean daily intake of fiber ranged from 11.0-23.0 grams (Table 3.4).

Mean daily food group intake were similar for boys and girls, except for fruit intake: a higher proportion of boys did not meet recommendations for fruit intake than girls (31.0% for boys vs 15.5% for girls, $p=0.048$) (Table 3.3); however, no significant gender difference was found for other food groups.

Two-to-three-year-old boys had the least daily food intake of all gender-age groups. The proportion of children not meeting recommended daily food intake levels, ranged from 23.3% for fruits to 98.3% for wholegrains (31.9% for legumes; 62.3% for dairy; 81.9% for fiber; and 92.2% for vegetables (not shown in table 3.3 and table 3.4).

A significantly higher proportion of the sample (except 9-to-10-year-old girls) met legume recommendations (Table 3.4); a significantly higher proportion of 4-to-8-year-old (17.9%) and 8-10-year-old (31.2%) girls met fruit and fiber recommendations; and a significantly higher proportion of 4-to-8-year-old boys met fiber recommendations, compared with corresponding gender-age group proportions in NHANES (Table 3.4). Apart from these differences, the sample's gender-age group proportions that did not meet recommendations for vegetables, wholegrains, fiber and dairy were in general as low as for the nation (Table 3.3 and Table 3.4).

About thirty four percent (33.6%) of the sample had elevated blood pressure (prehypertension/hypertension); 42.2% were overweight; 17.2% had low HDL-C; and 52.5% had hypertriglyceridemia (Table 3.5).

Children with elevated blood pressure had significantly less daily intake of fruits (mean±SD=1.73±0.90 vs 2.17±1.2; p=0.039); vegetables (mean±SD=0.50±0.37 vs 0.77±0.59; p=0.0030); dairy (mean±SD=1.93±0.80 vs 2.26±0.91; p=0.049); fiber (mean±SD=10.17±5.28 vs 15.18±8.03; p<0.000); and legumes (mean±SD=0.14±0.19 vs 0.26±0.27; p=0.0070), than children with normal blood pressure (Table 3.5).

Overweight children had significantly less fruit (mean±SD=1.74±1.02 vs 2.23±1.13; p=0.039) and fiber (mean±SD=11.55±6.65 vs 14.92±7.94; p=0.0010) intake than children with normal weight (Table 3.5).

In the univariate logistic regression analysis, higher fruit, vegetable, legume and fiber intake were protective against elevated blood pressure (Table 3.6); however, after adjusting for socio-demographic variables, only legume intake (OR: 0.052, 95% CI: 0.004 to 0.64; p=0.021), dairy intake (OR: 0.61; 95% CI: 0.37-0.99; p=0.045) and fiber intake (OR: 0.88; 95% CI: 0.81-0.96; p=0.003) were significantly protective against elevated blood pressure (Table 3.6). Similarly, fruit and fiber intake were protective against overweight in univariate analysis, but after adjusting for socio-demographic factors, only fiber intake (OR: 0.93; 95% CI: 0.87-0.99; p=0.018) was significantly protective against overweight (Table 3.6). There were no significant associations between fruit intake and dyslipidemia (Table 3.7).

Table 3.2. Children's sociodemographic characteristics and food intake (N=116) ^a

Characteristic	Large sample (N=116)	Small sample (N=99)	p-value
Age, mean(SD)	6.25(2.79)	6.35(2.76)	0.98 ^b
Age Group, n(%)			0.97 ^c
2-4 years	40(34.5)	33(33.3)	
5-7 years	26(22.4)	21(21.2)	
8-10 years	50(43.1)	45(45.5)	
Sex, n (%)			0.95 ^c
Female	58(50)	49(49.5)	
Male	58(50)	50(50.5)	
Parent's Education, n(%)			0.96 ^c
<9th grade	54(46.6)	45(45.5)	
9th-11th grade	17(14.7)	17(17.2)	
High school grad/GED	34(29.3)	28(28.3)	
>=Some college/AA	11(9.5)	9(9.1)	
Food Group, Mean(SD)			
Fruit(CE)	2.02(1.10)	2.05(1.11)	0.99 ^b
Vegetables no potato(CE)	0.68(0.54)	0.69(0.57)	1.00 ^b
Legumes(CE)	0.22(0.25)	0.22(0.26)	1.00 ^b
Wholegrain(OZE)	0.59(0.53)	0.57(0.51)	1.00 ^b
Dairy(CE)	2.15(0.88)	2.16(0.87)	1.00 ^b
Fiber(g)	13.49(7.58)	13.65(7.83)	.0.99 ^b

^a Data from study of metabolic syndrome in Hispanic children at a community health center in Johnson City, TN, 2015-2016

^b P-values from independent two sample t-test

^c P-values from chi-squared test

Table 3.3. Mean intake and proportion of children not meeting recommended daily fruit, vegetable and dairy intake compared with national proportions (NHANES, 2007 — 2010) by gender-age group (N=116) ^a

	Gender-Age Groups								M v F ^b
	Male (n=58)				Female (n=58)				
	2-3yrs	4-8yrs	9-10yrs	Total	2-3yrs	4-8yrs	9-10yrs	Total	
Food Group									
Fruits(CE)									
Mean(SD)	1.80(0.78)	1.90(1.03)	2.06(1.57)		2.07(1.03)	1.87(0.96)	2.61(1.11)	2.12(1.05)	0.18
RDI ^a (CE)	>=1	>=1	>=1.5		>=1	>=1	>=1.5		
Sample, n(%) not meet	1(9.1)	7(23.3)	10(58.8)	18(31.0)	2(14.3)	5(17.9)	2(12.5)	9(15.5)	0.048
National % not meet	23.9	39.6	75.6		25	41.5	75.5		
P-value ^c	ns		ns		ns	**	***		
Vegetables(CE)									
Mean(SD)	0.26(0.17)	0.71(0.46)	0.81(0.69)		0.49(0.34)	0.70(0.57)	0.89(0.61)		
RDI(CE)	>=1	>=1.5	>=2		>=1	>=1.5	>=1.5		
Sample, n(%) not meet	11(100)	28(93.3)	16(94.1)	55(94.8)	13(92.9)	25(89.3)	14(87.5)	52(89.7)	0.49
National % not meet	85	94.5	98.4		85.2	94.8	83.8		
P-value ^c	ns	ns	ns		ns	ns	ns		
Dairy(CE)									
Mean(SD)	1.54(0.92)	2.43(0.87)	1.98(0.92)		2.29(0.81)	2.01(0.85)	2.33(0.81)		
RDI(CE)	>=2	>=2.5	>=2.75		>=2	>=2.5	>=2.75		
Sample, n(%) not meet	7(63.6)	16(53.3)	12(70.6)	35(60.3)	6(42.9)	20(71.4)	11(68.8)	37(63.8)	0.7
National % not meet	34	65.5	72		37.8	70.2	75		
P-value ^c		ns	ns		ns	ns	ns		

