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Multifactorial correlates of blood pressure in South Asian children: a cross-sectional study.

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ABSTRACT

Objective: South Asian adults are at greater risk for cardiovascular disease risk factors. In South Asian children, studies have documented higher blood pressure (BP) values and hypertension rates than in Caucasian children. To effectively address the burden of hypertension in this population, an understanding of associated factors is necessary. We sought to explore various correlates of BP and hypertension in South Asian children.

Design: Cross-sectional study

Setting: Community-based recruitment in two Canadian cities (Hamilton and Surrey)

Participants: South Asian children (n=762) from two Canadian cities provided a range of physiological, behavioural and social variables. Blood pressure was assessed using an automated device. Body mass index, waist circumference, waist-to-height ratio and BP were transformed to z-scores using published standards.

Outcome measures: Regression analyses were used to explore associations among the range of physiological, behavioural and social factors with BP z-scores and hypertension and to identify the factors that provided the best explanatory capacity for systolic and diastolic BP z-scores.

Results: A range of physiological, social and behavioural factors were associated with BP z-score and hypertension in unadjusted analysis; however, upon adjustment for covariates, the association between most social and behavioural factors attenuated while the association between the physiological factors remained. In stepwise regression, age, sex, BMI z-score, heart rate and weight accounted for 30% of the variance of BP z-score, while age, BMI z-score, heart rate and daily intake of fast foods accounted for 23% of the diastolic BP z-score variance.

Conclusion: Our findings suggest that physiological variables such as age, sex, height, adiposity, and heart rate provide stronger explanatory capacity to BP variance and hypertension risk than other multifactorial variables in South Asian children.

ARTICLE SUMMARY

Strengths and limitations of this study

- The strengths of this study includes its large sample size of South Asian children and,
- Its examination of a wide range of physiological, behavioural and social risk factors in relation to BP z-scores and hypertension in South Asian children.
- Limitations of the study includes its cross-sectional design which limits the attribution of causality.

INTRODUCTION

South Asians comprise approximately 25% of the world's global population[1] and represent a significant portion of the visible ethnic minority groups in countries such as Canada, the United Kingdom and the United States (US) [2–4]. Individuals of South Asian origin are known to be at increased risk of cardiovascular disease (CVD) relative to other ethnic groups in Western countries[5,6]. These differences in CVD risk have also been shown to be present in South Asian children, suggesting that the risk differential in CVD risk factors and events experienced by this ethnic group starts from an early age[7].

One of the major physiological risk factors for CVDs is high blood pressure (BP) or hypertension[8]. Hypertension is also associated with an increased risk for stroke and kidney disease[8]. Moreover, multiple studies have shown that high BP in childhood typically continues into adulthood[9] — including in South Asian populations[10]. These findings suggest that it is essential to prevent hypertension in childhood in order to address the potential cardiovascular and metabolic sequelae later in life.

In South Asian children, studies have demonstrated increased prevalence of hypertension or higher BP levels relative to other ethnic groups[11,12]. While there is evidence suggesting a disproportionately higher BP burden for South Asians, the exact factors implicated are relatively unclear. Given the fact that causes of high BP are known to be multifactorial[8], it is vital to understand the various risk factors that might be responsible for the increased risk of high BP in South Asian children in general. Using a range of multifactorial variables that were identified in a recently published systematic review of children to be correlated with BP and hypertension in other children population groups[13], this study therefore aims: 1) to explore the associations between physiological, lifestyle and socio-demographic factors and BP in South Asian children; and 2) to identify the most important aggregate correlates of BP in South Asian children.

METHODS

Study Design

Participants included in this study were recruited as part of the Research in International Cardiovascular Health - Lifestyles, Environments and Genetic Attributes in Children and Youth (RICH-LEGACY) study. This cross-sectional study is designed to investigate risk factors for CVD across South Asian children in Canada. The study was approved by the Simon Fraser University Research Ethics Board (REB), Providence Health Care REB, and the Hamilton Integrated REB. Parents of participants provided written informed consent, while participants assented to take part in the study.

Recruitment

Elementary school and high-school children (n= 762) were recruited using community-based methods in two Canadian cities (Brampton, Ontario and Surrey, British Columbia) by convenience sampling between 2012 and 2016. Elementary schools with a high rate of South Asian enrolment were first identified by contacting the school boards. Once schools were identified, packages containing an invitation letter, a RICH-LEGACY study description and consent forms were sent to parents/guardians of children enrolled in the identified schools. Information stands were also placed at the participating elementary schools before and after school hours to reach out to parents with more information about the study. Additionally, the study was advertised through venues used by South Asian groups including newspapers, local television stations, community centres, worship centres and festivals. Inclusion criteria included:

children (in elementary or high school) having at least three grandparents of South Asian origin; and participants being able to provide consent (parents) and assent (children). Research assistants fluent in Hindi and Punjabi were responsible for participant recruitment and data collection. The research assistants who were involved in the measurements all undertook training together through simulator sessions and were retrained if variations in measurement protocol were observed by the research coordinator. This process was repeated for a few days to ensure accuracy and consistency amongst the research assistants in the assessment of the measurements collected in this study. In addition, written materials (including consent forms) were provided in English, Punjabi, Hindi and Urdu as needed.

Participant Assessment

Participants for the RICH-LEGACY study were assessed regarding socio-demographic variables including age, sex and parental education. In certain cases, parents or guardians helped complete certain sections of the child's questionnaire. Children's perception of body image was assessed using Stunkard's silhouettes, a rating scale from one to nine with increases related to increased silhouette size[14], that assesses perception of size and body dissatisfaction. This figure rating scale has been shown to be a valid indicator of determining weight status in children[15]. Feeding practices were assessed using the childhood feeding questionnaire[16]. Exposure to bullying was assessed by asking participants if they had experienced bullying or violence at school. This variable was assessed because of its role as a known stressor in children and its possible impact on pathways known to be involved in BP regulation such as the hypothalamic-pituitary-adrenal (HPA) axis[17]. Additionally, level of acculturation was assessed using the Acculturation Rating Scale for Mexican Americans-II (ARSMA- II) adapted for use in South Asians by Stigler *et al*[18]. This scale assesses an individual's identification with their heritage based on different domains including language preferences, media preferences, and preferences regarding food and other consumer goods using 24 questions[18]. The adapted questionnaire is grouped into two scales: the Western scale and the traditional scale. The traditional acculturation score measures children's acceptance of traditional Indian cultural attributes while the Westernized acculturation score measures the degree to which South Asian children identify with Western culture.

Participants completed a semi-quantitative food frequency questionnaire (FFQ) that assessed intake of fruits and vegetables and fast foods consumption. The FFQ was adapted from the INTERHEART FFQ, which was validated in an international cohort that included South Asians[19]. Physical activity was assessed using a questionnaire that quantified sports and other activities including leisure, household chores and sedentary factors (screen time and homework) during school and outside of school over the past month— with all activities then expressed as metabolic-equivalent-of-task (MET) minutes. Self-reported exposure to second-hand smoke was assessed to characterize children's passive exposure to smoking and defined as a minimum of five consecutive minutes during which inhalation of other people's smoke occurs. Hand-grip strength, a measure of muscular strength, was measured on the non-dominant hand by study personnel with a Jamar dynamometer utilizing standardized protocol[20].

Anthropometric Characteristics

Height was measured to the nearest 0.1cm using a right angle triangle and a calibrated wall mounted scale. Weight was measured to the nearest 0.1kg with the subject in light clothing using an electronic scale. Body mass index (BMI) was first calculated from weight in kilograms divided by height in meters squared before being converted to z-scores using WHO growth references for young people aged 5-19 years[21].

Waist circumference (WC) was recorded in centimetres as the average of two measures taken halfway between the lower rib margin and the iliac crest against the skin following a normal expiration. Waist circumference was assessed using non-stretching measuring tape by trained team members. Waist-to-height ratio (WtHR) was then calculated by dividing waist circumference by height. Both WC and WtHR were transformed to z scores using recently-published values for age and sex based on the third US National Health and Nutrition Examination Survey (NHANES III)[22]. Transforming the anthropometric measures to z-scores allowed for the standardized comparisons across populations of children of similar ages and sex.

Blood Pressure and Heart Rate

Blood pressure and heart rate were measured in the left arm using the Omron HEM-711DLX automated blood pressure monitor with appropriate sized cuffs following 10 minutes of seated rest. Three BP and heart rate measures were taken over a 10-minute period and the average of the three was recorded. Subsequently, BP was transformed to standard deviation scores and percentiles adjusted for age, sex and height according to the fourth National High Blood Pressure Education Program (NHBPEP) working group in children and adolescents[23]. Systolic and diastolic hypertension were defined using the NHBPEP recommendations as average systolic blood pressure or diastolic blood pressure equal to or greater than the 95th percentile for sex, age and height.

Parental Variables

Parents of the children recruited for this study provided information on parental education (father's and mother's education). In a smaller subset of the South Asian children (n=271), parental history of hypertension (yes or no) was assessed in order to explore the potential impact of heritable factors on children's BP z-scores and hypertension. Socioeconomic status was determined according to father's education, owing to widely reported cultural influences on gender structures in the South Asian population[24]. Fathers' education levels were categorized as: those with no formal education; those with primary/secondary school education; those with a trade school degree/diploma; and those with a college or university degree. Parent's smoking status was self-reported and categorized as non-smoker, former smoker, or current smoker.

Statistical Analysis

All continuous variables were examined using P-P plots and found to be normally distributed. For descriptive analysis, continuous variables were presented as means and standard deviations while categorical variables were reported as counts and percentages. Independent t-test analysis was used to assess sex differences in continuous variables, while chi-square tests were used to assess sex differences in categorical variables.

To explore the associations among the range of physiological, behavioural and sociodemographic variables with systolic and diastolic BP, unadjusted linear regression was used. These models were then adjusted for child age, sex and father's education. These confounders were selected based on their well –documented independent associations with the outcome variable in research studies. Although, the conversion to z-scores provides age and sex adjusted data, we chose to still include age and sex as confounders to adjust for potential residual effects because the growth chart used by the NHANES might not adequately reflect the growth profile of South Asian children. Similarly, unadjusted and adjusted (age, sex and father's education) logistic regression analysis was used to explore clinically-relevant associations among the multifactorial correlates with systolic and diastolic hypertension. To evaluate the independent effect of sex and age in the adjusted models, they were each removed from the list of covariates when exploring their effect on BP z-scores and hypertension (i.e., sex was adjusted for age and father's education), while age was adjusted for sex and father's education.

Following linear regression, stepwise multiple linear regression analyses were used to identify the combination of risk factors that best explained the variance in BP in South Asian children. The stepwise regression method enables the identification of the aggregate combination of correlates that has the highest contributory effect to the outcome variable. Specifically, for this analysis, we utilized the backward method to select the list of multifactorial correlates that provide significant contribution to the outcome (systolic and diastolic BP z-scores) using an entry criterion of $p < 0.05$ and a removal criterion of $p > 0.10$. The specific list of correlates (age, sex, height, weight, heart rate, BMI z-score, WC z-score, WHtR z-score, parental history of hypertension, parental education, exposure to bullying and violence, traditional and western acculturation scores, physical activity in school and outside school, dietary variables and second-hand smoking) considered for introduction in the backward stepwise regression model were chosen *a priori* based on literature evidence[13] and whether they had a p value <0.05 in univariate analysis. Using the aforementioned criteria, the following variables were considered in step-wise regression analysis: age, sex, height, weight, BMI z-score, WC z-score, WHtR z-score, heart rate, western acculturation score, child's perception of body image, and grip strength. In addition to these variables, father's education, daily intake of fast foods and total daily intake were considered in diastolic BP z-score models. The full lists of variables initially identified from literature search were considered in hypertension models. Statistical analysis was done using SPSS version 24.0. P values <0.05 were considered statistically significant. This study was written in line with the Strengthening the Reporting of Observational studies in Epidemiology (STROBE) guidelines[25]

Patient and Public Involvement

The research questions and outcome measures in this study were chosen by this team of researchers and clinicians with extensive experience working with the South Asian population to better understand the potential health risks faced by South Asian children. No patients were involved in setting the research question in development of the research question or study design. There are currently no plans to disseminate the results of this research study to study participants or to the relevant patient population.

RESULTS

This study included 360 boys and 402 girls ranging from 5.8 to 17.0 years (mean age 9.5 ± 3.0 years), with no statistically significant difference observed for age by sex. Mean non-transformed systolic BP was 109 ±11 mmHg while mean diastolic BP was 65 ± 8 mmHg. The prevalence of systolic hypertension in this population was 12%. South Asian boys were more physically active outside school than girls (p=0.04); were more likely to have a maternal history of hypertension (p=0.047); higher WC z-score (p<0.001); higher WHtR z-score (p=0.02); lower heart rate (p=0.047); higher systolic BP z-scores (p=0.001); higher non-transformed systolic BP (p<0.001); higher prevalence of systolic hypertension (p=0.01); had lower traditional acculturation score (p=0.02); and significantly higher exposure to bullying and violence at school (p=0.025) (Table 1).

Correlates of Systolic BP and Systolic Hypertension

In univariate linear regression analysis with systolic BP z-scores, weight (kg) (β= 0.005, 95% CI= 0.001, 0.01, p=0.022), BMI z-score (β= 0.289, 95% CI= 0.246, 0.333, p<0.001), WC z-score (β= 0.266, 95% CI= 0.213, 0.319, p<0.001), WHtR z-score (β= 0.271, 95% CI= 0.219, 0.324, p<0.001), heart rate (beats per minute) (β= 0.019, 95% CI= 0.015, 0.023, p<0.001), and the child's perception of their body image (using Stunkard's silhouettes) (β= 0.136, 95% CI= 0.083, 0.189, p<0.001) were found to be positively associated with systolic BP z-score. In contrast, we found that compared to male sex, female sex had lower systolic BP z-score (β= -0.246, 95% CI= -0.385, -0.108, p<0.001). Similarly, age (years) (β= -0.060, 95% CI= -0.084, -0.037, p<0.001), children's western acculturation score (β= -0.021, 95% CI= -0.036, -0.006, p=0.007) and height (cm) (β= -0.006, 95% CI= -0.010, -0.002, p=0.007) were negatively associated with systolic BP z-score. After adjustment for covariates the association between age, sex, weight, BMI z-score, WC z-score, WHtR z-score, heart rate and children's perception of body image with systolic BP z-scores remained— while the association with height became positive, and positive associations between children's grip strength and daily physical activity in school with systolic BP z-score was observed upon adjustment (Table 2).

In stepwise regression analysis, the combination of age, sex, BMI z-score, heart rate and weight were observed to be the most important correlates of systolic BP z-score, accounting for 30% of the systolic BP z-score variance of South Asian children (Table 3).

In unadjusted logistic regression analysis, female sex was associated with lower odds of developing systolic hypertension (odds ratio (OR) = 0.56, 95% CI= 0.36, 0.87, p=0.011). Associations were also observed with weight (kg) and systolic hypertension (OR= 1.02, 95% CI= 1.01, 1.04, p<0.001), BMI z-score and systolic hypertension (OR= 2.22, 95% CI= 1.84, 2.68, p<0.001), WC z-score and systolic hypertension (OR= 2.65, 95% CI= 2.06, 3.43, p<0.001) and WHtR z-score and systolic hypertension (OR= 2.47, 95% CI= 1.95, 3.13, p<0.001). Similarly, associations were observed between heart rate (beats per minute) and systolic hypertension (OR=1.04, 95% CI= 1.02, 1.06, p<0.001), child's perception of body image and systolic hypertension (OR= 1.50, 95% CI= 1.25, 1.79, p<0.001) and western acculturation score (OR= 0.95, 95% CI=0.90, 1.00, p=0.03). Upon adjustment for covariates, the associations between sex, height, weight, BMI z-score, WC z-score, WHtR z-score, heart rate and child's perception of body image remained — while the association between grip strength and systolic hypertension became significant upon adjustment (Figure 1).

