Original Article

Arterial stiffness in obese children: Role of adiposity and physical activity

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ABSTRACT

Objective: To explore association of adiposity and physical activity with arterial stiffness and to propose optimal waist circumference cutoffs, corresponding to 90th percentile of NHANES (National Health and Nutrition Examination Survey) for Indian children and adolescents. **Materials and Methods:** Data on weight, height, waist circumference, physical activity and right Carotid artery Intima-Media-Thickness (CIMT), pulse wave velocity (PWV), elasticity modulus (Ep), stiffness index(β), arterial compliance (AC) were assessed in 250 children (72 normal-weight and 178 overweight/obese) aged 6-17 years from Pune city, India. Body composition was measured using Dual energy X-ray absorptiometry. **Results:** Total, 37.1% normal-weight and 98.2% overweight/obese children had high adiposity (>95th body fat percentile). Positive association of PWV and Ep (r = 0.5) also β(r = 0.25) with BMI (Body Mass Index), waist circumference and body fat (P < 0.05) was observed. Physical activity was inversely associated with PWV (r =-0.2), β(r=-0.13), Ep (r=-0.12) and positively with AC (r= 0.12) (P < 0.05). PWV significantly increased with increasing body fat for each tertile of physical activity (P < 0.05). Regression analysis revealed waist circumference, BMI, body fat and physical activity as independent associates for PWV after adjusting for age (P < 0.05). The cutoff of waist circumference yielding sensitivity and specificity for predicting the risk of high PWV was (−0.43, −0.44) for boys and girls with sensitivity in boys (girls) of 78% (87%) and specificity in boys (girls) 51% (70%). The observed cutoffs are less than the NHANES-III cutoff values of waist circumference for 90th percentiles according to age and sex. **Conclusion:** High adiposity and low physical activity are adversely related to arterial stiffness in Indian children.

Key words: Arterial stiffness, body fat, physical activity

Introduction

In the past few years, prevalence of obesity in urban youth has reached striking levels[1] in India as a result of which children are exposed to health risks. A sedentary lifestyle is one of the major contributors to obesity that increases the risk of cardiovascular disease (CVD) in children in the latter[2,3] Further, high adiposity and sedentary lifestyle in childhood is associated with early development of dyslipidemia, insulin resistance and arterial stiffness[4] predicting the future risk of cardiovascular (CV) disease in adulthood.[5] Evidence suggests that the atherosclerotic process starts in childhood[6] and vascular status is abnormal even in overweight children and adolescents.[7,8] Studies have reported inverse and no correlation between physical activity and arterial stiffness in children.[9,10] Thus, limited work on the relationship between physical activity and arterial health in children has provided contradictory findings. Hence, a better understanding of structural and functional changes of arteries and its association with activity and adiposity in children will help in instituting preventive measures for atherosclerotic risk.

Waist circumference (WC), a measure of abdominal obesity, is more closely related to cardiovascular (CV) risk factors than BMI[11,12] in children and adults. WC is also considered a key component in defining the metabolic syndrome.[13] The increasing prevalence of obesity and metabolic syndrome worldwide in recent years demonstrates urgent need for appropriate cutoff points for WC in children and adolescents for early intervention.

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Ethnicity-specific cutoffs of WC for western adults[13] and Indian's have been suggested.[14] Similar cutoffs have been provided by NHANES-III for US children. However, for early detection of cardio-metabolic risk, such cutoffs in Asian children are not available. Further, the fact that body fat percentage and waist circumference (central adiposity) in Indian children are high,[15] makes them more vulnerable for arterial abnormalities; thus, the specific objectives of the present study were to explore the association of adiposity and physical activity with arterial stiffness in Indian obese children and to propose optimal WC cutoff points for Indian children which correspond to the 90th WC percentiles of NHANES-III for children in order to predict risk of arterial stiffness.

Materials and Methods

In a cross-sectional study, a total of 250 children and adolescents in the age range of 6 to 17 years (mean age: 11.4 ± 2.8 year) were selected randomly from private schools and routine health checks from tertiary care hospitals in Pune city and around suburbs, India on voluntary basis during 2008-2009 thus, representative sample. From the list of schools in Pune city, two schools were randomly selected then further using cluster sampling method class was selected and in a class all the children were enrolled for the study. For selection of children from health checks randomization was done by computer generated random number list.

Using the standard deviations of previous reported arterial and metabolic measurements (triglycerides, insulin, BMI, and carotid intima media thickness (CIMT)) in Indian youth;[16] sample size of 250 was estimated cross-sectionally to have overall power of the study to be 0.81 with level of significance 0.05. Children with frank type I or II Diabetes Mellitus (DM) and any endocrine disorders other than nutritional obesity (high body mass index but no endocrine issues) were excluded from the study. Children and adolescents who were suffering or those who had suffered with endocrine diseases [other than impaired glucose tolerance (IGT)], craniopharyngioma or those undergoing medication that alters blood pressure or glucose or lipid metabolism were excluded. Children with frank type II diabetes were also excluded. To rule out endocrinological causes of obesity, thyroid functioning test was carried out prior to selection of the children. The research protocol was approved by the Ethics Committee of Hirabai Cowasji Jehangir Medical Research Institute (HCJMRI), Pune, India. Clinical examination of all children was performed by a pediatrician to assess their health status. A written informed consent was obtained from the parents and assent was obtained from children prior to actual commencement of the study.