** p-value < 0.05, *** p-value < 0.001, ns p-value > 0.05

^a Data from study of metabolic syndrome in Hispanic children at a community health center in Johnson City, TN, 2015-2016

Abbreviations: RDI = Recommended daily intake; ns=not significant; Not meet= Not meeting recommendations for food intake

^b P-value from chi-squared test of number of girls versus boys who did not meet RDI; and independent samples t-test of mean food group intake by girls and boys

^c P-values from Binomial test proportions of sample gender-age-group that did not meet RDI versus NHANES (2007-2010) gender-age-group that did not meet RDI

Table 3.4. Mean intake and proportion of children not meeting recommended daily wholegrain, legume and fiber intake compared with national proportions (NHANES, 2007 — 2010) by gender-age group (N=116) ^a

	Gender-Age Groups								M v F ^b
	Male (n=58)				Female (n=58)				
	2-3yrs	4-8yrs	9-10yrs	Total	2-3yrs	4-8yrs	9-10yrs	Total	
Food Group									
Wholegrain(OZE)									
Mean(SD)	0.24(0.15)	0.69(0.46)	0.50(0.43)		0.34(0.28)	0.64(0.52)	0.85(0.15)		
RDA (OZE)	>=1.5	>=2	>=2.5		>=1.5	>=2	>=2.5		
Sample n(%) not meet ^c	11(100)	30(100)	17(100)	58(100)	14(100)	27(96.4)	15(93.8)	56(96.6)	0.5
National % not meet	97.7	99	99.3		99.1	99.7	99.5		
P-value	ns	ns	ns		ns	Ns	ns		
Legumes(CE)									
Mean(SD)	0.13(0.09)	0.22(0.21)	0.31(0.34)		0.19(0.29)	0.20(0.23)	0.22(0.26)		
RDA(CE)	>=0.054	>=0.054	>=0.14		>=0.054	>=0.054	>=0.054		
Sample, n(%) not meet	3(27.3)	9(30.0)	9(52.9)	21(36.2)	4(28.6)	5(17.9)	7(43.8)	16(27.6)	0.32
National % not meet	74.4	73.2	86.6		78.2	76.7	68.6		
P-value	***	***	****		***	***			
Fiber(grams)									
Mean(SD)	8.35(1.96)	14.53(6.51)	15.00(10.74)		9.71(4.66)	13.66(7.12)	16.51(8.70)		
AI	>=14	>=19.6	>=25.2		>=14	>=16.8	>=22.4		
Sample, n(%) not meet	11(100)	23(76.7)	15(88.2)	49(84.5)	12(85.7)	23(82.1)	11(68.8)	46(79.3)	0.47
National % not meet	97	97	97		97	97	97		
P-value	ns	***	ns		ns	***	***		

* P-value < 0.1, ** p-value < 0.05, *** p-value < 0.001, ns p-value > 0.1

^aData from study of metabolic syndrome in Hispanic children at a community health center in Johnson City, TN, 2015-2016

P-values from Binomial test of sample gender-age-group proportions that did not meet RDI/AI versus NHANES (2007-2010) gender-age-group proportions that did not meet RDI/AI

^b Not meeting recommended intake

^cP from chi-square test of number of girls versus boys who did not meet RDI/AI

Abbreviations: Sample (n, %) Not meet = the number and percentage of children in the study that did not meet food group RDI/AI; National % Not meet= NHANES (2007-2010) gender-age-group proportions that did not meet food group RDI/AI; RDA = Reference daily allowance, AI= Adequate intake; ns=p-value not significant

Table 3.5. Daily food intake by cardiometabolic risk category ^a

	Blood Pressure (N=116)		BMI (N=116)		HDL-C (N=99)		Triglycerides (N=99)	
	Normal	Elevated BP	Normal	Overweight	Normal	Low	Normal	Elevated
n(%)	77(66.4)	39(33.6)	67(57.8)	49(42.2)	82(82.8)	17(17.2)	47(47.5)	52(52.5)
Food Group, mean(SD)								
Fruits(CE)	2.17(1.16)	1.73(0.92)**	2.23(1.13)	1.74(1.02)**	2.06(1.15)	2.01(0.91)	2.02(1.23)	2.08(0.99)
Vegetables(CE)	0.77(0.59)	0.50(0.37)***	0.75(0.58)	0.57(0.47)	0.72(0.60)	0.56(0.34)	0.73(0.62)	0.66(0.52)
Dairy(CE)	2.26(0.91)	1.93(0.80)**	2.18(0.86)	2.09(.092)	2.23(0.88)	1.83(0.77)	2.00(0.77)	2.30(0.94)
Wholegrains(OZE)	0.65(0.58)	0.45(0.39)	0.63(0.58)	0.53(0.46)	0.58(0.53)	0.53(0.46)	0.49(0.47)	0.63(0.55)
Legumes(CE)	0.26(0.27)	0.14(0.19)***	0.25(0.27)	0.17(0.20)	0.22(0.27)	0.21(0.23)	0.25(0.28)	0.19(0.24)
Fiber(g)	15.19(8.03)	10.17(5.28) ***	14.92(7.94)	11.55(6.65)**	14.04(8.14)	11.77(6.00)	13.83(9.04)	13.48(6.64)

^a Data from study of metabolic syndrome in Hispanic children at a community health center in Johnson City, TN, 2015-2016

** p-value < 0.05, *** p-value < 0.01

P-values from independent two samples t-test

Table 3.6. Odds ratios and 95% confidence intervals for daily food intake and blood pressure and body mass index (N=116) ^a