Correlates of Diastolic BP and Diastolic Hypertension

In univariate linear regression analysis of multifactorial variables with diastolic BP z-score, negative associations with diastolic BP z-score were observed between age (years) (β= -0.061, p<0.001), height (cm) (β= -0.009, p<0.001), western acculturation score (β= -0.018, p=0.007), fathers' level of education (β= -0.054, p=0.047), total daily food intake (β= -0.016, p=0.005), fast foods (β= -0.065, p=0.048) and grip strength (kg) (β= -0.019, p<0.001). Conversely, significant positive associations with diastolic BP z-score were observed between heart rate (β= 0.018, p<0.001), BMI z-score (β= 0.156, p<0.001), WC z-score (β= 0.120, p<0.001), WHtR z-score (β= 0.128, p<0.001), and children's perception of their body image (using Stunkard's silhouettes) (β= 0.053, p=0.007). After adjustment for covariates the association remained between age, weight, BMI z-score, WC z-score, WHtR z-score, heart rate and children's perception of body image with diastolic BP z-score, while the association between physical activity in school with diastolic BP z-score became significant (Table 2).

In stepwise regression analysis, the combination of age, BMI z-score, heart rate and daily intake of fast foods were observed to be the most important aggregate correlates of diastolic BP z-score, accounting for 23% of the diastolic BP z-score variance of South Asian children (Table 3).

In unadjusted logistic regression analysis, associations were observed between age (years) (OR= 0.71, 95% CI= 0.55, 0.92, p=0.01), height (OR= 0.97, 95% CI= 0.94, 1.00, p=0.04), BMI z-score (OR= 1.68, 95% CI= 1.31, 2.17, p<0.001), WC z-score (OR= 1.89, 95% CI= 1.32, 2.70, p=0.001), WHtR z-score (OR= 1.77, 95% CI= 1.26, 2.47, p=0.001), heart rate (beats per minute) (OR=1.06, 95% CI= 1.03, 1.10, p<0.001) and grip strength (kg) (OR= 0.92, 95% CI= 0.86, 0.99, p=0.024) with diastolic BP z-score. The association with age, BMI z-score, WC z-score, WHtR z-score and heart rate remained significant after adjustment for covariates, while the association with weight became significant (Figure 2).

DISCUSSION

This study provides information on the multifactorial correlates of systolic and diastolic BP z-scores in a population of South Asian children. While results from unadjusted models highlight the presence of a multifactorial relationship for BP and hypertension, the disappearance of most of the social and lifestyle risk factors upon adjustment highlights the contribution of physiological variables such as age, sex, adiposity, height, heart rate, and grip strength to the risk of elevated BP and hypertension in South Asian children.

It is well documented that the burden of hypertension has precipitously increased in the pediatric population[26]. In addition, some studies have documented higher prevalence of hypertension in certain ethnic groups such as South Asians[11]. Although our sample was based on

convenience and non-representative given that sampling was restricted to two Canadian cities, the prevalence of hypertension in our study at 12% is consistent with age, sex and height adjusted estimates from Jafar *et al*[11] using a nationally-representative survey of Pakistani children age 5 to14 years, but higher than 5.2% prevalence from one cross-sectional study of Indian children ages 5 to 12 years[27]. Our estimates also appear higher than estimates from Canadian children ages 6 to 19 years where 4% of children were said to have hypertension and prehypertension[28]. When stratified by sex, we found significantly higher rates were observed for boys at 15% compared to girls at 9%. This is consistent with results from studies in other children which have reported higher hypertension prevalence in boys[29,30], and results from regression analysis which found female sex to be associated with lower odds of hypertension. This risk differential has been attributed to the presence of an anti-inflammatory immune profile in females and pro-inflammatory profile in males[31] — underscoring the potential for intervention efforts aimed at addressing sex-based disparities.

Consistent with research conducted in South Asian children[11,32] and research conducted in other childhood populations of different ethnicities [29,33–37], we observed positive associations between measures of adiposity and BP and hypertension after adjusting for covariates. The consistency of the association underscores the significant contribution of increasing adiposity to the prevalence of hypertension in young people. Moreover, the positive association between grip strength with systolic BP z-score and hypertension upon adjustment in this study raises questions about the benefits of strength training in children. The benefits of physical activity including aerobic exercise in relation to hypertension remain clear; however, the benefits of strength training in relation to hypertension risk, relative to the benefits of aerobic exercise, appear questionable[38]. It is unclear what might be responsible for the positive effect observed between grip strength and systolic BP z-score; however, findings from our study appear consistent with studies which have explored this association in Chinese[39] and American children[40].

Despite the fact that the BP z-scores values take into consideration age, height and sex values, we opted to test for residual correlations by examining the independent effect of these variables on BP z-scores and hypertension values. The significant independent association observed between age, sex and height with both BP z-scores and hypertension suggest that the NHANES growth charts which are used in the development of the blood pressure tables might not be well-suited to the South Asian population. Consequently, given the high rates of hypertension in this population as documented both in this research study and those in other studies of South-Asian children, the development of growth charts that reflect the growth trajectory and the unique physiological changes which have been documented in South Asian (such as a higher body fat at similar BMI levels when compared to Caucasians) will be necessary to ensuring that the epidemiology of hypertension in South Asian children is captured.

The consistent association between adiposity and hypertension, including the higher prevalence of hypertension in this population, reinforces their connections through well-established mechanisms. Specifically, the South Asian phenotype of higher body fat[7]—especially the visceral type which has been identified in adults[6]—when compared to their Caucasian peers, could activate the formation of pro-inflammatory cytokines such as Interleukin 6 (IL-6) which results in physiological changes that could lead to endothelial and vascular dysfunction through the development of insulin resistance[41], resulting in an increased predisposition for hypertension. The positive association between height and BP in this population could be explained by cerebral perfusion requirements where higher BP is needed in taller people to achieve optimal cerebral perfusion owing to hydrostatic pressure differences in taller and shorter individuals[42]. However, more research in South Asian children is warranted to corroborate our findings given the difference observed in direction of association in unadjusted and adjusted models.

The positive association we found between the child's perception of body image and BP may be due to this variable mirroring children's weight status or conversely, a marker for a graded increase in stress levels, owing to societal criticism of fatter body types, which could have insidious effects for hypertension risk through its impact on the neuro-endocrine system[43]. Additionally, a range of social and lifestyle variables were also found to be associated with BP z-score in univariate analysis but disappeared upon adjustment. While results from univariate associations may demonstrate links between risk factor and outcome, the disappearance of the association upon adjustment for socio-demographic variables highlights the links between these variables and suggests that the pathway linking these factors with BP might be interdependent.

The stepwise regression model shows that correlates from this study explained only about 30% of the variance of systolic BP z-score and 23% of the variability of diastolic BP z-scores. It is possible that some of this unexplained variance might be explained by genetics, as it has been suggested that about 30% to 60% of the variance in BP may be heritable[44,45]. Yet the lack of association between parental hypertension and child BP in the subset of parents of participants who provided this data would appear to contradict these findings for this population of South Asian children. However, it is likely that the subset of parents of child participants who provided this information might not be completely representative of the entire cohort, thereby biasing the results. Still, even accounting for potential genetic contributions, a significant amount of the BP variance remains unexplained. More research is needed to provide insight regarding the contributory effects of other potential variables that might contribute to risk of elevated BP in South Asian children.

Notably, null associations were also observed for certain variables in this study that have been found to be significantly associated with BP and hypertension in other child populations. For example, parental history of hypertension, dietary factors (such as consumption of fruit and vegetables) and exposure to second hand smoking have been linked in other studies to child BP but had no significant impact in this study. This could be reflective of the potential biases associated with using self-reports or may highlight how interactions between genes and environment/lifestyle shape risk factor susceptibilities — underscoring the need for more ethnic-based and ethnic comparison studies when exploring risk associations.

Study Limitations

This study has limitations. First, although we sought to recruit a representative sample of urban South Asian children, it was not a random sample. However, there is likely to be minimal effect on the relationships between the ranges of risk factors evaluated in this study. Second, this is a cross-sectional study and is therefore unable to provide insights into causal associations between the risk factor variables and long term CVD risk in South Asian children. Third, potential recall biases may have occurred as a result of using self-report data for some of the variables including diet and physical activity measures. Last, the lack of data collection on sexual maturity status could potential confound the study results obtained here. However, the adjustment for age in this study, which acts as a proxy variable for sexual maturity might help mitigate the bias. These limitations are in part addressed by strengths of this study which lies in its large sample size of South Asian children and in the wide range of risk factors examined.

Implications

Our findings underscore a range of factors that may contribute to risk of elevated BP and hypertension in South Asian children. Consequently, public health interventions such as those that emphasize prevention such as population-based health education and lifestyle modification that considers unique cultural contexts may provide significant potential in addressing the burden of hypertension in this population. There are also implications for clinical settings. Specifically, our findings suggest that while South Asian children may benefit from interventions aimed at reducing obesity to address the comparatively higher burden of hypertension in this population, there are certain sub-groups who could benefit from more targeted preventive interventions in primary care settings — such as males, children with increased adiposity, taller children, and children with increased heart rate, or children with a combination of these factors.

CONCLUSION

In this group of South Asian children, we found univariate associations between a range of physiological, social and lifestyle factors with BP z-scores and hypertension. However, in multivariate analysis, physiological variables remained consistently associated with BP and hypertension, and provided the strongest explanatory effect for the variance in BP. Given the sequelae associated with elevated BP, including BP tracking from childhood into adulthood, these results provide evidence on modifiable risk factors that might be targeted by prevention strategies in primary care to reduce the burden of high BP and hypertension in South Asian children.

Author contributions: Dr. Scott, Dr. Punthakee, Dr. Morrison, Dr. Gupta, Dr. Teo and Sumathy Rangarajan conceptualized the study, contributed to study design and reviewed the manuscript. Adeleke Fowokan conceptualized the study, drafted the initial manuscript, carried out statistical analysis and revised the manuscript. Dr. Waddell and Dr. Rosin contributed to the design of the study, reviewed and revised the manuscript.

All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

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Competing interests: None declared

Ethics Approval: Simon Fraser University Research Ethics Board (REB), Providence Health Care REB, and the Hamilton Integrated REB

Data sharing statement: Raw data are held by the lead author of the study in accordance with ethics guidelines.

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Table 1: Sociodemographic, anthropometric, risk factor characteristics of South Asian children stratified by sex.

	Total (n=762)	Boy (n=360)	Girl (n=402)	p value
Age (years)	9.5 ± 3.0	9.3 ± 2.8	9.7 ± 3.1	0.09
Paternal education				0.92
No formal education	5 (1%)	3 (1%)	2 (1%)	
Primary education	247 (34%)	115 (34%)	132 (35%)	
Trade school	21 (3%)	9 (3%)	12 (3%)	
College/university	444 (62%)	209 (62%)	235 (62%)	
Maternal education				0.363
No formal education	5 (1%)	4 (1%)	1 (0%)	
Primary education	223 (30%)	103 (30%)	120 (31%)	
Trade school	6 (1%)	4 (1%)	2 (1%)	
College/university	503 (68%)	235 (68%)	268 (69%)	
Acculturation score (western)	34.8 ± 4.7	34.6 ± 4.62	34.9 ± 4.74	0.426
Acculturation score (traditional)	26.7 ± 4.43	26.3 ± 4.35	27.1 ± 4.48	0.02
Daily physical activity in school (METmins/day)	35.7 ± 25.8	36.8 ± 27.0	34.8 ± 24.7	0.288
Daily physical activity outside school (METmins/day)	15.9 ± 33.9	18.5 ± 31.3	13.5 ± 35.9	0.04
Daily intake- servings of fruit and vegetables (daily mean intake)	3.16 ± 1.86	3.11 ± 1.81	3.21 ± 1.91	0.485
Daily intake- servings of fast foods (daily mean intake)	0.91 ± 0.78	0.86 ± 0.59	0.97 ± 0.91	0.067
Total daily intake- servings	12.0 ± 4.48	12.2 ± 4.9	11.8 ± 4.1	0.243
Exposure to bullying/violence at school				0.025
Yes	233 (34%)	126 (38%)	107 (30%)	

No	459 (66%)	207 (62%)	252 (70%)	
Exposure to second hand smoking*				0.616
None	712 (94%)	336 (94%)	376 (94%)	
1-2 times/week	33 (4%)	16 (5%)	17 (4%)	
3-6 times/week	5 (1%)	2 (1%)	3 (1%)	
At least once a day	7 (1%)	5 (1%)	2 (1%)	
2-3 times/day	1 (0%)	0 (0%)	1 (0%)	
Mother's history of hypertension				0.047
Yes	12 (4%)	9 (7%)	3 (2%)	
No	280 (96%)	128 (93%)	152 (98%)	
Father's history of hypertension				0.979
Yes	30 (10%)	14 (10%)	16 (10%)	
No	260 (90%)	122 (90%)	138 (90%)	
Height (cm)	138.3 ± 16.5	139.1 ± 17.6	137.7 ± 15.5	0.22
Weight (kg)	36.5 ± 15.8	36.9 ± 16.5	36.1 ± 15.3	0.46
BMI Z score	0.48 ± 1.44	0.57 ± 1.61	0.40 ± 1.28	0.11
WC Z score	-0.06 ± 1.23	0.11 ± 0.36	-0.21 ± 1.24	<0.001
WHtR Z score	-0.38 ± 1.24	-0.27 ± 1.27	-0.48 ± 1.21	0.02
Heart rate	87 ± 12	86 ± 12	87 ± 13	0.047
SBP Z score	0.57 ± 0.97	0.70 ± 0.99	0.46 ± 0.95	0.001
DBP Z score	0.37 ± 0.71	0.35 ± 0.68	0.39 ± 0.73	0.41
SBP (non-transformed)	109 ± 11	111 ± 12	107± 10	<0.001

DBP (non-transformed)	65 ± 8	65 ± 8	65 ± 8	0.849
Systolic hypertension	90 (12%)	54 (15%)	36 (9%)	0.01
Diastolic hypertension	31 (4%)	13 (4%)	18 (5%)	0.55

**Exposure defined as a minimum of five consecutive minutes during which inhalation of other people's smoke occurs*

BP=Blood pressure, BMI=body mass index, WC= waist circumference, WHtR= waist to height ratio, SBP= systolic blood pressure, DBP= diastolic blood pressure

Table 2: Adjusted linear regression between multifactorial risk factors with systolic and diastolic BP z scores

	Systolic BP z score	Diastolic BP z score
Age[a]	-0.054 (-0.078, -0.029), p<0.001	-0.057 (-0.075, -0.039), p<0.001
Female sex (vs Male)[b]	-0.208 (-0.350, -0.067), p=0.004	0.078 (-0.023, 0.179), p=0.132
Height	0.022 (0.011, 0.033), p<0.001	0.007 (-0.001, 0.015), p=0.077
Weight	0.047 (0.040, 0.055), p<0.001	0.022 (0.016, 0.027), p<0.001
BMI z score	0.292 (0.249, 0.336), p<0.001	0.160 (0.127, 0.193), p<0.001
WC z score	0.273 (0.219, 0.326), p<0.001	0.137 (0.098, 0.177), p<0.001
WHtR z score	0.289 (0.236, 0.342), p<0.001	0.153 (0.114, 0.192), p<0.001
Heart rate	0.016 (0.010, 0.022), p<0.001	0.015 (0.011, 0.019), p<0.001
Acculturation (western score)	-0.010 (-0.026, 0.006), p=0.211	-0.005 (-0.016, 0.006), p=0.373
Acculturation (traditional score)	0.010 (-0.006, 0.026), p=0.227	0.003 (-0.008, 0.015), p=0.582
Child's perception of body image	0.183 (0.128, 0.239), p<0.001	0.104 (0.064, 0.144), p<0.001
Exposure to bullying/violence at school	0.021 (-0.138, 0.181), p=0.794	-0.071 (-0.183, 0.042), p=0.218
Father's smoking status	0.118 (-0.056, 0.292), p=0.184	0.082 (-0.053, 0.218), p=0.233
Exposure to second hand smoke	-0.052 (-0.240, 0.136), p=0.587	0.018 (-0.117, 0.152), p=0.795
Father's history of	-0.127 (-0.484, 0.230), p=0.484	-0.063 (-0.336, 0.209), p=0.648

hypertension		
Mother's history of hypertension	-0.003 (-0.524, 0.518), p=0.991	0.354 (-0.042, 0.750), p=0.079
Grip strength (non-dominant hand)	0.025 (0.007, 0.043), p=0.007	0.006 (-0.007, 0.019), p=0.381
Daily physical activity in school (METmins/day)	0.005 (0.002, 0.008), p=0.003	0.003 (0.001, 0.005), p=0.009
Daily physical activity outside school (METmins/day)	0.001 (-0.001, 0.003), p=0.363	0.000 (-0.002, 0.002), p=0.994
Daily intake- fruit and vegetables (daily mean intake)	-0.008 (-0.049, 0.033), p=0.717	-0.011 (-0.040, 0.018), p=0.466
Daily intake-fast foods (daily mean intake)	0.004 (-0.086, 0.093), p=0.937	-0.053 (-0.117, 0.011), p=0.104