	Elevated Blood Pressure		Overweight/Obese	
	Crude ORs (95% CI)	Adjusted ORs (95% CI) ^b	Crude ORs (95% CI)	Adjusted ORs (95% CI) ^b
Male v Female	1.73(0.80-3.76)	3.11(1.16-8.35) **	1.07(0.51-2.24)	0.95(0.42-1.31)
Age Group				
2-4 years	3.55(1.42-8.83) ***	3.15(1.06-9.37) **	0.72(0.31-1.68)	0.52(0.42-2.17)
5-7 years	1.58(0.54-4.59)	1.54(0.46-5.13)	0.57(0.22-1.53)	0.44(0.15-1.31)
8-10 years(ref)				
Parent's Education				
<9th grade(ref)				
9th-12th	0.86(0.28-2.67)	0.97(0.26-3.71)	0.63(0.21-1.96)	0.67(0.20-2.28)
High school grad	0.66(0.26-1.64)	0.62(0.21-1.83)	0.56(0.23-1.36)	0.53(0.20-1.40)
>=Some college	0.35(0.070-1.78)	0.15(0.24-0.98) **	2.03(0.53-7.75)	1.61(0.37-6.94)
Fruit(CE)	0.67(0.45-0.99) **	0.67(0.44-1.03)	0.65(0.45-0.93)**	0.62(0.42-0.91)
Vegetables(CE)	0.29(0.11-0.79) **	0.38(0.14-1.06)	0.50(0.23-1.10)	0.45(0.19-1.06)
Legumes(CE)	0.072(0.007-0.69) **	0.052(0.004-0.64)**	0.20(0.036-1.15)	0.18(0.03-1.17)
Wholegrain(OZE)	0.40(0.16-1.03)	0.41(0.15-1.14)	0.71(0.34-1.48)	0.71(0.33-1.55)
Dairy(CE)	0.65(0.41-1.02)	0.61(0.37-0.99)**	0.88(0.58-1.3)	0.88(0.57-1.36)
Fiber(g)	0.879(0.71-0.95)***	0.88(0.81-0.96)***	0.93(0.88-0.99)**	0.93(0.87-0.99)**

^a Data from study of metabolic syndrome in Hispanic children at a community health center in Johnson City, TN, 2015-2016

** p-value < 0.05, *** p-value < 0.001

^b adjusted for child's age, sex and parent's education

Table 3.7. Odds ratios and 95% confidence intervals for daily food intake and lipid levels ^a

	Low High Density Lipoprotein		Hypertriglyceridemia	
	Crude ORs (95% CI)	Adjusted ORs (95% CI) ^b	Crude ORs (95% CI)	Adjusted ORs (95% CI) ^b
Male v Female	0.64(0.22-1.83)	1.84(0.52-6.53)	1.44(0.65-3.19)	1.65(0.68-3.97)
Age Group				
2-4 years	1.74(0.56-5.39)	1.98(0.49-7.97)	1.15(0.47-2.83)	1.14(0.42-3.15)
5-7 years	0.57(0.11-3.02)	0.81(0.13-5.15)	1.05(0.37-2.97)	1.16(0.37-3.66)
8-10 years(ref)				
Parent's Education				
< 9th grade(ref)				
9th-12th	1.16(0.264-5.14)	1.41(0.26-7.53)	0.93(0.30-2.84)	0.81(0.24-2.71)
High school grad	0.65(0.15-2.76)	0.53(0.11-2.67)	1.39(0.54-3.60)	1.86(0.64-5.41)
>= Some college	4.34(0.93-20.30)	4.28(0.73-25.06)	2.09(0.47-9.41)	1.98(0.39-10.08)
Fruit(CE)	0.88(0.60-1.55)	1.0(0.61-1.63)	1.05(0.73-1.50)	1.11(0.76-1.61)
Vegetables(CE)	0.53(0.17-1.67)	0.76(0.23-2.55)	0.82(0.41-1.66)	0.85(0.40-1.81)
Legumes(CE)	0.84(0.11-6.45)	1.40(0.16-12.38)	0.40(0.083-1.89)	0.38(0.076-1.92)
Wholegrain(OZE)	0.73(0.23-2.32)	0.94(0.27-3.35)	1.78(0.75-4.21)	1.98(0.8-4.90)
Dairy(CE)	0.57(0.30-1.10)	0.57(0.28-1.15)	1.50(0.94-2.40)	1.60(0.98-2.59)
Fiber (g)	0.96(0.88-1.04)	0.98(0.90-1.06)	0.99(0.95-1.05)	1.00(0.95-1.05)

^a Data from study of metabolic syndrome in Hispanic children at a community health center in Johnson City, TN, 2015-2016

^b adjusted for child's age, sex and parent's education

Discussion

In this study, we found that mean daily intake of legumes and fruits by all sample gender age groups exceeded the minimum DGA recommendations (DGA, 2015). Because of the high legume intake by the sample, a significantly lower proportion of all sample gender-age groups (except 9-to-10-year-old girls) did not meet legume recommendations compared with similar gender-age groups of a nationally representative sample (National Cancer Institute, 2015). Similarly, a significantly lower proportion of 4-to-8-year-old girls and 9-to-10-year-old girls did not meet fruit recommendations compared with similar gender-age groups of a nationally representative sample (National Cancer Institute, 2015). These findings are consistent with results from previous studies which have reported higher intake of fruits in Mexican-American children compared to non-Hispanic White and non-Hispanic Black children (Kong et al., 2013; Salvo et al., 2012). To the best of our knowledge, this study is the first to compare intake of legumes in pre-adolescent Hispanic children to intake in corresponding national gender age-groups. Although a significantly lower proportion of boys than girls did not meet fruit recommendations, there was no gender difference in mean fruit intake, consistent with findings by Lorson and colleagues (Lorson, Melgar-Quinonez, & Taylor, 2009).

In contrast to the high intake of legumes and fruits by the sample, mean daily intake of vegetables, dairy (except for 2-to-3-year-old girls), wholegrains and fiber were well below the minimum recommendations. These findings are consistent with findings from nationally representative studies which show U.S children do not eat enough vegetables, wholegrains, dairy and fiber (Lorson et al., 2009; Munoz, Krebs-smith,

Billard-Barbash, & Cleveland, 1997; National Cancer Institute, 2015; Nielsen et al., 2014; Salvo et al., 2012). Given the similarities between our sample and nation in mean daily intake of these food groups, gender-age group proportions observed not to meet wholegrain, fiber, dairy and vegetable recommendations were not significantly different from corresponding proportions of nationally representative samples (National Cancer Institute, 2015). The exceptions were with fiber consumption, where the proportions of 4-to-8-year-old boys, and 4-to-10-year-old girls were significantly lower than corresponding nationally representative sample proportions (National Cancer Institute, 2015). Vegetable intake increased significantly with age in the sample. This finding contrasts with findings reported by studies which used nationally representative samples. For example, in the study by Lorson and colleagues, 6-to-11-year-olds were 1.5 times more likely than 2-to-5-year-olds to not meet MyPyramid vegetable recommendations (Lorson et al., 2009). Also, unlike previous studies, we did not find significant gender difference in vegetable consumption (Nielsen et al., 2014).