Model adjusted for age, sex and father's education
Values presented are β (95% confidence intervals), and p values
BMI= body mass index, WC= waist circumference, WHtR= waist to height ratio, BP =blood pressure, MET=Metabolic equivalent of task
[a]Age was adjusted for sex and father's education
[b]Sex was for adjusted for age and father's education

Table 3: Stepwise linear regression analysis showing the aggregate correlates of BP z-score in South Asian children

Stepwise multiple linear regression models					
	Variable	B	95%	P value	Adjusted R^2
Systolic BP z-score	Child's age	-0.132	-0.202 -0.062	<0.001	
	Sex	-0.293	-0.461, -0.126	0.001	
	BMI z-score	0.125	0.022, 0.228	0.017	
	Heart rate	0.014	0.007, 0.021	<0.001	
	Weight	0.027	0.012, 0.041	<0.001	
					0.294
Diastolic BP z-score	Child's age	-0.027	-0.048, -0.007	0.01	
	BMI z-score	0.125	0.081, 0.170	<0.001	
	Heart rate	0.015	0.010, 0.021	<0.001	
	Daily fast food intake	-0.013	-0.028, 0.001	0.072	
					0.228

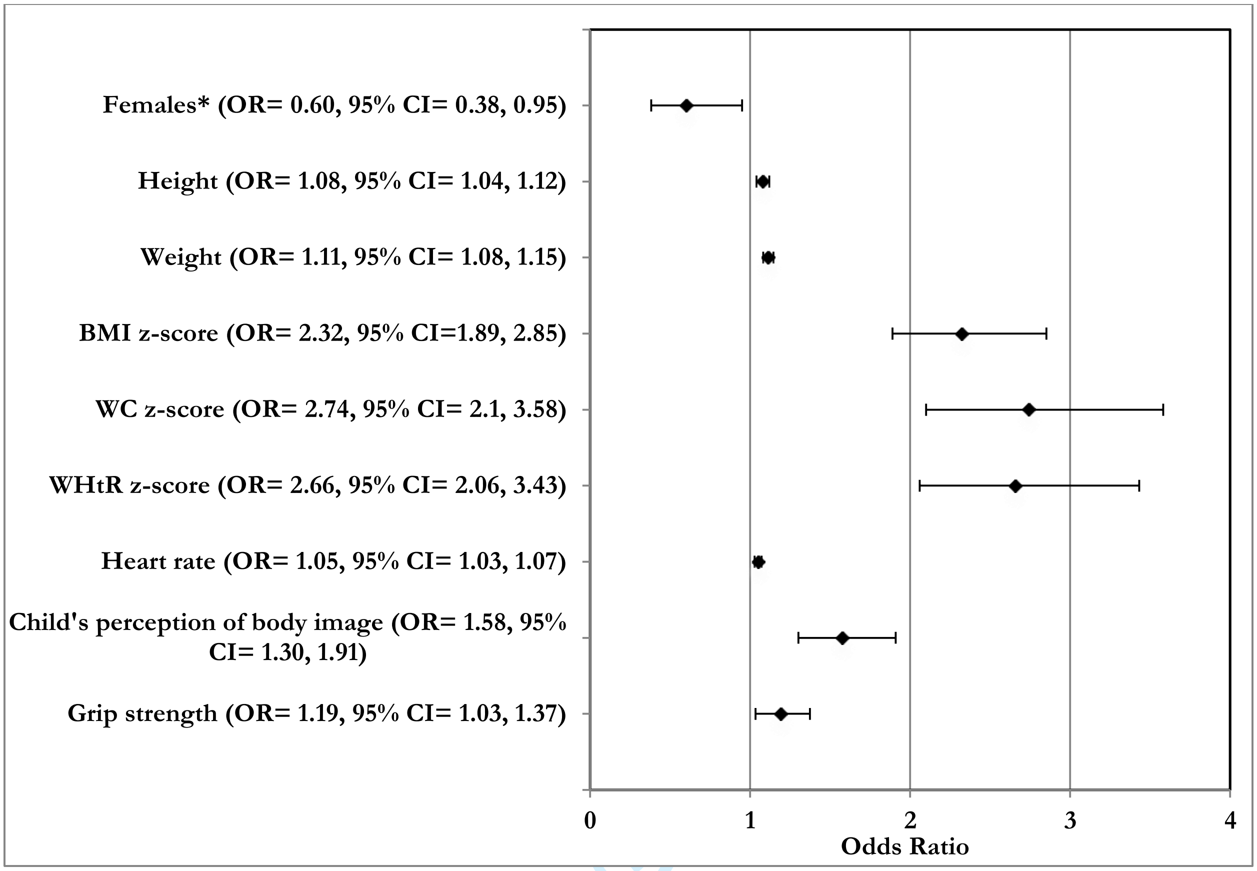
BMI=body mass index, BP= blood pressure

Figure 1: Adjusted odds ratio for the association between the multifactorial variables with systolic hypertension

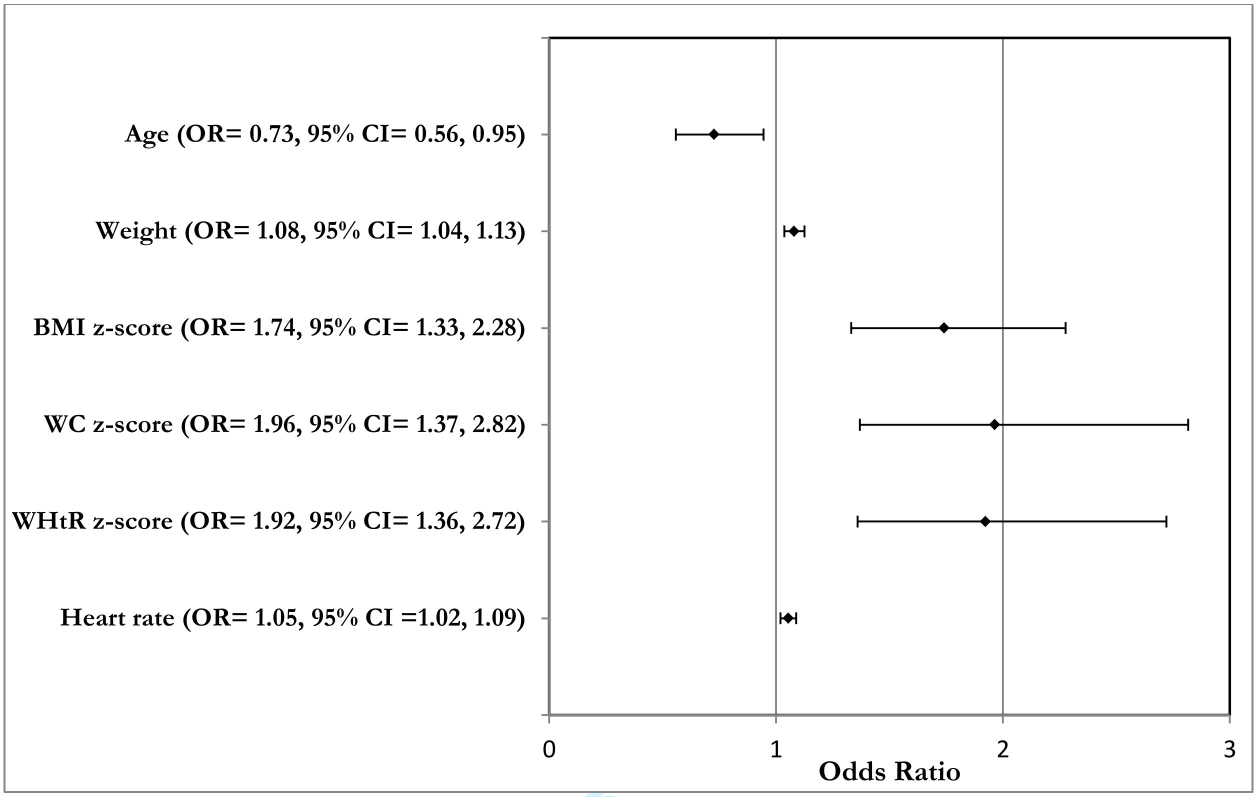
Model adjusted for age, sex and father's education
Values presented are odds ratio (95% confidence intervals)
BMI= body mass index, WC= waist circumference, WHtR= waist to height ratio, BP =blood pressure
**compared to males*

Figure 2: Adjusted odds ratio for the association between the multifactorial variables with diastolic hypertension

Model adjusted for age, sex and father's education
Values presented are odds ratio (95% confidence intervals)
BMI= body mass index, WC= waist circumference, WHtR= waist to height ratio, BP =blood pressure



Model adjusted for age, sex and father's education
Values presented are odds ratio (95% confidence intervals)
BMI= body mass index, WC= waist circumference, WHtR= waist to height ratio, BP =blood pressure
**compared to males*



Model adjusted for age, sex and father's education
Values presented are odds ratio (95% confidence intervals)
BMI= body mass index, WC= waist circumference, WHtR= waist to height ratio, BP =blood pressure

STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1-2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	3	State specific objectives, including any prespecified hypotheses	3-4
Methods			
Study design	4	Present key elements of study design early in the paper	4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	4
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5-8
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	*5-8*
Bias	9	Describe any efforts to address potential sources of bias	5
Study size	10	Explain how the study size was arrived at	
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	8
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	8-9
		(*b*) Describe any methods used to examine subgroups and interactions	N/A
		(*c*) Explain how missing data were addressed	7
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	N/A
		(*e*) Describe any sensitivity analyses	N/A
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	9
		(b) Give reasons for non-participation at each stage	N/A
		(c) Consider use of a flow diagram	N/A
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	9
		(b) Indicate number of participants with missing data for each variable of interest	24
Outcome data	15*	Report numbers of outcome events or summary measures	9
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	8-11

		(*b*) Report category boundaries when continuous variables were categorized	N/A
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	N/A
Discussion			
Key results	18	Summarise key results with reference to study objectives	12
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	16
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	17
Generalisability	21	Discuss the generalisability (external validity) of the study results	16
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	18

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Multifactorial correlates of blood pressure in South Asian children in Canada: a cross-sectional study.

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ABSTRACT

Objective: In South Asian children, studies have documented higher blood pressure (BP) values and hypertension rates than in Caucasian children. To effectively address the burden of hypertension in this population, an understanding of associated factors is necessary. We sought to explore various correlates of BP and hypertension, and to identify the most important aggregate combination of correlates for BP in South Asian children.

Design: Cross-sectional study

Setting: Community-based recruitment in two Canadian cities (Hamilton and Surrey)

Participants: South Asian children (n=762) provided a range of physiological, behavioural and social variables. BP was assessed using an automated device. Body mass index (BMI), waist circumference (WC), waist-to-height ratio (WHtR) and BP were transformed to z-scores using published standards.

Outcome measures: Linear and logistic regression analyses were used to explore associations among the range of physiological, behavioural and social factors with BP z-scores and hypertension while stepwise regression was used to identify aggregate factors that provided explanatory capacity for systolic BP (SBP) and diastolic BP (DBP) z-scores.

Results: A range of variables were associated with BP z-score and hypertension in unadjusted analysis. Upon adjustment for confounders, the association between age, weight, BMI z-score, WC z-score, WHtR z-score, heart rate and child's perception of body image with SBP and DBP z-score ($p<0.001$ for all); sex with SBP z-score ($p=0.004$); height with SBP z-score ($p<0.001$); and grip strength with SBP z-score ($p=0.007$) remained. In stepwise regression, age, sex, BMI z-score, heart rate and weight accounted for 30% of the variance of SBP z-score, while age, BMI z-score, heart rate and daily fast food intake accounted for 23% of the DBP z-score variance.

Conclusion: Our findings suggest that variables such as age, sex, height, adiposity, and heart rate provide stronger explanatory capacity to BP variance and hypertension risk than other variables in South Asian children.

ARTICLE SUMMARY

Strengths and limitations of this study

- The strengths of this study includes its large sample size of South Asian children and,
- Its examination of a wide range of physiological, behavioural and social risk factors in relation to BP z-scores and hypertension in South Asian children.
- Limitations of the study includes its cross-sectional design which limits the attribution of causality.

INTRODUCTION

South Asians comprise approximately 25% of the world's global population[1] and represent a significant portion of the visible ethnic minority groups in countries such as Canada, the United Kingdom and the United States (US) [2–4]. Individuals of South Asian origin are known to be at increased risk of cardiovascular disease (CVD) relative to other ethnic groups in Western countries[5,6]. These differences in CVD risk have also been shown to be present in South Asian children, suggesting that the risk differential in CVD risk factors and events experienced by this ethnic group starts from an early age[7].

One of the major physiological risk factors for CVDs is high blood pressure (BP) or hypertension[8]. Hypertension is also associated with an increased risk for stroke and kidney disease[8]. Moreover, multiple studies have shown that high BP in childhood typically continues into adulthood[9] — including in South Asian populations[10]. These findings suggest that it is important to prevent hypertension in childhood in order to address the potential cardiovascular and metabolic sequelae later in life.

In South Asian children, studies have demonstrated increased prevalence of hypertension or higher BP levels relative to other ethnic groups[11,12]. While there is evidence suggesting a disproportionately higher BP burden for South Asians, the exact factors implicated are relatively unclear. Given the fact that causes of high BP are known to be multifactorial[8], it is important to understand the various risk factors that might be responsible for the increased risk of high BP in South Asian children in general. Using a range of multifactorial variables (i.e. variables across a range of different factors) that were identified in a recently published systematic review of children to be correlated with BP and hypertension in other children population groups[13], this study therefore aims: 1) to explore the associations between physiological (factors relating to biology), lifestyle (factors relating to behaviour) and social factors (factors relating to conditions in which people live, attend school, grow, and develop) and BP in South Asian children; and 2) to identify the most important aggregate correlates of BP in South Asian children.

METHODS

Study Design

Participants included in this study were recruited as part of the Research in International Cardiovascular Health - Lifestyles, Environments and Genetic Attributes in Children and Youth (RICH-LEGACY) study. This cross-sectional study is designed to investigate risk factors for CVD across South Asian children in Canada. The study was approved by the Simon Fraser University Research Ethics Board (REB), Providence Health Care REB, and the Hamilton Integrated REB. Parents of participants provided written informed consent, while participants assented to take part in the study.

Recruitment

Elementary school and high-school children (n= 762) were recruited using community-based methods in two Canadian cities (Brampton, Ontario and Surrey, British Columbia) by convenience sampling between 2012 and 2016. Letters were first sent to school boards to identify elementary schools with a high rate of South Asian enrolment. Once schools were identified, packages containing an invitation letter, a RICH-LEGACY study description and consent forms were sent to parents/guardians of children enrolled in the identified schools. Information stands were also placed at the participating elementary schools before and after school hours to reach out to parents with more information about the study. Additionally, the study was advertised through venues used by South Asian groups including newspapers, local television stations, community centres, worship centres and festivals. Inclusion criteria included: children (in elementary or high school) having at least three grandparents of South Asian origin; and participants being able to provide consent (parents) and assent (children). Research assistants fluent in Hindi and Punjabi were responsible for participant recruitment and data collection. The research assistants who were involved in the measurements all undertook training together through simulator sessions and were retrained if variations in measurement protocol were observed by the research coordinator. This process was repeated for a few days to ensure accuracy and consistency amongst the research assistants in the assessment of the measurements collected in this study. In addition, written materials (including consent forms) were provided in English, Punjabi, Hindi and Urdu as needed.

Participant Assessment

Participants for the RICH-LEGACY study were assessed regarding socio-demographic variables including age, sex and parental education. In certain cases, parents or guardians helped complete certain sections of the child's questionnaire. Children's perception of body image was assessed using Stunkard's silhouettes, a rating scale from one to nine with increases related to increased silhouette size[14], that assesses perception of size and body dissatisfaction. This figure rating scale has been shown to be a valid indicator of determining weight status in children[15]. Feeding practices were assessed using the childhood feeding questionnaire[16]. Exposure to bullying was assessed by asking participants if they had experienced bullying or violence at school. This variable was assessed because of its role as a known stressor in children and its possible impact on pathways known to be involved in BP regulation such as the hypothalamic-pituitary-adrenal (HPA) axis[17]. Additionally, level of acculturation was assessed using the Acculturation Rating Scale for Mexican Americans-II (ARSMA- II) adapted for use in South

Asians by Stigler *et al*[18]. This scale assesses an individual's identification with their heritage based on different domains including language preferences, media preferences, and preferences regarding food and other consumer goods using 24 questions[18]. The adapted questionnaire is grouped into two scales: the Western scale and the traditional scale. The traditional acculturation score measures children's acceptance of traditional Indian cultural attributes while the Westernized acculturation score measures the degree to which South Asian children identify with Western culture.

Participants completed a semi-quantitative food frequency questionnaire (FFQ) that assessed intake of fruits and vegetables and fast foods consumption. The FFQ was adapted from the INTERHEART FFQ, which was validated in an international cohort that included South Asians[19]. Physical activity was assessed using a standardized questionnaire that quantified sports and other activities including leisure, household chores and sedentary factors (screen time and homework) during school and outside of school over the past month. All activities were then expressed as metabolic-equivalent-of-task (MET) minutes. Self-reported exposure to second-hand smoke was assessed to characterize children's passive exposure to smoking and defined as a minimum of five consecutive minutes during which inhalation of other people's smoke occurs. Hand-grip strength, a measure of muscular strength, was measured on the non-dominant hand by study personnel with a Jamar dynamometer utilizing standardized protocol[20].

Anthropometric Characteristics

Height was measured to the nearest 0.1cm using a right angle triangle and a calibrated wall mounted scale. Weight was measured to the nearest 0.1kg with the subject in light clothing using an electronic scale. Body mass index (BMI) was first calculated from weight in kilograms divided by height in meters squared before being converted to z-scores using WHO growth references for young people aged 5-19 years[21].

Waist circumference (WC) was recorded in centimetres as the average of two measures taken halfway between the lower rib margin and the iliac crest against the skin following a normal expiration. Waist circumference was assessed using non-stretching measuring tape by trained team members. Waist-to-height ratio (WtHR) was then calculated by dividing waist circumference by height. Both WC and WtHR were transformed to z scores using published lambda-mu-sigma (LMS) values for age and sex based on the third US National Health and Nutrition Examination Survey (NHANES III)[22]. Transforming the anthropometric measures to z-scores allowed for the standardized comparisons across populations of children of similar ages and sex.

Blood Pressure and Heart Rate

Blood pressure and heart rate were measured in the left arm using the Omron HEM-711DLX automated blood pressure monitor with appropriate sized cuffs following 10 minutes of seated rest. Three BP and heart rate measures were taken over a 10-minute period and the average of the three was recorded. Subsequently, BP was transformed to standard deviation scores and percentiles adjusted for age, sex and height according to the fourth National High Blood Pressure Education Program (NHBPEP) working group in children and adolescents[23]. Systolic and diastolic hypertension were defined using the NHBPEP recommendations as average systolic blood pressure or diastolic blood pressure equal to or greater than the 95th percentile for sex, age and height.

Parental Variables

Parents of the children recruited for this study provided information on parental education (father's and mother's education). In a smaller subset of the South Asian children (n=271), parental history of hypertension (yes or no) was assessed in order to explore the potential impact of heritable factors on children's BP z-scores and hypertension. Father's education was used as a proxy variable for socioeconomic status in this study. Fathers' education levels were categorized as: those with no formal education; those with primary/secondary school education; those with a trade school degree/diploma; and those with a college or university degree. Parent's smoking status was self-reported and categorized as non-smoker, former smoker, or current smoker.

Statistical Analysis

All continuous variables were examined using P-P plots and found to be normally distributed. For descriptive analysis, continuous variables were presented as means and standard deviations while categorical variables were reported as counts and percentages. Independent t-test analysis was used to assess sex differences in continuous variables, while chi-square tests were used to assess sex differences in categorical variables.

To explore the associations among the range of physiological, behavioural and sociodemographic variables with systolic and diastolic BP, unadjusted linear regression was used. These models were then adjusted for potential confounding effect of child age, sex and father's education. These confounders were selected based on their well –documented independent associations with the outcome variable in research studies[11,13]. Although, the conversion of to z-scores provides age and sex adjusted data, we chose to still include age and sex as confounders to adjust for potential residual effects unaccounted for by the reference chart used in this study. Similarly, unadjusted and adjusted (age, sex and father's education) logistic regression analysis was used to explore clinically-relevant associations among the multifactorial variables with systolic and diastolic hypertension. While age and sex were identified as potential confounders in the association between the other variables assessed in this study with BP and hypertension, we also wanted to examine their independent associations with BP and hypertension. To do this, they were each removed from the list of confounders we adjusted for when exploring their effect on BP z-scores and hypertension (i.e., sex was adjusted for age and father's education, while age was adjusted for sex and father's education.)

To address the second study objective, stepwise multiple linear regression analyses were used to identify the combination of risk factors that best explained the variance in BP in South Asian children. The stepwise regression method enables the identification of the aggregate combination of correlates that has the highest contributory effect to the outcome variable. Specifically, for this analysis, we utilized the backward method to select the list of multifactorial correlates that provide significant contribution to the outcome (systolic and diastolic BP z-scores) using an entry criterion of $p < 0.05$ and a removal criterion of $p > 0.10$. The specific list of correlates (age, sex, height, weight, heart rate, BMI z-score, WC z-score, WHtR z-score, parental history of hypertension, parental education, exposure to bullying and violence, traditional and western acculturation scores, physical activity in school and outside school, dietary variables and second-hand smoking) considered for introduction in the backward stepwise regression model were chosen *a priori* based on literature evidence[13] and whether they had a p value <0.05 in unadjusted analysis. Using the aforementioned criteria, the following variables were considered in step-wise regression analysis: age, sex, height, weight, BMI z-score, WC z-score, WHtR z-score, heart rate, western acculturation score, child's perception of body image, and grip strength. In addition to these variables, father's education, daily intake of fast foods and total daily intake were considered in diastolic BP z-score models. The adjusted R squared value for each model provides the combined contribution of the variables in the model to the variance in BP z-scores. The full list of variables initially identified from literature search were also considered in logistic regression models with hypertension. Statistical analysis was done using SPSS version 24.0. P values <0.05 were considered statistically significant. This study was written in line with the Strengthening the Reporting of Observational studies in Epidemiology (STROBE) guidelines[24]

Patient and Public Involvement

The research questions and outcome measures in this study were chosen by this team of researchers and clinicians with extensive experience working with the South Asian population to better understand the potential health risks faced by South Asian children. No patients were involved in setting the research question in development of the research question or study design. There are currently no plans to disseminate the results of this research study to study participants or to the relevant patient population.

RESULTS

This study included 360 boys (47%) and 402 girls ranging from 5.8 to 17.0 years (mean age 9.5 ± 3.0 years), with no statistically significant difference observed for age by sex (table 1). The prevalence of systolic hypertension in this population was 12%. South Asian boys were more physically active outside school than girls (p=0.04); higher WC z-score (p<0.001); higher WHtR z-score (p=0.02); lower heart rate (p=0.047); higher systolic BP z-scores (p=0.001); higher prevalence of systolic hypertension (p=0.01); had lower traditional acculturation score (p=0.02); and significantly higher exposure to bullying and violence at school (p=0.025).

Correlates of Systolic BP and Systolic Hypertension

In unadjusted linear regression analysis with systolic BP z-scores, weight (kg) (β= 0.005, 95% CI= 0.001, 0.01, p=0.022), BMI z-score (β= 0.289, 95% CI= 0.246, 0.333, p<0.001), WC z-score (β= 0.266, 95% CI= 0.213, 0.319, p<0.001), WHtR z-score (β= 0.271, 95% CI= 0.219, 0.324, p<0.001), heart rate (beats per minute) (β= 0.019, 95% CI= 0.015, 0.023, p<0.001), and the child's perception of their body image (using Stunkard's silhouettes) (β= 0.136, 95% CI= 0.083, 0.189, p<0.001) were found to be positively associated with systolic BP z-score. In contrast, we found that compared to male sex, female sex had lower systolic BP z-score (β= -0.246, 95% CI= -0.385, -0.108, p<0.001). Similarly, age (years) (β= -0.060, 95% CI= -0.084, -0.037, p<0.001), children's western acculturation score (β= -0.021, 95% CI= -0.036, -0.006, p=0.007) and height (cm) (β= -0.006, 95% CI= -0.010, -0.002, p=0.007) were negatively associated with systolic BP z-score. After adjustment for confounders, the association between western acculturation attenuated and became non-significant, while the association observed between height and systolic BP z-score became positive. Associations between children's grip strength and daily physical activity in school with systolic BP z-score also became significant upon adjustment (table 2).

In stepwise regression analysis, the combination of age, sex, BMI z-score, heart rate and weight were observed to be the most important correlates of systolic BP z-score, accounting for 30% of the systolic BP z-score variance of South Asian children (Table 3).

In unadjusted logistic regression analysis, female sex was associated with lower odds of developing systolic hypertension (odds ratio (OR) = 0.56, 95% CI= 0.36, 0.87, p=0.011). Associations were also observed with weight (kg) and systolic hypertension (OR= 1.02, 95%

CI= 1.01, 1.04, p<0.001), BMI z-score and systolic hypertension (OR= 2.22, 95% CI= 1.84, 2.68, p<0.001), WC z-score and systolic hypertension (OR= 2.65, 95% CI= 2.06, 3.43, p<0.001) and WHtR z-score and systolic hypertension (OR= 2.47, 95% CI= 1.95, 3.13, p<0.001). Similarly, associations were observed between heart rate (beats per minute) and systolic hypertension (OR=1.04, 95% CI= 1.02, 1.06, p<0.001), child's perception of body image and systolic hypertension (OR= 1.50, 95% CI= 1.25, 1.79, p<0.001) and western acculturation score with systolic hypertension (OR= 0.95, 95% CI=0.90, 1.00, p=0.03). Upon adjustment for confounders, the associations between western acculturation score and systolic hypertension attenuated and became non-significant. The association between grip strength and systolic hypertension became significant upon adjustment (Figure 1).

Correlates of Diastolic BP and Diastolic Hypertension

In unadjusted linear regression analysis of multifactorial variables with diastolic BP z-score, negative associations with diastolic BP z-score were observed between age (years) (β= -0.061, p<0.001), height (cm) (β= -0.009, p<0.001), western acculturation score (β= -0.018, p=0.007), fathers' level of education (β= -0.054, p=0.047), total daily food intake (β= -0.016, p=0.005), fast foods (β= -0.065, p=0.048) and grip strength (kg) (β= -0.019, p<0.001). Conversely, significant positive associations with diastolic BP z-score were observed between heart rate (β= 0.018, p<0.001), BMI z-score (β= 0.156, p<0.001), WC z-score (β= 0.120, p<0.001), WHtR z-score (β= 0.128, p<0.001), and children's perception of their body image (using Stunkard's silhouettes) (β= 0.053, p=0.007). After adjustment for confounders the association between height, western acculturation score, father's level of education, total daily food intake, fast food consumption and grip strength attenuated and became non-significant (Table 2).

In stepwise regression analysis, the combination of age, BMI z-score, heart rate and daily intake of fast foods were observed to be the most important aggregate correlates of diastolic BP z-score, accounting for 23% of the diastolic BP z-score variance of South Asian children (Table 3).

In unadjusted logistic regression analysis, associations were observed between age (years) (OR= 0.71, 95% CI= 0.55, 0.92, p=0.01), height (OR= 0.97, 95% CI= 0.94, 1.00, p=0.04), BMI z-score (OR= 1.68, 95% CI= 1.31, 2.17, p<0.001), WC z-score (OR= 1.89, 95% CI= 1.32, 2.70, p=0.001), WHtR z-score (OR= 1.77, 95% CI= 1.26, 2.47, p=0.001), heart rate (beats per minute) (OR=1.06, 95% CI= 1.03, 1.10, p<0.001) and grip strength (kg) (OR= 0.92, 95% CI= 0.86, 0.99, p=0.024) with diastolic hypertension. Upon adjustment for confounders, the association between height, grip strength and diastolic hypertension attenuated and became non-significant (Figure 2).

DISCUSSION

This study provides information on a range of correlates of systolic and diastolic BP z-scores in a population of South Asian children. While results from unadjusted models highlight the presence of a multifactorial relationship for BP and hypertension, the disappearance of most of the social and lifestyle risk factors upon adjustment highlights the contribution of variables such as age, sex, adiposity, height, heart rate, and grip strength to the risk of elevated BP and hypertension in South Asian children.

It is well documented that the burden of hypertension has precipitously increased in the pediatric population[25]. In addition, some studies have documented higher prevalence of hypertension in certain ethnic groups such as South Asians[11]. Although our sample was based on

convenience and non-representative given that sampling was restricted to two Canadian cities, the prevalence of hypertension in our study at 12% is consistent with age, sex and height adjusted estimates from Jafar *et al*[11] using a nationally-representative survey of Pakistani children age 5 to14 years, but higher than 5.2% prevalence from one cross-sectional study of Indian children ages 5 to 12 years[26]. Our estimates also appear higher than estimates from Canadian children ages 6 to 19 years where 4% of children were said to have hypertension and prehypertension[27]. When stratified by sex, we found significantly higher rates were observed for boys at 15% compared to girls at 9%. This is consistent with results from studies in other children which have reported higher hypertension prevalence in boys[28,29], and results from regression analysis which found female sex to be associated with lower odds of hypertension. This risk differential has been attributed to the presence of an anti-inflammatory immune profile in females and pro-inflammatory profile in males[30] — underscoring the potential for intervention efforts aimed at addressing sex-based disparities.

Consistent with research conducted in South Asian children[11,31] and research conducted in other childhood populations of different ethnicities [28,32–36], we observed positive associations between measures of adiposity and BP and hypertension after adjusting for covariates. The consistency of the association observed across the range of adiposity metrics assessed underscores the significant contribution of increasing adiposity to the prevalence of hypertension in South Asian children. Moreover, the positive association between grip strength (a measure of muscle strength) with systolic BP z-score and hypertension upon adjustment in this study raises questions about the benefits of strength training in children. The benefits of physical activity including aerobic exercise in relation to hypertension remain clear; however, the benefits of strength training in relation to hypertension risk, relative to the benefits of aerobic exercise, appear questionable[37]. It is unclear what might be responsible for the positive effect observed between grip strength and systolic BP z-score; however, findings from our study appear consistent with studies which have explored this association in Chinese[38] and American children[39].