Although mean daily fiber consumption by children was well below minimum recommendations, we found that with the exception of 2-to-3-year-olds, a lower proportion of all sample gender-age groups than corresponding nationally representative sample gender-age group proportions (National Cancer Institute, 2015) did not meet fiber recommendations. Indeed, the proportion of 4-to-8-year-old boys, 4-to-8-year-old girls and 9-to-10-year-old girls who did not meet fiber recommendations were significantly lower than corresponding nationally representative sample gender-age group proportions.

The cardio-protective benefit of under-consumed food groups such as legumes, vegetables, fruits, wholegrains, fiber and dairy is well-documented in previous studies (Afshin et al., 2014). Previous studies also provide evidence of a diet quality disparity in children by cardiometabolic risk status, where those at greater risk are more likely than their healthier peers to have a less healthy diet. Our findings are consistent with these previous studies. After adjusting for child's age, gender and socio-economic status we found that increased fiber consumption decreased the odds of elevated blood pressure (OR: 0.88 95% CI: 0.81-0.96) and overweight (OR: 0.93: 95% CI: 0.87-0.99); increased legume consumption reduced the odds of elevated blood pressure (OR: 0.052: 95% CI: 0.004-0.64); and increased dairy intake was protective against elevated blood pressure (OR: 0.61: 95% CI: 0.37-0.99). In addition to supporting findings by previous studies, this study advances the literature on the association between dietary intake and cardiometabolic risk in pre-pubertal children in general and specifically in Hispanic children.

The low sample intake of vegetables, wholegrains, dairy and fiber is concerning; however, it is even more concerning when taken together with findings from previous studies which show that children's under-consumption of healthy food usually goes together with over-consumption of unhealthy food such as sugar sweetened beverages, sodas, and fries and other empty calories (Munoz et al., 1997). In practice, what this means is that effective dietary interventions for cardiometabolic risk must promote both increased consumption of 'short fall' food groups and reduction in the intake of unhealthy food.

Not many studies have examined the relationship between under-consumed foods and cardiometabolic risk in young children. This study therefore makes an important contribution to the literature on the subject. However, this study has a few limitations. First the sample size was small and that may have led to under-estimation of risk factors prevalence and lack of associations. Second, the sample is predominantly Mexican-American, therefore, our findings may not apply to other Hispanic groups. Finally, because of the cross-sectional design, reported associations do not indicate a causal relationship.

In this study daily mean intake of legumes and fruits by pre-adolescent Hispanic children exceeded the minimum daily recommendation. The proportions of sample gender-age groups who did not meet legume recommendations were significantly lower than corresponding nationally representative gender-age proportions. However, daily intake of vegetables, wholegrains, dairy and fiber by the sample were generally well below recommended levels. At-risk children had less intake of fruits, vegetables, legumes and fiber than their healthy peers. Legume, dairy and fruit intake were protective against elevated blood pressure; whereas increased fruit intake was protective against overweight. While Hispanic children have higher intake of fruits and legumes, they do share a common need with non-Hispanic Black and non-Hispanic White children for dietary interventions to increase their intake of wholegrains, dairy, vegetables and fiber. This study confirmed the protective effect of these food groups, suggesting that increasing their consumption could enhance cardiometabolic health among Hispanic children.

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CHAPTER 4

EVALUATING THE EFFICACY OF NON-TRADITIONAL BIOMARKERS FOR DETECTING CARDIOMETABOLIC RISK IN HISPANIC CHILDREN

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Abstract

Background: Non-traditional biomarkers could be used for detecting cardiometabolic risk; however, their efficacy and optimal cut-offs have not been established, especially in minority children. This study aimed to assess the efficacy and optimal cut-offs of seven non-traditional biomarkers for detecting cardiometabolic risk in Hispanic children.

Methods: A control group of 23 children and an at-risk group (having ≥ 3 of: elevated blood pressure (BP), large waist circumference (WC), hypertriglyceridemia, and low high density lipoprotein (HDL-C)) of 15 children, participated in a cross-sectional study of metabolic syndrome at a community health center, from 2015 to 2016. T-test, Mann-Whitney U and Chi-squared tests were used to assess differences in characteristics of the two groups. Spearman's correlation analysis was used to assess correlations between biomarkers and cardiometabolic risks. Receiver operating characteristic analysis and the Youden's J statistic= $\text{maximum (sensitivity + (specificity-1))}$ were used to determine biomarker cut-offs for optimal sensitivity and specificity.

Results: The mean age of the sample was 6.48 years ($SD=2.74$); 50.5% were girls. The at-risk group had significantly higher systolic blood pressure, triglycerides, waist circumference, leptin and C-peptide levels, but significantly lower HDL-C than children in the control group. Leptin and C-peptide were positively correlated with triglycerides ($r=0.30, p<0.05$; $r=0.30, p<0.05$, respectively) and WC ($r=0.39, p<0.05$; $r=0.30, p<0.05$, respectively). Leptin, IL-6 and TNF- α were positively correlated with systolic BP ($r=0.32, p<0.05$; $r=0.34, p<0.05$; $r=0.37, p<0.05$, respectively). TNF- α was inversely correlated with HDL-C ($r=0.37, p<0.05$). Biomarkers with overall efficacy to identify at-risk children were: C-peptide (AUC=70, 95% CI=0.52, 0.89; $p=0.03$) and TNF- α (AUC=75, 95%

CI=0.58, 0.92; p=0.0035). Biomarkers with overall efficacy to identify at-risk children were: C-peptide (AUC=70, 95% CI=0.52, 0.89; p=0.03) and TNF- α (AUC=75, 95% CI=0.58, 0.92; p=0.0035). Optimal cut-offs were: C-peptide, 0.73 ng/ml (sensitivity=100%, specificity=48%); and TNF- α , 4.28 pg/ml (sensitivity=93%, specificity=58%).

Conclusions: C-peptide (cut-off, 0.73 ng/ml); and TNF- α (cut-off, 4.28 pg/ml) could help identify cardiometabolic risk in pre-adolescent Hispanic children.