The consistent association between adiposity and hypertension, including the higher prevalence of hypertension in this population, reinforces their connections through a range of complex mechanistic pathways. Some of these pathways involve the activation of the renin-angiotensin-aldosterone system (RAAS) or sympathetic nervous system. Specifically, the South Asian phenotype of higher body fat[7]—especially the visceral type which has been identified in adults[6]—when compared to their Caucasian peers, could activate the formation of pro-inflammatory cytokines such as Interleukin 6 (IL-6) which results in physiological changes that could lead to endothelial and vascular dysfunction through the development of insulin resistance[40], resulting in an increased predisposition for hypertension. The positive association between height and BP in this population could be explained by cerebral perfusion requirements where higher BP is needed in taller people to achieve optimal cerebral perfusion owing to hydrostatic pressure differences in taller and shorter individuals[41]. However, more research in South Asian children is warranted to corroborate our findings given the difference observed in direction of association in unadjusted and adjusted models.

The positive association we found between the child's perception of body image and BP may be due to this variable mirroring children's weight status or conversely, a marker for a graded increase in stress levels, owing to societal criticism of fatter body types, which could have insidious effects for hypertension risk through its impact on the neuro-endocrine system[42]. Additionally, a range of social and lifestyle variables were also found to be associated with BP z-score in unadjusted analysis but became non-significant upon adjustment for confounders. While results from unadjusted associations may demonstrate links between risk factor and outcome, the disappearance of the association upon adjustment for socio-demographic variables highlights the links between these variables and suggests that the pathway linking these factors with BP might be interdependent.

The stepwise regression model shows that correlates from this study explained only about 30% of the variance of systolic BP z-score and 23% of the variability of diastolic BP z-scores. It is possible that some of this unexplained variance might be explained by genetics, as it has been suggested that about 30% to 60% of the variance in BP may be heritable[43,44]. Yet the lack of association between parental hypertension and child BP in the subset of parents of participants who provided this data would appear to contradict these findings for this population of South Asian children. However, it is likely that the subset of parents of child participants who provided this information might not be completely representative of the entire cohort, thereby biasing the results. Still, even accounting for potential genetic contributions, a significant amount of the BP variance remains unexplained. More research is needed to provide insight regarding the contributory effects of other potential variables that might contribute to risk of elevated BP in South Asian children.

Notably, null associations were also observed for certain variables in this study that have been found to be significantly associated with BP and hypertension in other child populations. For example, parental history of hypertension, dietary factors (such as consumption of fruit and vegetables) and exposure to second hand smoking have been linked in other studies to child BP but had no significant impact in this study. This could be reflective of the potential biases associated with using self-reports or may highlight how interactions between genes and environment/lifestyle shape risk factor susceptibilities — underscoring the need for more ethnic-based and ethnic comparison studies when exploring risk associations.

Study Limitations

This study has limitations. First, although we sought to recruit a representative sample of urban South Asian children, it was not a random sample. However, there is likely to be minimal effect on the relationships between the ranges of risk factors evaluated in this study. Second, this is a cross-sectional study and is therefore unable to provide insights into causal associations between the risk factor variables and long term CVD risk in South Asian children. Third, potential recall biases may have occurred as a result of using self-report data for some of the variables including diet and physical activity measures. Fourth, the use of father's education as a measure of socioeconomic status pose limitations. Variables like household income would have been preferred, however only a subset of participants provided data on household income, thus its use would have excluded a significant portion of children in this study. However, as a means to confirm the results, we separately adjusted for mother's education and no deviation in study results was observed. Last, the lack of data collection on sexual maturity status could potential confound the study results obtained here. However, the adjustment for age in this study, which acts as a proxy variable for sexual maturity might help mitigate the bias. These limitations are in part addressed by strengths of this study which lies in its large sample size of South Asian children and in the wide range of risk factors examined.

Implications

Our findings underscore a range of factors that may contribute to risk of elevated BP and hypertension in South Asian children. Consequently, public health interventions such as those that emphasize prevention such as population-based health education and lifestyle modification that considers unique cultural contexts may provide significant potential in addressing the burden of hypertension in this population. There are also implications for clinical settings. Specifically, our findings suggest that while South Asian children may benefit from interventions aimed at reducing obesity to address the comparatively higher burden of hypertension in this population, there are certain sub-groups who could benefit from more targeted preventive interventions in primary care settings — such as males, children with increased adiposity, taller children, and children with increased heart rate, or children with a combination of these factors.

CONCLUSION

In this group of South Asian children, we found associations between a range of physiological, social and lifestyle factors with BP z-scores and hypertension. However, upon adjustment for confounders, physiological variables such as age, sex, height, adiposity and heart rate remained consistently associated with BP and hypertension, and provided the strongest explanatory effect for the variance in BP. Given the sequelae associated with elevated BP, including BP tracking from childhood into adulthood, these results provide evidence on modifiable risk factors that might be targeted by prevention strategies in primary care to reduce the burden of high BP and hypertension in South Asian children.

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All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

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Data sharing statement: Raw data are held by the lead author of the study in accordance with ethics guidelines.

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Table 1: Sociodemographic, anthropometric, risk factor characteristics of South Asian children stratified by sex.

	Total (n=762)	Boy (n=360)	Girl (n=402)	p value
Age (years)	9.5 ± 3.0	9.3 ± 2.8	9.7 ± 3.1	0.09
Paternal education				0.92
No formal education	5 (1%)	3 (1%)	2 (1%)	
Primary education	247 (34%)	115 (34%)	132 (35%)	
Trade school	21 (3%)	9 (3%)	12 (3%)	
College/university	444 (62%)	209 (62%)	235 (62%)	
Maternal education				0.363
No formal education	5 (1%)	4 (1%)	1 (0%)	
Primary education	223 (30%)	103 (30%)	120 (31%)	
Trade school	6 (1%)	4 (1%)	2 (1%)	
College/university	503 (68%)	235 (68%)	268 (69%)	
Acculturation score (western)	34.8 ± 4.7	34.6 ± 4.62	34.9 ± 4.74	0.426
Acculturation score (traditional)	26.7 ± 4.43	26.3 ± 4.35	27.1 ± 4.48	0.02
Daily physical activity in school (METmins/day)	35.7 ± 25.8	36.8 ± 27.0	34.8 ± 24.7	0.288
Daily physical activity outside school (METmins/day)	15.9 ± 33.9	18.5 ± 31.3	13.5 ± 35.9	0.04
Daily intake- servings of fruit and vegetables (daily mean intake)	3.16 ± 1.86	3.11 ± 1.81	3.21 ± 1.91	0.485
Daily intake- servings of fast foods (daily mean intake)	0.91 ± 0.78	0.86 ± 0.59	0.97 ± 0.91	0.067
Total daily intake- servings	12.0 ± 4.48	12.2 ± 4.9	11.8 ± 4.1	0.243
Exposure to bullying/violence at school				0.025
Yes	233 (34%)	126 (38%)	107 (30%)	

No	459 (66%)	207 (62%)	252 (70%)	
Exposure to second hand smoking*				0.616
None	712 (94%)	336 (94%)	376 (94%)	
1-2 times/week	33 (4%)	16 (5%)	17 (4%)	
3-6 times/week	5 (1%)	2 (1%)	3 (1%)	
At least once a day	7 (1%)	5 (1%)	2 (1%)	
2-3 times/day	1 (0%)	0 (0%)	1 (0%)	
Mother's history of hypertension				0.047
Yes	12 (4%)	9 (7%)	3 (2%)	
No	280 (96%)	128 (93%)	152 (98%)	
Father's history of hypertension				0.979
Yes	30 (10%)	14 (10%)	16 (10%)	
No	260 (90%)	122 (90%)	138 (90%)	
Height (cm)	138.3 ± 16.5	139.1 ± 17.6	137.7 ± 15.5	0.22
Weight (kg)	36.5 ± 15.8	36.9 ± 16.5	36.1 ± 15.3	0.46
BMI Z score	0.48 ± 1.44	0.57 ± 1.61	0.40 ± 1.28	0.11
WC Z score	-0.06 ± 1.23	0.11 ± 0.36	-0.21 ± 1.24	<0.001
WHtR Z score	-0.38 ± 1.24	-0.27 ± 1.27	-0.48 ± 1.21	0.02
Heart rate	87 ± 12	86 ± 12	87 ± 13	0.047
SBP Z score	0.57 ± 0.97	0.70 ± 0.99	0.46 ± 0.95	0.001
DBP Z score	0.37 ± 0.71	0.35 ± 0.68	0.39 ± 0.73	0.41
SBP (non-transformed)	109 ± 11	111 ± 12	107± 10	<0.001

DBP (non-transformed)	65 ± 8	65 ± 8	65 ± 8	0.849
Systolic hypertension	90 (12%)	54 (15%)	36 (9%)	0.01
Diastolic hypertension	31 (4%)	13 (4%)	18 (5%)	0.55

**Exposure defined as a minimum of five consecutive minutes during which inhalation of other people's smoke occurs*

BP=Blood pressure, BMI=body mass index, WC= waist circumference, WHtR= waist to height ratio, SBP= systolic blood pressure, DBP= diastolic blood pressure

1 Table 2: Adjusted linear regression between multifactorial risk factors with systolic and diastolic
2 BP z scores

	Systolic BP z score	Diastolic BP z score
Age[a]	-0.054 (-0.078, -0.029), p<0.001	-0.057 (-0.075, -0.039), p<0.001
Female sex (vs Male)[b]	-0.208 (-0.350, -0.067), p=0.004	0.078 (-0.023, 0.179), p=0.132
Height	0.022 (0.011, 0.033), p<0.001	0.007 (-0.001, 0.015), p=0.077
Weight	0.047 (0.040, 0.055), p<0.001	0.022 (0.016, 0.027), p<0.001
BMI z score	0.292 (0.249, 0.336), p<0.001	0.160 (0.127, 0.193), p<0.001
WC z score	0.273 (0.219, 0.326), p<0.001	0.137 (0.098, 0.177), p<0.001
WHtR z score	0.289 (0.236, 0.342), p<0.001	0.153 (0.114, 0.192), p<0.001
Heart rate	0.016 (0.010, 0.022), p<0.001	0.015 (0.011, 0.019), p<0.001
Acculturation (western score)	-0.010 (-0.026, 0.006), p=0.211	-0.005 (-0.016, 0.006), p=0.373
Acculturation (traditional score)	0.010 (-0.006, 0.026), p=0.227	0.003 (-0.008, 0.015), p=0.582
Child's perception of body image	0.183 (0.128, 0.239), p<0.001	0.104 (0.064, 0.144), p<0.001
Exposure to bullying/violence at school	0.021 (-0.138, 0.181), p=0.794	-0.071 (-0.183, 0.042), p=0.218
Father's smoking status	0.118 (-0.056, 0.292), p=0.184	0.082 (-0.053, 0.218), p=0.233
Exposure to second hand smoke	-0.052 (-0.240, 0.136), p=0.587	0.018 (-0.117, 0.152), p=0.795
Father's history of	-0.127 (-0.484, 0.230), p=0.484	-0.063 (-0.336, 0.209), p=0.648

hypertension		
Mother's history of hypertension	-0.003 (-0.524, 0.518), p=0.991	0.354 (-0.042, 0.750), p=0.079
Grip strength (non-dominant hand)	0.025 (0.007, 0.043), p=0.007	0.006 (-0.007, 0.019), p=0.381
Daily physical activity in school (METmins/day)	0.005 (0.002, 0.008), p=0.003	0.003 (0.001, 0.005), p=0.009
Daily physical activity outside school (METmins/day)	0.001 (-0.001, 0.003), p=0.363	0.000 (-0.002, 0.002), p=0.994
Daily intake- fruit and vegetables (daily mean intake)	-0.008 (-0.049, 0.033), p=0.717	-0.011 (-0.040, 0.018), p=0.466
Daily intake-fast foods (daily mean intake)	0.004 (-0.086, 0.093), p=0.937	-0.053 (-0.117, 0.011), p=0.104

Model adjusted for age, sex and father's education
Values presented are β (95% confidence intervals), and p values
BMI= body mass index, WC= waist circumference, WHtR= waist to height ratio, BP =blood pressure, MET=Metabolic equivalent of task
[a]*Age was adjusted for sex and father's education*
[b]*Sex was for adjusted for age and father's education*

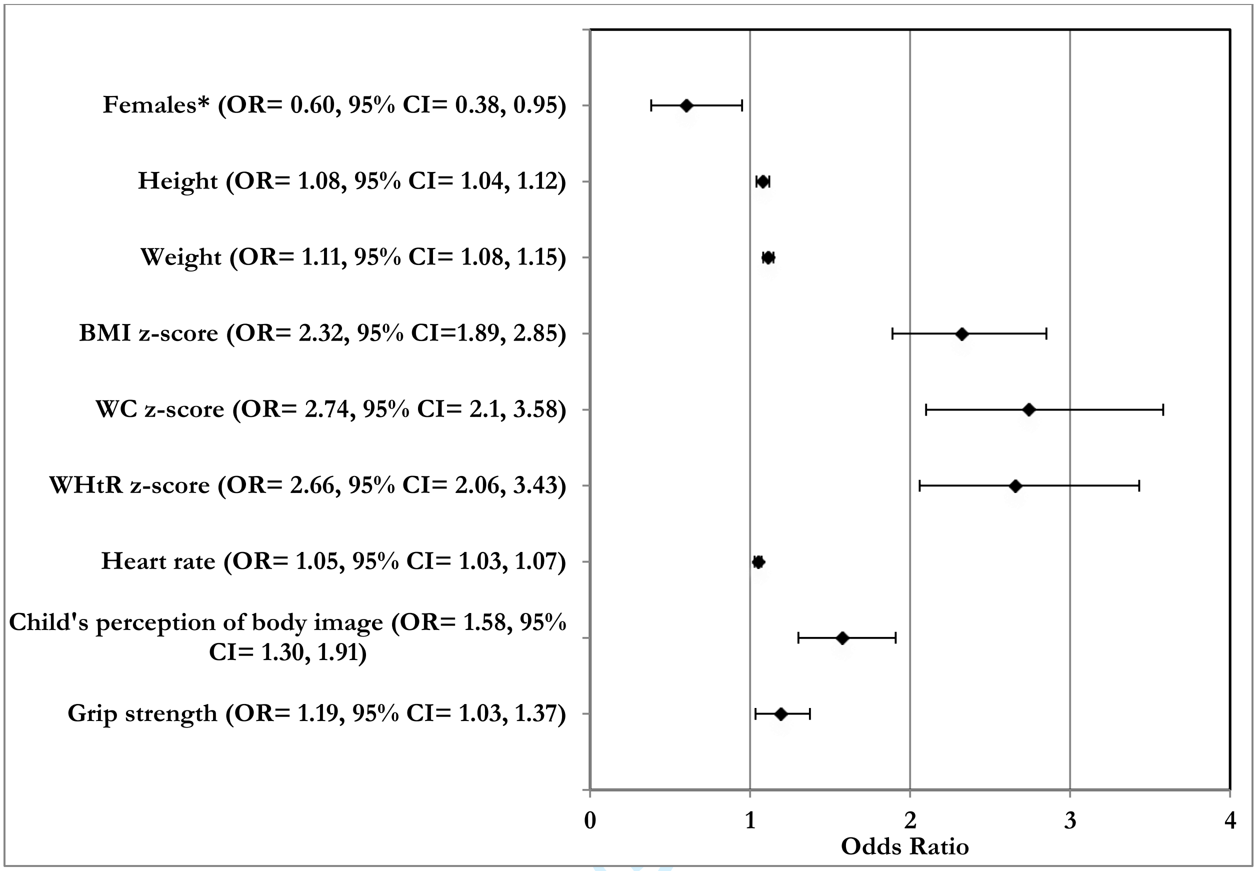
Table 3: Stepwise linear regression analysis showing the aggregate correlates of BP z-score in South Asian children

Stepwise multiple linear regression models					
	Variable	B	95%	P value	Adjusted R^2
Systolic BP z-score	Child's age	-0.132	-0.202 -0.062	<0.001	
	Sex	-0.293	-0.461, -0.126	0.001	
	BMI z-score	0.125	0.022, 0.228	0.017	
	Heart rate	0.014	0.007, 0.021	<0.001	
	Weight	0.027	0.012, 0.041	<0.001	
					0.294
Diastolic BP z-score	Child's age	-0.027	-0.048, -0.007	0.01	
	BMI z-score	0.125	0.081, 0.170	<0.001	
	Heart rate	0.015	0.010, 0.021	<0.001	
	Daily fast food intake	-0.013	-0.028, 0.001	0.072	
					0.228

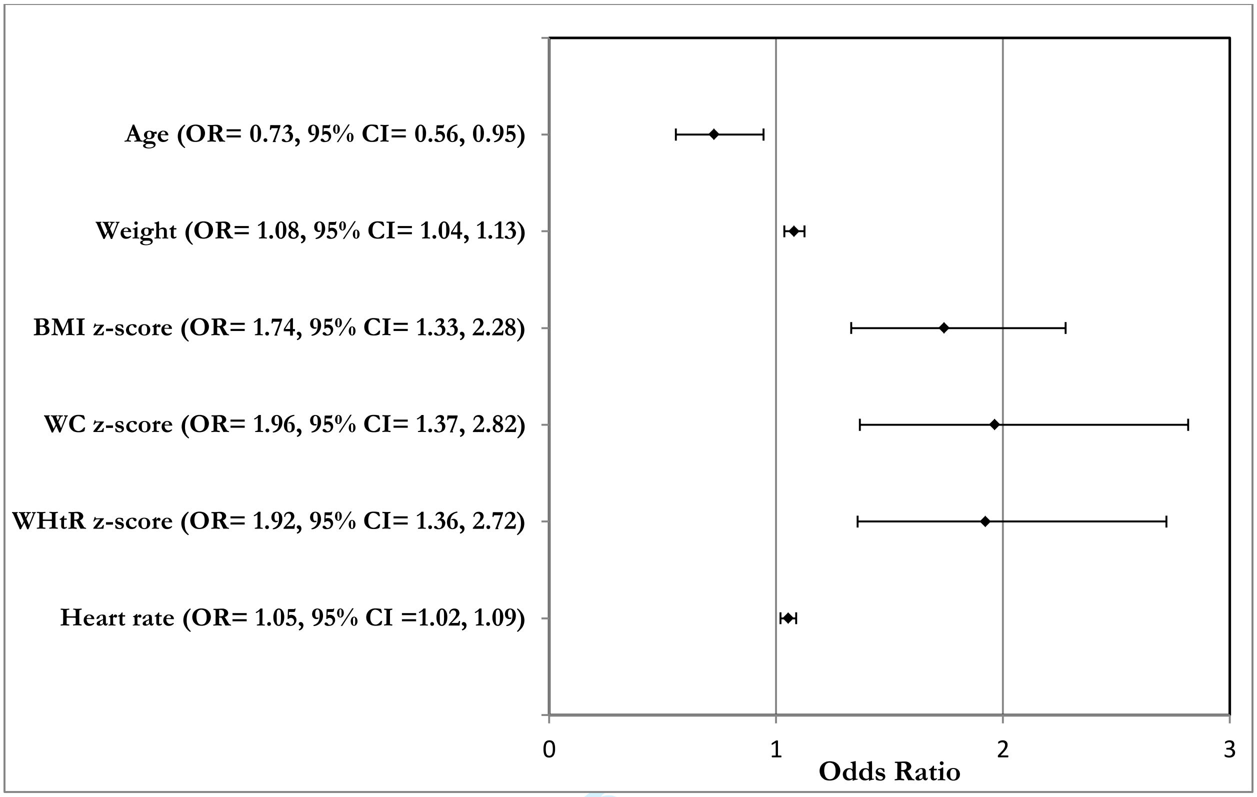
BMI=body mass index, BP= blood pressure

Figure 1: Adjusted odds ratio for the association between the multifactorial variables with systolic hypertension

Figure 2: Adjusted odds ratio for the association between the multifactorial variables with diastolic hypertension



Model adjusted for age, sex and father's education
Values presented are odds ratio (95% confidence intervals)
BMI= body mass index, WC= waist circumference, WHtR= waist to height ratio, BP =blood pressure
**compared to males*



Model adjusted for age, sex and father's education
Values presented are odds ratio (95% confidence intervals)
BMI= body mass index, WC= waist circumference, WHtR= waist to height ratio, BP =blood pressure

STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1-2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	3	State specific objectives, including any prespecified hypotheses	3-4
Methods			
Study design	4	Present key elements of study design early in the paper	4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	4
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5-8
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	*5-8*
Bias	9	Describe any efforts to address potential sources of bias	5
Study size	10	Explain how the study size was arrived at	
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	8
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	8-9
		(*b*) Describe any methods used to examine subgroups and interactions	N/A
		(*c*) Explain how missing data were addressed	7
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	N/A
		(*e*) Describe any sensitivity analyses	N/A
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	9
		(b) Give reasons for non-participation at each stage	N/A
		(c) Consider use of a flow diagram	N/A
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	9
		(b) Indicate number of participants with missing data for each variable of interest	24
Outcome data	15*	Report numbers of outcome events or summary measures	9
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	8-11

		(*b*) Report category boundaries when continuous variables were categorized	N/A
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	N/A
Discussion			
Key results	18	Summarise key results with reference to study objectives	12
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	16
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	17
Generalisability	21	Discuss the generalisability (external validity) of the study results	16
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	18

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Multifactorial correlates of blood pressure in South Asian children in Canada: a cross-sectional study

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Multifactorial correlates of blood pressure in South Asian children in Canada: a cross-sectional study.

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ABSTRACT

Objective: We sought to explore various correlates of BP and hypertension, and to identify the most important aggregate combination of correlates for BP in South Asian children.

Design: Cross-sectional study

Setting: Community-based recruitment in two Canadian cities

Participants: South Asian children (n=762) provided a range of physiological, lifestyle and social variables. BP was assessed using an automated device. Body mass index (BMI), waist circumference (WC), waist-to-height ratio (WHtR) and BP were transformed to z-scores using published standards.

Outcome measures: Linear and logistic regression analyses were used to explore associations between the range of variables with BP z-scores and hypertension while stepwise regression was used to identify aggregate factors that provided explanatory capacity for systolic BP (SBP) and diastolic BP (DBP) z-scores.

Results: A range of variables were associated with BP z-score and hypertension in unadjusted analysis. Upon adjustment for confounders, the association between age (β =-0.054, 95% CI -0.078, 0.029, female sex (β= -0.208, 95% CI= -0.350, -0.067), height (β= 0.022, 95% CI= 0.011, 0.033), weight (β= 0.047, 95% CI= 0.040, 0.055) BMI z-score (β= 0.292, 95% CI 0.249, 0.336), WC z-score (β= 0.273, 95% CI= 0.219, 0.326), WHtR z-score (β= 0.289, 95% CI= 0.236, 0.342), heart rate (β= 0.016, 95% CI= 0.010, 0.022), child's perception of body image (β= 0.183, 95% CI= 0.128, 0.239) and grip strength (β= 0.025, 95% CI= 0.007, 0.043) with SBP z-score remained. In stepwise regression, age, sex, BMI z-score, heart rate and weight accounted for

30% of the variance of SBP z-score, while age, BMI z-score, heart rate and daily fast food intake accounted for 23% of the DBP z-score variance.

Conclusion: Our findings suggest that variables such as age, sex, height, adiposity, and heart rate provide stronger explanatory capacity to BP variance and hypertension risk than other variables in South Asian children.

ARTICLE SUMMARY

Strengths and limitations of this study

- The strengths of this study includes its large sample size of South Asian children and,
- Its examination of a wide range of physiological, lifestyle and social risk factors in relation to BP z-scores and hypertension in South Asian children.
- Limitations of the study includes its cross-sectional design which limits the attribution of causality.

INTRODUCTION

South Asians comprise approximately 25% of the world's global population[1] and represent a significant portion of the visible ethnic minority groups in countries such as Canada, the United Kingdom and the United States (US) [2–4]. Individuals of South Asian origin are known to be at increased risk of cardiovascular disease (CVD) relative to other ethnic groups in Western countries[5,6]. These differences in CVD risk have also been shown to be present in South Asian children, suggesting that the risk differential in CVD risk factors and events experienced by this ethnic group starts from an early age[7].

One of the major physiological risk factors for CVDs is high blood pressure (BP) or hypertension[8]. Hypertension is also associated with an increased risk for stroke and kidney disease[8]. Moreover, multiple studies have shown that high BP in childhood typically continues into adulthood[9] — including in South Asian populations[10]. These findings suggest that it is important to prevent hypertension in childhood in order to address the potential cardiovascular and metabolic sequelae later in life.

In South Asian children, studies have demonstrated increased prevalence of hypertension or higher BP levels relative to other ethnic groups[11,12]. While there is evidence suggesting a disproportionately higher BP burden for South Asians, the exact factors implicated are relatively unclear. Given the fact that causes of high BP are known to be multifactorial[8], it is important to understand the various risk factors that might be responsible for the increased risk of high BP in South Asian children in general. Using a range of multifactorial variables (i.e. variables across a range of different factors) that were identified in a recently published systematic review of children to be correlated with BP and hypertension in other children population groups[13], this study therefore aims: 1) to explore the associations between physiological (factors relating to biology), lifestyle (factors relating to behaviour) and social factors (factors relating to conditions in which people live, attend school, grow, and develop) and BP in South Asian children; and 2) to identify the most important aggregate correlates of BP in South Asian children.

METHODS

Study Design

Participants included in this study were recruited as part of the Research in International Cardiovascular Health - Lifestyles, Environments and Genetic Attributes in Children and Youth (RICH-LEGACY) study. This cross-sectional study is designed to investigate risk factors for CVD across South Asian children in Canada. The study was approved by the Simon Fraser University Research Ethics Board (REB), Providence Health Care REB, and the Hamilton Integrated REB. Parents of participants provided written informed consent, while participants assented to take part in the study.

Recruitment

Elementary school and high-school children (n= 762) were recruited using community-based methods in two Canadian cities (Brampton, Ontario and Surrey, British Columbia) by convenience sampling between 2012 and 2016. Letters were first sent to school boards to identify elementary schools with a high rate of South Asian enrolment. Once schools were identified, packages containing an invitation letter, a RICH-LEGACY study description and consent forms were sent to parents/guardians of children enrolled in the identified schools. Information stands were also placed at the participating elementary schools before and after school hours to reach out to parents with more information about the study. Additionally, the study was advertised through venues used by South Asian groups including newspapers, local television stations, community centres, worship centres and festivals. Inclusion criteria included: children (in elementary or high school) having at least three grandparents of South Asian origin; and participants being able to provide consent (parents) and assent (children). Research assistants fluent in Hindi and Punjabi were responsible for participant recruitment and data collection. The research assistants who were involved in the measurements all undertook training together through simulator sessions and were retrained if variations in measurement protocol were observed by the research coordinator. This process was repeated for a few days to ensure accuracy and consistency amongst the research assistants in the assessment of the measurements collected in this study. In addition, written materials (including consent forms) were provided in English, Punjabi, Hindi and Urdu as needed.

Participant Assessment

Participants for the RICH-LEGACY study were assessed regarding socio-demographic variables including age, sex and parental education. In certain cases, parents or guardians helped complete certain sections of the child's questionnaire. Children's perception of body image was assessed using Stunkard's silhouettes, a rating scale from one to nine with increases related to increased silhouette size[14], that assesses perception of size and body dissatisfaction. This figure rating scale has been shown to be a valid indicator of determining weight status in children[15]. Feeding practices were assessed using the childhood feeding questionnaire[16]. Exposure to bullying was assessed by asking participants if they had experienced bullying or violence at school. This variable was assessed because of its role as a known stressor in children and its possible impact on pathways known to be involved in BP regulation such as the hypothalamic-pituitary-adrenal (HPA) axis[17]. Additionally, level of acculturation was assessed using the Acculturation Rating Scale for Mexican Americans-II (ARSMA- II) adapted for use in South

Asians by Stigler *et al*[18]. This scale assesses an individual's identification with their heritage based on different domains including language preferences, media preferences, and preferences regarding food and other consumer goods using 24 questions[18]. The adapted questionnaire is grouped into two scales: the Western scale and the traditional scale. The traditional acculturation score measures children's acceptance of traditional Indian cultural attributes while the Westernized acculturation score measures the degree to which South Asian children identify with Western culture.

Participants completed a semi-quantitative food frequency questionnaire (FFQ) that assessed intake of fruits and vegetables and fast foods consumption. The FFQ was adapted from the INTERHEART FFQ, which was validated in an international cohort that included South Asians[19]. Physical activity was assessed using a standardized questionnaire that quantified sports and other activities including leisure, household chores and sedentary factors (screen time and homework) during school and outside of school over the past month. All activities were then expressed as metabolic-equivalent-of-task (MET) minutes. Self-reported exposure to second-hand smoke was assessed to characterize children's passive exposure to smoking and defined as a minimum of five consecutive minutes during which inhalation of other people's smoke occurs. Hand-grip strength, a measure of muscular strength, was measured on the non-dominant hand by study personnel with a Jamar dynamometer utilizing standardized protocol[20].

Anthropometric Characteristics

Height was measured to the nearest 0.1cm using a right angle triangle and a calibrated wall mounted scale. Weight was measured to the nearest 0.1kg with the subject in light clothing using an electronic scale. Body mass index (BMI) was first calculated from weight in kilograms divided by height in meters squared before being converted to z-scores using WHO growth references for young people aged 5-19 years[21].

Waist circumference (WC) was recorded in centimetres as the average of two measures taken halfway between the lower rib margin and the iliac crest against the skin following a normal expiration. Waist circumference was assessed using non-stretching measuring tape by trained team members. Waist-to-height ratio (WtHR) was then calculated by dividing waist circumference by height. Both WC and WtHR were transformed to z scores using published lambda-mu-sigma (LMS) values for age and sex based on the third US National Health and Nutrition Examination Survey (NHANES III)[22]. Transforming the anthropometric measures to z-scores allowed for the standardized comparisons across populations of children of similar ages and sex.

Blood Pressure and Heart Rate

Blood pressure and heart rate were measured in the left arm using the Omron HEM-711DLX automated blood pressure monitor with appropriate sized cuffs following 10 minutes of seated rest. Three BP and heart rate measures were taken over a 10-minute period and the average of the three was recorded. Subsequently, BP was transformed to standard deviation scores and percentiles adjusted for age, sex and height according to the fourth National High Blood Pressure Education Program (NHBPEP) working group in children and adolescents[23]. Systolic and diastolic hypertension were defined using the NHBPEP recommendations as average systolic blood pressure or diastolic blood pressure equal to or greater than the 95th percentile for sex, age and height.

Parental Variables

Parents of the children recruited for this study provided information on parental education (father's and mother's education). In a smaller subset of the South Asian children (n=271), parental history of hypertension (yes or no) was assessed in order to explore the potential impact of heritable factors on children's BP z-scores and hypertension. Father's education was used as a proxy variable for socioeconomic status in this study. Fathers' education levels were categorized as: those with no formal education; those with primary/secondary school education; those with a trade school degree/diploma; and those with a college or university degree. Parent's smoking status was self-reported and categorized as non-smoker, former smoker, or current smoker.

Statistical Analysis

All continuous variables were examined using P-P plots and found to be normally distributed. For descriptive analysis, continuous variables were presented as means and standard deviations while categorical variables were reported as counts and percentages. Independent t-test analysis was used to assess sex differences in continuous variables, while chi-square tests were used to assess sex differences in categorical variables.