Keywords: non-traditional biomarker; cardiometabolic risk; sensitivity; specificity; Hispanic children

Introduction

Cardio-metabolic risk factors such as overweight, low high density lipoprotein cholesterol (HDL-C), hypertriglyceridemia, and hypertension are important health risks in children because of their association with the development of serious and costly health outcomes later in life. The clustering of three or more cardiometabolic risk factors, also referred to as the metabolic syndrome, has been found to be more detrimental to cardiovascular health than individual cardiometabolic risk factors. According to recent National Health and Nutrition Examination Survey (NHANES) estimates, the prevalence of three or more cardiometabolic risk factors among 12-to-19-year-old U.S children decreased from 7.3% in 1988-1994 to 6.5% in 2003-2006 (Jang et al., 2013).

Despite consensus on the clinical significance of the clustering of cardiometabolic risk factors, there is no agreed upon definition in children. Many pediatric studies have applied sex- and age-dependent normative values to adult criteria, which is the presence of ≥ 3 of the following: (1) an elevated TG level, (2) a reduced HDL-C level, (3) a raised BP, (4) an elevated fasting plasma glucose concentration, and (5) obesity (Weiss, Bremer, & Lustig, 2013). Others have used different criteria, such as the International Diabetes Criteria exist (Ford, Li, Pearson, & Okdad, 2008).

It is important that we can accurately assess the clustering of cardiometabolic risk in children. All current definitions require measurements on five different biochemical and anthropometric scales, with the logistics involved making it less than an ideal screening test of children's cardiometabolic health status. What if a single

biochemical marker could accurately screen for cardiometabolic risk. Non-traditional biomarkers, such as adipocytokines, ghrelin and C-peptide have emerged as important markers of cardiometabolic risk, and have potential use in screening for cardiometabolic risk. Leptin, adiponectin, resistin and interleukin 6 (IL-6) are important adipocytokines associated with cardiometabolic risk. High levels of Adiponectin is protective against obesity, hypertension and dyslipidemia (Shaibi et al., 2007; Winer et al., 2006). In contrast, hyperleptinemia, elevated IL-6 and TNF- α increase the risk for obesity and hypertension. However, the correlation between resistin and cardiometabolic risk in humans is less clear. Some studies have reported a positive correlation (M. Li et al., 2009; Takata et al., 2008), while other studies showed no correlation (De Luis et al., 2011; Heilbronn et al., 2004). C-peptide and ghrelin are non-adipocytokine non-traditional biomarkers. C-peptide is a protein which is co-secreted with insulin in a one-to-one ratio by the pancreatic beta cells. Like other markers of insulin resistance, it is positively correlated with cardiometabolic risk (Li, Li, Meng, & Zheng, 2015; McFarlin, Johnson, Moreno, & Foreyt, 2013; Patel, Taveira, Choudhary, Whitlatch, & Wu, 2012). Ghrelin is produced mainly in the stomach and exhibits an inverse correlation with cardiometabolic risk.

Levels of biomarkers and cardiometabolic risk are influenced by age, sex and ethnicity (Ford et al., 2008; Srikanthan et al., 2016). Females have higher levels of adiponectin, ghrelin and resistin compared to males (Srikanthan et al., 2016; Yaturu, Daberry, Rains, & Jain, 2006). The prevalence of elevated blood pressure, obesity, dyslipidemia and the clustering of cardiometabolic risk increases with age (Ford et al., 2008). Levels of all adipokines are correlated with fat mass (Srikanthan et al., 2016).

Levels of adiponectin, and ghrelin are inversely correlated with fat mass whereas levels of leptin, IL-6 and TNF- α are directly correlated with fat mass (Srikanthan et al., 2016).

Previous studies have found leptin to have low-to-high accuracy, specificity and sensitivity for detecting the metabolic syndrome in adults and children (Li et al., 2011; Madeira et al., 2016; Obeidat, Ahmad, Haddad, & Azzeh, 2016; Zhuo et al., 2009). In a cross sectional study of 630 Jordanian adults, Obeidat et al. (2016) found a leptin cut-off of 7.55 ng/ml to have moderate efficacy for detecting the metabolic syndrome among men (AUC=0.721, sensitivity=72%, specificity=72.1%, $p<0.001$); a leptin cut-off of 21.5 ng/ml, had low efficacy for detecting the metabolic syndrome among women (AUC=0.683 sensitivity=64%, specificity=70.8%, $p<0.001$ for women). A study of over 900 Taiwanese adults (Li et al., 2011) found that independent of age and body mass index, leptin had high accuracy for detecting the metabolic syndrome among men (AUC=0.9) and moderate accuracy as a test of metabolic syndrome among women (AUC=0.714). Among 275 Brazilian boys and girls, mean age 93.7 months ($SD=178$ months), Madeira et al. (2016) found a leptin cut-off of 13.4 ng/ml adjusted for age and sex to have moderate accuracy for detecting the metabolic syndrome (AUC = 0.721; sensitivity 67.6%; specificity 68.9). Adiponectin has also been shown to have low-to-moderate sensitivity and specificity for detecting the metabolic syndrome in adults and children. In a study of 9-18 year-old Italian boys and girls, Gilardini et al. (2006) found that a cut-off of 8.3ug/ml had a sensitivity of 77% (95% CI 46–95%) and a specificity of 79% (95% CI 67–88%) in girls; and a cut-off of 8.1ug/ml had a sensitivity of 82% (95% CI 48–98%) and a specificity of 57% (95% CI 39–74%) in boys. In 8-13-year-old obese Japanese boys Ogawa et al. (2005) reported an adiponectin cut-off of 6.6 ug/ml had a

sensitivity of 63.9% and specificity of 66.7% for detecting those with three or more cardiometabolic complications of obesity.

Studies on the diagnostic ability of ghrelin are few. In one study of adult Saudi-Arabians with type II diabetes, a ghrelin cut-off of 33.65 pg/ml had a sensitivity of 39.1%, a specificity of 62.9% and an accuracy of 0.48 (Ahmed, Ismail, & Meki, 2015) for detecting metabolic syndrome.

However, few studies have examined the association between non-traditional biomarkers and cardiometabolic risk in pre-adolescent Hispanic children. This study sought to examine the association between non-traditional biomarkers and the clustering of three or more cardiometabolic risk factors in pre-adolescent Hispanic children; and to propose cut-offs with optimal sensitivity and specificity for detecting risk. Strengths of this study include the young age (2-10 years) of the sample; the novelty of this type of inquiry in Hispanic children; and the potential direct application of findings for risk control in Hispanic children who experience higher prevalence of cardiometabolic risk compared to their non-Hispanic White (NHW) and non-Hispanic Black (NHB) peers.

Methods

Data Source and Study Population

Data for this study came from a cross-sectional study of metabolic syndrome in Hispanic Children, ages 2-10 years, receiving well-child care at a community health center in Johnson City, TN. The study was conducted by an interdisciplinary group of researchers at East Tennessee State University. Funding was provided by the

Tennessee Board of Regents. The study was reviewed and approved by the Institutional Review Board at East Tennessee State University.