To explore the associations among the range of physiological, lifestyle and social variables with systolic and diastolic BP, unadjusted linear regression was used. These models were then adjusted for potential confounding effect of child age, sex and father's education. These confounders were selected based on their well –documented independent associations with the outcome variable in research studies[11,13]. Although, the conversion of to z-scores provides age and sex adjusted data, we chose to still include age and sex as confounders to adjust for potential residual effects unaccounted for by the reference charts used in this study. Similarly, unadjusted and adjusted (age, sex and father's education) logistic regression analysis was used to explore clinically-relevant associations among the multifactorial variables with systolic and diastolic hypertension. While age and sex were identified as potential confounders in the association between the other variables assessed in this study with BP and hypertension, we also wanted to examine their independent associations with BP and hypertension. To do this, they were each removed from the list of confounders we adjusted for when exploring their effect on BP z-scores and hypertension (i.e., sex was adjusted for age and father's education, while age was adjusted for sex and father's education.)

To address the second study objective, stepwise multiple linear regression analyses were used to identify the combination of risk factors that best explained the variance in BP in South Asian children. The stepwise regression method enables the identification of the aggregate combination of correlates that has the highest contributory effect to the outcome variable. Specifically, for this analysis, we utilized the backward method to select the list of multifactorial correlates that provide significant contribution to the outcome (systolic and diastolic BP z-scores) using an entry criterion of $p < 0.05$ and a removal criterion of $p > 0.10$. The specific list of correlates (age, sex, height, weight, heart rate, BMI z-score, WC z-score, WHtR z-score, parental history of hypertension, parental education, exposure to bullying and violence, traditional and western acculturation scores, physical activity in school and outside school, dietary variables and second-hand smoking) considered for introduction in the backward stepwise regression model were chosen *a priori* based on literature evidence[13] and whether they had a p value <0.05 in unadjusted analysis. Using the aforementioned criteria, the following variables were considered in step-wise regression analysis: age, sex, height, weight, BMI z-score, WC z-score, WHtR z-score, heart rate, western acculturation score, child's perception of body image, and grip strength. In addition to these variables, father's education, daily intake of fast foods and total daily intake were considered in diastolic BP z-score models. The adjusted R squared value for each model provides the combined contribution of the variables in the model to the variance in BP z-scores. The full list of variables initially identified from literature search were also considered in logistic regression models with hypertension. Statistical analysis was done using SPSS version 24.0. P values <0.05 were considered statistically significant. This study was written in line with the Strengthening the Reporting of Observational studies in Epidemiology (STROBE) guidelines[24]

Patient and Public Involvement

The research questions and outcome measures in this study were chosen by this team of researchers and clinicians with extensive experience working with the South Asian population to better understand the potential health risks faced by South Asian children. No patients were involved in setting the research question in development of the research question or study design. There are currently no plans to disseminate the results of this research study to study participants or to the relevant patient population.

RESULTS

This study included 360 boys (47%) and 402 girls ranging from 5.8 to 17.0 years (mean age 9.5 ± 3.0 years), with no statistically significant difference observed for age by sex (table 1). The prevalence of systolic hypertension in this population was 12%. South Asian boys were more physically active outside school than girls (p=0.04); higher WC z-score (p<0.001); higher WHtR z-score (p=0.02); lower heart rate (p=0.047); higher systolic BP z-scores (p=0.001); higher prevalence of systolic hypertension (p=0.01); had lower traditional acculturation score (p=0.02); and significantly higher exposure to bullying and violence at school (p=0.025).

Correlates of Systolic BP and Systolic Hypertension

In unadjusted linear regression analysis with systolic BP z-scores, weight (kg) (β= 0.005, 95% CI= 0.001, 0.01, p=0.022), BMI z-score (β= 0.289, 95% CI= 0.246, 0.333, p<0.001), WC z-score (β= 0.266, 95% CI= 0.213, 0.319, p<0.001), WHtR z-score (β= 0.271, 95% CI= 0.219, 0.324, p<0.001), heart rate (beats per minute) (β= 0.019, 95% CI= 0.015, 0.023, p<0.001), and the child's perception of their body image (using Stunkard's silhouettes) (β= 0.136, 95% CI= 0.083, 0.189, p<0.001) were found to be positively associated with systolic BP z-score. In contrast, we found that compared to male sex, female sex had lower systolic BP z-score (β= -0.246, 95% CI= -0.385, -0.108, p<0.001). Similarly, age (years) (β= -0.060, 95% CI= -0.084, -0.037, p<0.001), children's western acculturation score (β= -0.021, 95% CI= -0.036, -0.006, p=0.007) and height (cm) (β= -0.006, 95% CI= -0.010, -0.002, p=0.007) were negatively associated with systolic BP z-score. After adjustment for confounders, the association between western acculturation attenuated and became non-significant, while the association observed between height and systolic BP z-score became positive. Associations between children's grip strength and daily physical activity in school with systolic BP z-score also became significant upon adjustment (table 2).

In stepwise regression analysis, the combination of age, sex, BMI z-score, heart rate and weight were observed to be the most important correlates of systolic BP z-score, accounting for 30% of the systolic BP z-score variance of South Asian children (Table 3).

In unadjusted logistic regression analysis, female sex was associated with lower odds of developing systolic hypertension (odds ratio (OR) = 0.56, 95% CI= 0.36, 0.87, p=0.011). Associations were also observed with weight (kg) and systolic hypertension (OR= 1.02, 95%

CI= 1.01, 1.04, p<0.001), BMI z-score and systolic hypertension (OR= 2.22, 95% CI= 1.84, 2.68, p<0.001), WC z-score and systolic hypertension (OR= 2.65, 95% CI= 2.06, 3.43, p<0.001) and WHtR z-score and systolic hypertension (OR= 2.47, 95% CI= 1.95, 3.13, p<0.001). Similarly, associations were observed between heart rate (beats per minute) and systolic hypertension (OR=1.04, 95% CI= 1.02, 1.06, p<0.001), child's perception of body image and systolic hypertension (OR= 1.50, 95% CI= 1.25, 1.79, p<0.001) and western acculturation score with systolic hypertension (OR= 0.95, 95% CI=0.90, 1.00, p=0.03). Upon adjustment for confounders, the associations between western acculturation score and systolic hypertension attenuated and became non-significant. The association between grip strength and systolic hypertension became significant upon adjustment (Figure 1).

Correlates of Diastolic BP and Diastolic Hypertension

In unadjusted linear regression analysis of multifactorial variables with diastolic BP z-score, negative associations with diastolic BP z-score were observed between age (years) (β= -0.061, p<0.001), height (cm) (β= -0.009, p<0.001), western acculturation score (β= -0.018, p=0.007), fathers' level of education (β= -0.054, p=0.047), total daily food intake (β= -0.016, p=0.005), fast foods (β= -0.065, p=0.048) and grip strength (kg) (β= -0.019, p<0.001). Conversely, significant positive associations with diastolic BP z-score were observed between heart rate (β= 0.018, p<0.001), BMI z-score (β= 0.156, p<0.001), WC z-score (β= 0.120, p<0.001), WHtR z-score (β= 0.128, p<0.001), and children's perception of their body image (using Stunkard's silhouettes) (β= 0.053, p=0.007). After adjustment for confounders the association between height, western acculturation score, father's level of education, total daily food intake, fast food consumption and grip strength attenuated and became non-significant (Table 2).

In stepwise regression analysis, the combination of age, BMI z-score, heart rate and daily intake of fast foods were observed to be the most important aggregate correlates of diastolic BP z-score, accounting for 23% of the diastolic BP z-score variance of South Asian children (Table 3).

In unadjusted logistic regression analysis, associations were observed between age (years) (OR= 0.71, 95% CI= 0.55, 0.92, p=0.01), height (OR= 0.97, 95% CI= 0.94, 1.00, p=0.04), BMI z-score (OR= 1.68, 95% CI= 1.31, 2.17, p<0.001), WC z-score (OR= 1.89, 95% CI= 1.32, 2.70, p=0.001), WHtR z-score (OR= 1.77, 95% CI= 1.26, 2.47, p=0.001), heart rate (beats per minute) (OR=1.06, 95% CI= 1.03, 1.10, p<0.001) and grip strength (kg) (OR= 0.92, 95% CI= 0.86, 0.99, p=0.024) with diastolic hypertension. Upon adjustment for confounders, the association between height, grip strength and diastolic hypertension attenuated and became non-significant (Figure 2).

DISCUSSION

This study provides information on a range of correlates of systolic and diastolic BP z-scores in a population of South Asian children. While results from unadjusted models highlight the presence of a multifactorial relationship for BP and hypertension, the disappearance of most of the social and lifestyle risk factors upon adjustment highlights the contribution of variables such as age, sex, adiposity, height, heart rate, and grip strength to the risk of elevated BP and hypertension in South Asian children.

It is well documented that the burden of hypertension has precipitously increased in the pediatric population[25]. In addition, some studies have documented higher prevalence of hypertension in certain ethnic groups such as South Asians[11]. Although our sample was based on

convenience and non-representative given that sampling was restricted to two Canadian cities, the prevalence of hypertension in our study at 12% is consistent with age, sex and height adjusted estimates from Jafar *et al*[11] using a nationally-representative survey of Pakistani children age 5 to14 years, but higher than 5.2% prevalence from one cross-sectional study of Indian children ages 5 to 12 years[26]. Our estimates also appear higher than estimates from Canadian children ages 6 to 19 years where 4% of children were said to have hypertension and prehypertension[27]. When stratified by sex, we found significantly higher rates were observed for boys at 15% compared to girls at 9%. This is consistent with results from studies in other children which have reported higher hypertension prevalence in boys[28,29], and results from regression analysis which found female sex to be associated with lower odds of hypertension. This risk differential has been attributed to the presence of an anti-inflammatory immune profile in females and pro-inflammatory profile in males[30] — underscoring the potential for intervention efforts aimed at addressing sex-based disparities.

Consistent with research conducted in South Asian children[11,31] and research conducted in other childhood populations of different ethnicities [28,32–36], we observed positive associations between measures of adiposity and BP and hypertension after adjusting for covariates. The consistency of the association observed across the range of adiposity metrics assessed underscores the significant contribution of increasing adiposity to the prevalence of hypertension in South Asian children. Moreover, the positive association between grip strength (a measure of muscle strength) with systolic BP z-score and hypertension upon adjustment in this study raises questions about the benefits of strength training in children. The benefits of physical activity including aerobic exercise in relation to hypertension remain clear; however, the benefits of strength training in relation to hypertension risk, relative to the benefits of aerobic exercise, appear questionable[37]. It is unclear what might be responsible for the positive effect observed between grip strength and systolic BP z-score; however, findings from our study appear consistent with studies which have explored this association in Chinese[38] and American children[39].

The consistent association between adiposity and hypertension, including the higher prevalence of hypertension in this population, reinforces their connections through a range of complex mechanistic pathways. Some of these pathways involve the activation of the renin-angiotensin-aldosterone system (RAAS) or sympathetic nervous system. Specifically, the South Asian phenotype of higher body fat[7]—especially the visceral type which has been identified in adults[6]—when compared to their Caucasian peers, could activate the formation of pro-inflammatory cytokines such as Interleukin 6 (IL-6) which results in physiological changes that could lead to endothelial and vascular dysfunction through the development of insulin resistance[40], resulting in an increased predisposition for hypertension. The positive association between height and BP in this population could be explained by cerebral perfusion requirements where higher BP is needed in taller people to achieve optimal cerebral perfusion owing to hydrostatic pressure differences in taller and shorter individuals[41]. However, more research in South Asian children is warranted to corroborate our findings given the difference observed in direction of association in unadjusted and adjusted models.

The positive association we found between the child's perception of body image and BP may be due to this variable mirroring children's weight status or conversely, a marker for a graded increase in stress levels, owing to societal criticism of fatter body types, which could have insidious effects for hypertension risk through its impact on the neuro-endocrine system[42]. Additionally, a range of social and lifestyle variables were also found to be associated with BP z-score in unadjusted analysis but became non-significant upon adjustment for confounders. While results from unadjusted associations may demonstrate links between risk factor and outcome, the disappearance of the association upon adjustment for socio-demographic variables highlights the links between these variables and suggests that the pathway linking these factors with BP might be interdependent.

The stepwise regression model shows that correlates from this study explained only about 30% of the variance of systolic BP z-score and 23% of the variability of diastolic BP z-scores. It is possible that some of this unexplained variance might be explained by genetics, as it has been suggested that about 30% to 60% of the variance in BP may be heritable[43,44]. Yet the lack of association between parental hypertension and child BP in the subset of parents of participants who provided this data would appear to contradict these findings for this population of South Asian children. However, it is likely that the subset of parents of child participants who provided this information might not be completely representative of the entire cohort, thereby biasing the results. Still, even accounting for potential genetic contributions, a significant amount of the BP variance remains unexplained. More research is needed to provide insight regarding the contributory effects of other potential variables that might contribute to risk of elevated BP in South Asian children.

Notably, null associations were also observed for certain variables in this study that have been found to be significantly associated with BP and hypertension in other child populations. For example, parental history of hypertension, dietary factors (such as consumption of fruit and vegetables) and exposure to second hand smoking have been linked in other studies to child BP but had no significant impact in this study. This could be reflective of the potential biases associated with using self-reports or may highlight how interactions between genes and environment/lifestyle shape risk factor susceptibilities — underscoring the need for more ethnic-based and ethnic comparison studies when exploring risk associations.

Study Limitations

This study has limitations. First, although we sought to recruit a representative sample of urban South Asian children, it was not a random sample. However, there is likely to be minimal effect on the relationships between the ranges of risk factors evaluated in this study. Second, this is a cross-sectional study and is therefore unable to provide insights into causal associations between the risk factor variables and long term CVD risk in South Asian children. Third, potential recall biases may have occurred as a result of using self-report data for some of the variables including diet and physical activity measures. Fourth, the use of father's education as a measure of socioeconomic status pose limitations. Variables like household income would have been preferred, however only a subset of participants provided data on household income, thus its use would have excluded a significant portion of children in this study. However, as a means to confirm the results, we separately adjusted for mother's education and no deviation in study results was observed. Last, the lack of data collection on sexual maturity status could potential confound the study results obtained here. However, the adjustment for age in this study, which acts as a proxy variable for sexual maturity might help mitigate the bias. These limitations are in part addressed by strengths of this study which lies in its large sample size of South Asian children and in the wide range of risk factors examined.

Implications

Our findings underscore a range of factors that may contribute to risk of elevated BP and hypertension in South Asian children. Consequently, public health interventions such as those that emphasize prevention such as population-based health education and lifestyle modification that considers unique cultural contexts may provide significant potential in addressing the burden of hypertension in this population. There are also implications for clinical settings. Specifically, our findings suggest that while South Asian children may benefit from interventions aimed at reducing obesity to address the comparatively higher burden of hypertension in this population, there are certain sub-groups who could benefit from more targeted preventive interventions in primary care settings — such as males, children with increased adiposity, taller children, and children with increased heart rate, or children with a combination of these factors.

CONCLUSION

In this group of South Asian children, we found associations between a range of physiological, social and lifestyle factors with BP z-scores and hypertension. However, upon adjustment for confounders, physiological variables such as age, sex, height, adiposity and heart rate remained consistently associated with BP and hypertension, and provided the strongest explanatory effect for the variance in BP. Given the sequelae associated with elevated BP, including BP tracking from childhood into adulthood, these results provide evidence on modifiable risk factors that might be targeted by prevention strategies in primary care to reduce the burden of high BP and hypertension in South Asian children.

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All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

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Table 1: Physiological, lifestyle and sociodemographic characteristics of South Asian children stratified by sex.

	Total (n=762)	Boy (n=360)	Girl (n=402)	p value
Age (years)	9.5 ± 3.0	9.3 ± 2.8	9.7 ± 3.1	0.09
Paternal education				0.92
No formal education	5 (1%)	3 (1%)	2 (1%)	
Primary education	247 (34%)	115 (34%)	132 (35%)	
Trade school	21 (3%)	9 (3%)	12 (3%)	
College/university	444 (62%)	209 (62%)	235 (62%)	
Maternal education				0.363
No formal education	5 (1%)	4 (1%)	1 (0%)	
Primary education	223 (30%)	103 (30%)	120 (31%)	
Trade school	6 (1%)	4 (1%)	2 (1%)	
College/university	503 (68%)	235 (68%)	268 (69%)	
Acculturation score (western)	34.8 ± 4.7	34.6 ± 4.62	34.9 ± 4.74	0.426
Acculturation score (traditional)	26.7 ± 4.43	26.3 ± 4.35	27.1 ± 4.48	0.02
Daily physical activity in school (METmins/day)	35.7 ± 25.8	36.8 ± 27.0	34.8 ± 24.7	0.288
Daily physical activity outside school (METmins/day)	15.9 ± 33.9	18.5 ± 31.3	13.5 ± 35.9	0.04
Daily intake- servings of fruit and vegetables (daily mean intake)	3.16 ± 1.86	3.11 ± 1.81	3.21 ± 1.91	0.485
Daily intake- servings of fast foods (daily mean intake)	0.91 ± 0.78	0.86 ± 0.59	0.97 ± 0.91	0.067
Total daily intake- servings	12.0 ± 4.48	12.2 ± 4.9	11.8 ± 4.1	0.243
Exposure to bullying/violence at school				0.025
Yes	233 (34%)	126 (38%)	107 (30%)	

No	459 (66%)	207 (62%)	252 (70%)	
Exposure to second hand smoking*				0.616
None	712 (94%)	336 (94%)	376 (94%)	
1-2 times/week	33 (4%)	16 (5%)	17 (4%)	
3-6 times/week	5 (1%)	2 (1%)	3 (1%)	
At least once a day	7 (1%)	5 (1%)	2 (1%)	
2-3 times/day	1 (0%)	0 (0%)	1 (0%)	
Mother's history of hypertension				0.047
Yes	12 (4%)	9 (7%)	3 (2%)	
No	280 (96%)	128 (93%)	152 (98%)	
Father's history of hypertension				0.979
Yes	30 (10%)	14 (10%)	16 (10%)	
No	260 (90%)	122 (90%)	138 (90%)	
Height (cm)	138.3 ± 16.5	139.1 ± 17.6	137.7 ± 15.5	0.22
Weight (kg)	36.5 ± 15.8	36.9 ± 16.5	36.1 ± 15.3	0.46
BMI Z score	0.48 ± 1.44	0.57 ± 1.61	0.40 ± 1.28	0.11
WC Z score	-0.06 ± 1.23	0.11 ± 0.36	-0.21 ± 1.24	<0.001
WHtR Z score	-0.38 ± 1.24	-0.27 ± 1.27	-0.48 ± 1.21	0.02
Heart rate	87 ± 12	86 ± 12	87 ± 13	0.047
SBP Z score	0.57 ± 0.97	0.70 ± 0.99	0.46 ± 0.95	0.001
DBP Z score	0.37 ± 0.71	0.35 ± 0.68	0.39 ± 0.73	0.41
SBP (non-transformed)	109 ± 11	111 ± 12	107± 10	<0.001

DBP (non-transformed)	65 ± 8	65 ± 8	65 ± 8	0.849
Systolic hypertension	90 (12%)	54 (15%)	36 (9%)	0.01
Diastolic hypertension	31 (4%)	13 (4%)	18 (5%)	0.55

**Exposure defined as a minimum of five consecutive minutes during which inhalation of other people's smoke occurs*

BP=Blood pressure, BMI=body mass index, WC= waist circumference, WHtR= waist to height ratio, SBP= systolic blood pressure, DBP= diastolic blood pressure

Table 2: Adjusted linear regression between multifactorial risk factors with systolic and diastolic BP z scores

	Systolic BP z score	Diastolic BP z score
Age[a]	-0.054 (-0.078, -0.029), p<0.001	-0.057 (-0.075, -0.039), p<0.001
Female sex (vs Male)[b]	-0.208 (-0.350, -0.067), p=0.004	0.078 (-0.023, 0.179), p=0.132
Height	0.022 (0.011, 0.033), p<0.001	0.007 (-0.001, 0.015), p=0.077
Weight	0.047 (0.040, 0.055), p<0.001	0.022 (0.016, 0.027), p<0.001
BMI z score	0.292 (0.249, 0.336), p<0.001	0.160 (0.127, 0.193), p<0.001
WC z score	0.273 (0.219, 0.326), p<0.001	0.137 (0.098, 0.177), p<0.001
WHtR z score	0.289 (0.236, 0.342), p<0.001	0.153 (0.114, 0.192), p<0.001
Heart rate	0.016 (0.010, 0.022), p<0.001	0.015 (0.011, 0.019), p<0.001
Acculturation (western score)	-0.010 (-0.026, 0.006), p=0.211	-0.005 (-0.016, 0.006), p=0.373
Acculturation (traditional score)	0.010 (-0.006, 0.026), p=0.227	0.003 (-0.008, 0.015), p=0.582
Child's perception of body image	0.183 (0.128, 0.239), p<0.001	0.104 (0.064, 0.144), p<0.001
Exposure to bullying/violence at school	0.021 (-0.138, 0.181), p=0.794	-0.071 (-0.183, 0.042), p=0.218
Father's smoking status	0.118 (-0.056, 0.292), p=0.184	0.082 (-0.053, 0.218), p=0.233
Exposure to second hand smoke	-0.052 (-0.240, 0.136), p=0.587	0.018 (-0.117, 0.152), p=0.795
Father's history of	-0.127 (-0.484, 0.230), p=0.484	-0.063 (-0.336, 0.209), p=0.648

hypertension		
Mother's history of hypertension	-0.003 (-0.524, 0.518), p=0.991	0.354 (-0.042, 0.750), p=0.079
Grip strength (non-dominant hand)	0.025 (0.007, 0.043), p=0.007	0.006 (-0.007, 0.019), p=0.381
Daily physical activity in school (METmins/day)	0.005 (0.002, 0.008), p=0.003	0.003 (0.001, 0.005), p=0.009
Daily physical activity outside school (METmins/day)	0.001 (-0.001, 0.003), p=0.363	0.000 (-0.002, 0.002), p=0.994
Daily intake- fruit and vegetables (daily mean intake)	-0.008 (-0.049, 0.033), p=0.717	-0.011 (-0.040, 0.018), p=0.466
Daily intake-fast foods (daily mean intake)	0.004 (-0.086, 0.093), p=0.937	-0.053 (-0.117, 0.011), p=0.104

Model adjusted for age, sex and father's education
Values presented are β (95% confidence intervals), and p values
BMI= body mass index, WC= waist circumference, WHtR= waist to height ratio, BP =blood pressure, MET=Metabolic equivalent of task
[a]*Age was adjusted for sex and father's education*
[b]*Sex was for adjusted for age and father's education*

1 Table 3: Stepwise linear regression analysis showing the aggregate correlates of BP z-score in
2 South Asian children

Stepwise multiple linear regression models					
	Variable	B	95%	P value	Adjusted R^2
Systolic BP z-score	Child's age	-0.132	-0.202 -0.062	<0.001	
	Sex	-0.293	-0.461, -0.126	0.001	
	BMI z-score	0.125	0.022, 0.228	0.017	
	Heart rate	0.014	0.007, 0.021	<0.001	
	Weight	0.027	0.012, 0.041	<0.001	
					0.294
Diastolic BP z-score	Child's age	-0.027	-0.048, -0.007	0.01	
	BMI z-score	0.125	0.081, 0.170	<0.001	
	Heart rate	0.015	0.010, 0.021	<0.001	
	Daily fast food intake	-0.013	-0.028, 0.001	0.072	
					0.228

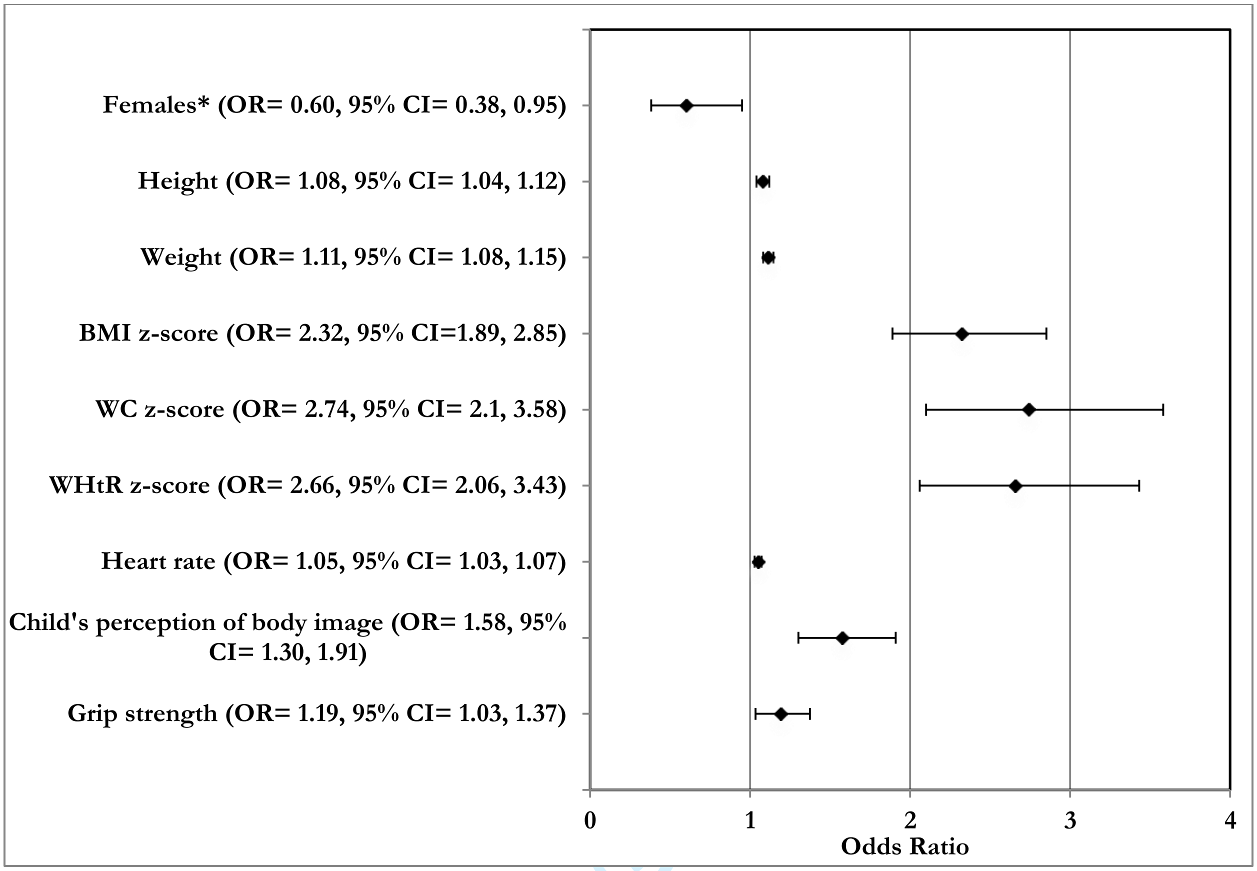
3 *BMI=body mass index, BP= blood pressure*

4

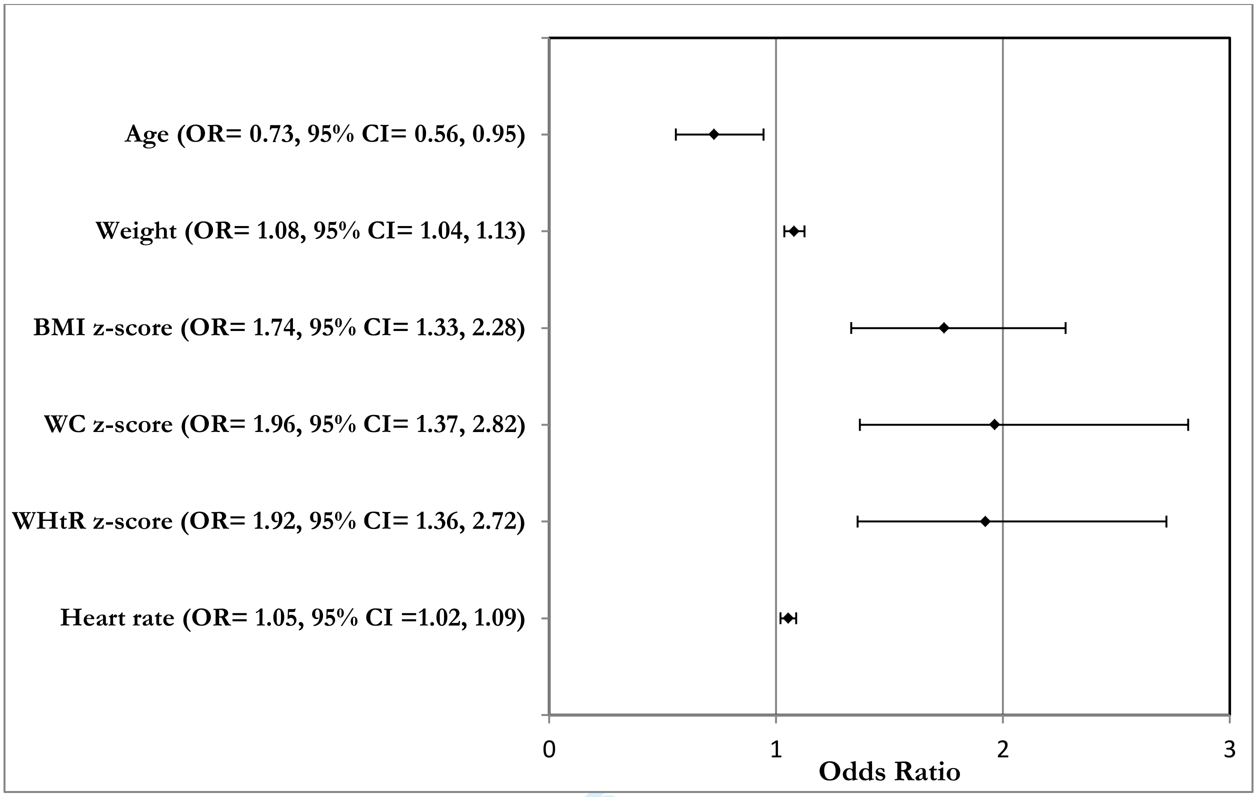
5

Figure 1: Adjusted odds ratio for the association between the multifactorial variables with systolic hypertension

Figure 2: Adjusted odds ratio for the association between the multifactorial variables with diastolic hypertension



Model adjusted for age, sex and father's education
Values presented are odds ratio (95% confidence intervals)
BMI= body mass index, WC= waist circumference, WHtR= waist to height ratio, BP =blood pressure
**compared to males*



Model adjusted for age, sex and father's education
Values presented are odds ratio (95% confidence intervals)
BMI= body mass index, WC= waist circumference, WHtR= waist to height ratio, BP =blood pressure

STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1-2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	3	State specific objectives, including any prespecified hypotheses	3-4
Methods			
Study design	4	Present key elements of study design early in the paper	4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	4
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5-8
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	*5-8*
Bias	9	Describe any efforts to address potential sources of bias	5
Study size	10	Explain how the study size was arrived at	
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	8
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	8-9
		(*b*) Describe any methods used to examine subgroups and interactions	N/A
		(*c*) Explain how missing data were addressed	7
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	N/A
		(*e*) Describe any sensitivity analyses	N/A
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	9
		(b) Give reasons for non-participation at each stage	N/A
		(c) Consider use of a flow diagram	N/A
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	9
		(b) Indicate number of participants with missing data for each variable of interest	24
Outcome data	15*	Report numbers of outcome events or summary measures	9
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	8-11

		(*b*) Report category boundaries when continuous variables were categorized	N/A
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	N/A
Discussion			
Key results	18	Summarise key results with reference to study objectives	12
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	16
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	17
Generalisability	21	Discuss the generalisability (external validity) of the study results	16
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	18

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.