Inclusion criteria for participation included: being 2-10 years of age; being of Hispanic origin by self-identification; and not having a serious physical or mental illness. A total of 150 children were recruited in the study, beginning from June 2015 and ending in September 2016.

A total of 150 children were recruited in the study. Of the 150, 21 of a set of 21 pairs of siblings and 4 of two sets of three siblings were randomly eliminated from the analytic set. Two children with BMI less than the fifth percentile, were also excluded from the analytic set because this study's focus on children who either had normal BMI or were overweight. An additional 24 children had incomplete data for either biomarkers or lipids and were therefore excluded; the final analytic set comprised 99 children. Of these, a healthy group of 23 had no risk factors, whereas an at-risk group of 15 children had three or more risk factors.

Data Collection Methods

Parents of potentially eligible children were approached by a trained research assistant about participating in the study. Informed consent was obtained from interested parents in either Spanish or English Language and a child assent from children seven years and older.

A pediatric nurse practitioner measured children's height, weight and blood pressure using standard protocol: a standard scale which was tested and calibrated daily for accuracy was used to measure weight to the nearest 0.2 pounds; a stadiometer

was used to measure height to the nearest on-eighth of an inch; and auscultation with a stethoscope and a standard clinical mercury sphygmomanometer was used to measure blood pressure. Waist circumference was measured with a non-elastic tape half-way between the lower border of the ribs and the iliac crest to the nearest one-sixteenth of an inch. A laboratory technician drew four milliliters (4mls) of blood from the ante-cubital fossa of each child into each of a serum separator tube (SST) and an ethylenediamine tetra-acetic acid (EDTA) tube. The blood samples were stored at -80°C and later analyzed for HDL-C, triglyceride and IL-6, TNF- α , adiponectin, leptin, ghrelin, and C-peptide).

Risk Groups

Participants were grouped into an at-risk group, based on the presence of three or more of the following cardiometabolic risk factors: 1. Systolic or diastolic blood pressure $\geq 90^{\text{th}}$ percentile for age and sex (Falkner et al., 2004); 2. Triglyceride \geq the 95th percentile for age and sex; 3. HDL-C levels less than the 5th percentile for age and sex (Daniels & Greer, 2008b) and; waist circumference $>90^{\text{th}}$ percentile for age and sex (C. Li, Ford, Mokdad, & Cook, 2006). Participants with no risk factor were grouped into the healthy or control group.

Statistical Analyses

Risk group differences in cardiometabolic factors were assessed by t-tests. The distribution of leptin in the two groups was skewed and so group difference was assessed using the Mann-Whitney test. Chi-squared test was used to assess sex

differences in cardiometabolic risk status. Spearman's correlation analysis was used to assess the association between biomarkers and cardiometabolic risk factors. Receiver operating characteristic analyses (ROC) were conducted to determine the efficacy of biomarkers for detecting three cardiometabolic risk factors. Area under the curve (AUC), sensitivity and specificity were reported from ROC analyses. The optimal biomarker cut-offs for detecting three or more cardiometabolic risk factors were determined using the Youden's J statistic, calculated as: Youden's J statistic=maximum (sensitivity + (specificity-1)). All tests were two-sided and a p-value < 0.05 was set as the level of statistical significance. All data analysis was done in statistical analyst system (version 9.4, SAS Institute Inc., Cary, NC, USA).

Results

The mean sample age was 6.48 years ($SD=2.74$); about half (50.5%) the children were girls (Table 4.1). Of the four cardiometabolic risk factors assessed (elevated blood pressure, obesity, low high density lipoprotein and hypertriglyceridemia), 23.5% had no risk factor (control or healthy group) whereas 15.2% had three risk factors (Table 4.1).

The at-risk group was younger than the control group ($M=4.93$, $SD=2.82$ vs $M=7.65$, $SD=2.23$; $p = 0.001$). The at-risk group also had higher systolic blood pressure, triglyceride, waist circumference, leptin and C-peptide, but significantly lower HDL-C levels than participants in the control group (Table 4.1).

Table 4.2 shows Spearman's correlation coefficients between biomarkers and cardiometabolic risk factors adjusted for age and sex. Leptin and C-peptide were positively correlated with triglycerides ($r =0.30$, $p<0.05$; $r =0.30$, $p< 0.05$, respectively)

and WC ($r=0.39$, $p<0.05$; $r=0.30$, $p<0.05$, respectively); but adiponectin had an inverse correlation with triglyceride ($r=-0.43$, $p<0.01$). Leptin, IL-6 and TNF- α were positively correlated with systolic BP ($r=0.32$, $p<0.05$; $r=0.34$, $p<0.05$; $r=0.37$, $p<0.05$, respectively). TNF- α was inversely correlated with HDL-C ($r=0.37$, $p<0.05$). No biomarker had significant correlation with diastolic blood pressure. Ghrelin had no significant correlation with any cardiometabolic risk factor. Biomarkers that showed an overall efficacy to identify at-risk children were: Leptin (AUC=70, 95% CI=0.50, 0.89; $p=0.05$); C-peptide (AUC=70, 95% CI=0.52, 0.89; $p=0.03$) and TNF- α (AUC=75, 95% CI=0.58, 0.92; $p=0.0035$). Optimal cut-offs were: Leptin, 5.95 ng/ml (sensitivity=68%, specificity=79%); C-peptide, 0.73 ng/ml (sensitivity=100%, specificity=48%); and TNF- α , 4.28 pg/ml (sensitivity=93%, specificity=58%). Overall, leptin, IL-6, TNF-alpha, adiponectin and ghrelin were not efficacies for identifying at-risk children (Table 4.3). IL-6, resistin, adiponectin, resistin and ghrelin had poor to fair overall efficacy for detecting three or more cardiometabolic risk factors (Table 4.3).

Table 4.1. Characteristics of children by cardiometabolic risk group (N=38) ^a

	Total Sample	Control Group	>=3 Risk Factors	P-value ^b
n(%) of total	99(100)	23(23.2)	15(15.2)	
Sex, n(%)				0.089
Male	49(49.5)	6(26.1)	8(53.3)	
Female	50(50.5)	17(73.9)	7(46.7)	
Age, mean(SD)	6.48(2.74)	7.65(2.23)	4.93(2.82)	0.001
WC, mean(SD)	63.64(12.01)	59.43(7.06)	65.83(10.64)	0.027
SBP, mean(SD)	102.78(10.64)	97.83(9.03)	107.13(9.07)	0.002
DBP, mean(SD)	64.72(7.90)	63.00(6.29)	66.27(11.04)	0.16
TG, mean(SD)	121.25(61.65)	76.57(20.15)	172.87(68.34)	0.000
HDL, mean(SD)	49.30(11.25)	57.00(11.00)	41.07(11.14)	0.000
Leptin, mean(SD)	6163.30(8020.38)	3557.58(3236.34)	10158.74(11193.22)	
Median		1970.7	6489.31	0.021 ^{&}
Adiponectin (ug/ml)	27.44(14.34)	27.62(16.75)	27.17(10.12)	0.46
C-peptide (pg/ml)	1444.22(883.72)	1234.50(786.93)	1765.77(952.80)	0.035
Ghrelin (pg/ml)	247.49(188.66)	247.17(172.81)	247.97(217.12)	0.5
TNF- α (pg/ml)	11.78(26.65)	11.10(30.07)	12.83(21.30)	0.42
Resistin (pg/ml)	6190.53(4474.44)	5592.54(2647.09)	7107.45(6357.06)	0.16
IL-6 (pg/ml)	5.26(13.47)	3.19(7.11)	8.44(19.55)	0.12

^a Data from study of metabolic syndrome in Hispanic children at a community health center in Johnson City, TN, 2015-2016

^b P-value from t-test

[&] P-value calculated using the Mann-Whitney U test

Abbreviations: TG =Triglycerides; HDL-C= High Density Lipoprotein Cholesterol; SBP=Systolic Blood Pressure; DBP=Diastolic Blood Pressure; WC=Waist Circumference

Table 4.2. Partial correlation coefficients between biomarkers and cardiometabolic risk factors (N=38) ^a

	Leptin (pg/ml)	Adiponectin (ug/ml)	C-peptide (pg/ml)	Ghrelin (pg/ml)	Resistin (pg/ml)	IL-6 (pg/ml)	TNF- α (pg/ml)
TG (mg/dl)	0.30**	-0.43***	0.30**	-0.065	0.073	0.15	0.21
HDL-C (mg/dl)	-0.21	0.15	-0.26	-0.15	-0.15	-0.22	-0.37**
SBP(mmHg)	0.32**	-0.033	0.24	-0.12	0.13	0.34**	0.37**
DBP (mmHg)	0.22	-0.027	0.22	-0.046	-0.17	0.032	0.049
WC(cm)	0.39**	-0.21	0.30**	-0.092	0.0014	0.19	0.2

^a Data from study of metabolic syndrome in Hispanic children at a community health center in Johnson City, TN, 2015-2016

** p-value < 0.05, *** p-value < 0.01

Abbreviations: TG=Triglycerides; HDL-C= High Density Lipoprotein Cholesterol; SBP=Systolic Blood Pressure; DBP=Diastolic Blood Pressure; WC=Waist Circumference

Table 4.3. The effectiveness of biomarkers as diagnostic test for three or more cardiometabolic risk in children (N=38) ^a

Biomarker	Cut-off ^{&}	AUC (95% CI)	Sensitivity%	Specificity%
Leptin (pg/ml)	5954	0.70(0.50-0.89)*	64	79
C-peptide (pg/ml)	727	0.70(0.52-0.89)**	100	42
Resistin (pg/ml)	3715	0.59(0.39-0.79)	93	42
Ghrelin (pg/ml)	359.5	0.53(0.33-0.74)	100	21
TNF-alpha (pg/ml)	4.28	0.75(0.58-0.92)***	93	58
Adiponectin (ug/ml)	31.3	0.53(0.32-0.73)	71	47
IL_6 (pg/ml)	1.28	0.62(0.42-0.82)	79	58

^a Data from study of metabolic syndrome in Hispanic children at a community health center in Johnson City, TN, 2015-2016

[&] Youden's J statistic used to estimate cut-off level

* P-value < 0.1, ** p-value <0.05, *** p-value < 0.001

Discussion

The cumulative evidence from the literature shows that leptin, C-peptide, TNF- α , and IL-6 are positively correlated with cardiometabolic risk factors and metabolic syndrome (Deng et al., 2015; González, del Mar Bibiloni, Pons, Llompарт, & Tur, 2012; Indulekha et al., 2011; Valle et al., 2005; Winer et al., 2006); whereas adiponectin and ghrelin have an inverse correlation with cardiometabolic risk and metabolic syndrome (Gilardini et al., 2006; Winer et al., 2006). However, few studies have examined the association between non-traditional biomarkers and cardiometabolic risk in Hispanic children (McFarlin et al., 2013; Pérez et al., 2014; Shaibi et al., 2007). In this study, we found that independent of age and sex, Leptin and C-peptide were significantly positively correlated with triglycerides and waist circumference, but adiponectin and TNF- α had significant inverse correlation with triglyceride level and HDL-C level respectively; leptin and TNF- α had significant positive correlation with systolic blood pressure. Our findings comport with results from the few studies in Hispanic children. For example, in a study of 175 overweight Hispanic children, of mean age 11.1 years (SD= 1.7), Shaibi et al. (2007) reported significant inverse correlations between adiponectin and systolic blood pressure, triglycerides and waist circumference. Pérez et al. (2014) found significant inverse correlations between adiponectin and systolic, and diastolic blood pressure, but a significant positive correlation between adiponectin and HDL-C in a study of 101 Puerto Rican adolescents (mean age 15.3 years). They also found a significant positive correlation between leptin and systolic blood pressure; and a significant positive correlation between C-peptide and systolic and diastolic blood pressure. To our knowledge, this study is the first to examine the correlation between

nontraditional biomarkers and cardiometabolic risk in pre-adolescent Hispanic children in Tennessee. We also believe that it is the first to evaluate the efficacy of nontraditional biomarkers to detect three cardiometabolic risk factors in pre-adolescent Hispanic children in Tennessee.

The diagnostic accuracy of a screening test is determined by its sensitivity and specificity; however, the sensitivity and specificity of a screening test are determined by the test cut-off which is chosen to discriminate between normal and abnormal. In this study, we found that a Leptin cut-off 5.95 ng/ml had 68% sensitivity and 79% sensitivity ; a C-peptide cut-off of 0.73 ng/ml had 100% sensitivity and 42% specificity for detecting three or more cardiometabolic risk factors in the sample; for TNF- α , optimal sensitivity (93%) and specificity (58%) occurred at a cut-off of 4.28 pg/ml. Across the full range of cut-offs, leptin ($AUC=0.7$), c-peptide ($AUC=0.7$) and TNF- α ($AUC=0.75$) showed moderate discrimination between healthy and at-risk groups. Although not statistically significant, the AUC, sensitivity and specificity which we found for leptin are similar to findings from previous studies (Madeira et al., 2016; Obeidat et al., 2016); however, this study's cut-offs for detecting cardiometabolic risk differs from the ones reported by Madeira et al. (2016). In their study of 275 pre-pubertal Brazilian children ($M=93.7\pm 178$ months) Madeira et al. (2016) reported a leptin cut-off of 13.4 ng/ml. One methodological difference between this study and the study by Madeira and colleagues is that our definition of metabolic syndrome was based on the ATP III (Weiss et al., 2013) criteria for adults, while theirs was based on the International Diabetes Federation criteria (Ford et al., 2008).

This study has some limitations. First, although we did not find significant sex difference in biomarker levels, the literature shows there is sex difference; however, because the study sample size was small, we could not stratify ROC analysis by sex. Our findings from the ROC analysis could therefore be confounded by sex. Second, being a cross-sectional study of predominantly Mexican-Americans, our findings do not indicate causality and may not be generalizable to all Hispanic children. Third, biochemical measures used in this study were obtained from non-fasting participants and care must be taken in comparing our findings with those of studies that used fasted measures. However, these weaknesses should be weighed against the strengths of this study. Most of our findings comport with the general literature, are plausible; and to our knowledge, this study is the first of its kind in pre-adolescent Hispanic children.

In conclusion, this study found significant correlations between leptin, C-peptide, adiponectin, TNF- α , IL-6 and cardiometabolic risk factors. Leptin cut-off 5.95 ng/ml, C-peptide cut-off of 0.73 ng/ml and TNF- α cut-off of 4.28 pg/ml were identified as having optimal sensitivity and specificity for detecting three or more cardiometabolic risk factors in pre-adolescent Hispanic children. Findings suggest that TNF- α , and C-peptide could help in identifying at-risk Hispanic children.

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CHAPTER 5

DISCUSSION AND CONCLUSION

Using data from a study of metabolic syndrome in pre-adolescent children receiving well-child care at a community health center, this study examined social, dietary and biochemical correlates and predictors of cardiometabolic risk. This study confirmed the high prevalence of overweight, elevated blood pressure and dyslipidemia in Hispanic children reported by other studies: about 4 out of 10 (40.7%) were overweight or obese; about a third (31.4%) had elevated blood pressure; more than half (52.5%) had elevated triglycerides and about a fifth (17.2%) had low high density lipoprotein cholesterol (HDL-C). Particularly concerning were the proportions of at-risk 2-to-5-year-olds: with 45.7% having elevated blood pressure; 39.1% being overweight or obese; a fifth having low HDL-C; and 57% having hypertriglyceridemia. The risk profile of 2-to-5-year-olds in this study is therefore worse than estimates from other studies. One explanation for the high prevalence of cardiometabolic risk in the sample in general, but especially in 2-to-5-year-olds could be due to the limitations of this study as a convenient, cross-sectional study which used non-fasting biochemical measures. However, there are other explanations. About 85% of household incomes were below the 2017 federal poverty level; and 89% of all mothers had a high school education or less. The low socio-economic status of the study sample can also partly explain the high at-risk proportions.

Some of the study's findings have potential practical utility for improving Hispanic children's cardiovascular health. We found that maternal obesity and physical inactivity

were predictors of increased cardiometabolic risk in children. This suggests that helping Hispanic mothers to achieve and maintain a healthy weight, and to model physical activity, as part of health promotion and education, could reduce cardiometabolic risk in Hispanic children.

Regarding dietary intake, in general, the study sample exceeded minimum daily reference intake for legumes and fruits. Compared with similar NHANES gender-age proportions, higher proportions of all children in this study met recommendations for legume intake; higher proportions of 4-to-10-year-old girls met recommendations for fruit and fiber intake; and higher proportions of 4-to-8-year-old boys met recommendations for fiber intake. However, in general, our sample's intake of vegetables, wholegrains, dairy and fiber were as low as for the nation. This study confirmed the cardio-protective effects of fruits, legumes, and dairy. The practical implication of these findings is that increasing consumption of under-consumed food groups could help reduce cardiometabolic risk in Hispanic children.

It is important to have a quick and easy screening tool for detecting important health risks and conditions, such as the clustering of cardiometabolic risk; however, the way the clustering of cardiometabolic risk is currently measured makes it less desirable as a screening tool. Part of the attention non-traditional biomarkers are receiving is because of their potential for detecting the clustering of cardiometabolic risk. In this study, we found significant correlations between non-traditional biomarkers and cardiometabolic risk factors in children and report the following biomarker cut-offs as having the most optimal sensitivity and specificity for detecting three or more cardiometabolic risk factors in pre-adolescent Hispanic children: leptin, 5.95 ng/ml

($AUC=70$, sensitivity=68%, specificity=79%, $p=0.05$); C-peptide, 0.73 ng/ml ($AUC=70$, sensitivity=100%, specificity=48%); and TNF-alpha, 4.28 pg/ml ($AU=75$, sensitivity=93%, specificity=58%, $p=0.0035$). To the best of our knowledge this study is the first to propose cut-offs of non-traditional biomarkers with optimal sensitivity and specificity for detecting cardiometabolic risk in pre-adolescent Hispanic children. While our findings are far from confirmatory of the utility of non-traditional biomarkers in identifying at-risk children, they however provide the initial evidence of the efficacy of non-traditional biomarkers to identify at-risk Hispanic children. Our work can be built upon by further research.

Findings of this study must be interpreted bearing its limitations in mind. Optimal biomarker cut-offs were not stratified by gender because of the small sample size; the associations between child food group intake and cardiometabolic risk were not adjusted for child physical activity; and likewise, the associations between child physical activity and cardiometabolic risk were not adjusted for dietary intake. Confounding and residual confounding are therefore possible biases in our findings. Nonetheless, our study's findings can potentially help improve the cardiometabolic health of Hispanic children.

To summarize, we found high prevalence of cardiometabolic risk in 2-to-10-year-old Hispanic girls and boys receiving well-child care at a community health center in Johnson City, TN. The study found potential leverage points for reducing Hispanic children's risk, such as, helping mothers to achieve and maintain a healthy BMI; helping mothers to become more physically active; and promoting the consumption of more vegetables, legumes, fruits and fiber by children.

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