Anthropometric measures

Weight, height, waist and hip circumference were measured using standard methods.[10] Waist to hip ratio (WHR) was computed. Body mass index [BMI] was computed according to the current available Indian growth monitoring guidelines, the reference values at 85th and 95th percentile of nationally representative data were used to define overweight and obesity respectively.[17]

Physical activity

Activity was assessed by using the Activity Questionnaire,[18] which was adapted for Indian children and adolescents' lifestyle. Each participant was asked to report the usual amount of time spent in different daily activities.[19] Time spent by the subjects in personal activities, school activities, reading and commuting was considered as light activity. Time spent in sports activities (e.g., walking, jogging, swimming, dancing, and playing outdoor games) was considered as moderate activity. Total amount of time spent in watching television was considered as inactivity. The questionnaire was validated against a 24 hour activity recall on a pilot sample of 15 children. Test-retest reliability of these measures was calculated (intra-class correlation coefficient, $r = 0.94$, $P < 0.01$ for inactivity; $r = 0.92$, $P < 0.01$ for light activity; $r = 0.99$, $P < 0.01$ for moderate activity)

Body composition

Dual Energy X-ray Absorptiometry (DEXA) was used for measurement of body fat percentage. DEXA measurements were performed using Lunar DPX-PRO total body pencil beam Densitometer (GE Healthcare, Wisconsin, USA) using a medium mode scan (software encore 2005 version 9.30.044) for total body fat percentage. Measurements were standardized in children and adolescents by running daily quality assurance scans and reproducibility was established.[20] The amount of effective dose of radiation exposure for a whole body DEXA is 0.02 μSv which is safe (Personal Communication with Dr Qi Zhou, GE Lunar, Evidence Based Marketing Manager Asia Lunar, January 2010).

Blood pressure

Blood pressure was measured in the right arm with child lying down quietly for 10 min. Measurements were made by auscultation with a mercury-column sphygmomanometer and a cuff appropriately sized for the arm size of the participant. The average of 3 measurements was used as the final reading.

Carotid arterial measurement

Arterial measurements were carried out at right carotid artery using an Aloka alfa-10 ultrasound apparatus (EchoTracking) (Model SSD- α 10; No: M00542; 2007; Aloka Co. Ltd. Japan) to track the vessel wall motion and automatically construct the diameter change curve in real time by a radiologist.[10] The 4 physiological parameters; stiffness (β), elastic modulus (Ep), arterial compliance (AC) and pulse wave velocity (PWV) of the right common carotid artery along with CIMT were analyzed in the present study. A Chinese study has provided reference stiffness data for each gender across age groups (<10 years, 10-19 and so on)[21] considering the comparable ethnicity and no availability of Indian cutoffs, stiffness parameters in the present study were compared with age-gender specific healthy reference Chinese for determining high and low PWV.

Statistical analyses

Analyses were performed using SPSS software for Windows (version 11.0, 2001, SPSS Inc, Chicago, IL). Descriptive statistics for general characteristics and arterial parameters were calculated for 2 groups of normal weight and overweight/obese children. Differences in means amongst normal weight and overweight/obese children were tested using independent student *t*-test. Pearson's correlation coefficients were computed to explore association between anthropometric, stiffness and physical activity parameters. As PWV is considered as an important marker for evaluation of early functional changes of the carotid artery in children and adolescents,[8] multivariate regression analysis carried out with PWV as dependent variables and BMI, waist circumference, body fat and moderate physical activity as independent variable.

Waist Z scores were computed by standardizing the variable (waist circumference) and by regressing it onto age to account for any age related differences. Regressions were carried out separately for both the genders. The standardized residual (Z-score) for waist circumference were then used as a test variable in receiver operating characteristic curve (ROC) curve analyses. ROC curve is a plot of the true positive rate (sensitivity) against the false positive rate (1-specificity) across range of values from the diagnostic test. The decision threshold is the criterion value with the highest accuracy that maximizes the sum of the sensitivity and specificity. ROC analysis was utilized to determine cutoff values of waist circumference that minimize the total number of misclassification errors and to provide an evaluation of the global performance of the waist circumference cutoffs to discriminate between those with or without risk of high PWV (stiffness).

Results

Children and adolescents in the present study were classified as normal weight, overweight and obese according to the 85th and 95th reference BMI percentiles of Indian children.[17] Table 1 presents anthropometric characteristics and activity pattern of the study population across 2 groups of normal weight and overweight/obese children. Mean age of normal weight and overweight/obese children was similar ($P > 0.1$). Amongst anthropometric parameters, average weight, body mass index, waist and hip circumference, waist to hip ratio and waist to height ratio were significantly higher in overweight/obese children than normal weight children ($P < 0.05$) [Table 1]. Mean total body fat percentage was significantly higher in overweight/obese children in comparison to normal weight children ($P < 0.05$). As there is no Indian reference database for body fat percentage, western cutoffs for body fat have been used. High adiposity was defined as body fat percentage greater than the 95th percentile of McCarthy's body fat reference database for each yearly age-sex group.[22] Moreover, children when classified using McCarthy body fat cutoff, 37.1% normal weight children and 98.2% overweight/obese children had high adiposity. Various types of daily activity are presented in Table 1. Median time spent in sleep 480 min (8 h), personal work (30 min) and average class room hours in school and reading hours was similar in both normal weight and overweight/

Table 1: Characteristics of the study population

Characteristic	Normal weight children (*n*=72)	Overweight/ obese children (*n*=178)
Age (years)	11.9±0.3	11.2±0.2
Weight (kg)	35.3±1.3	54.5±1.4***
Height (cm)	145.6±1.7	144.6±1.1
Body mass index (kg/m^2)	16.1±0.3	25.4±0.4***
Waist circumference (cm)	63.5±1.1	83.4±1.0***
Hip circumference (cm)	77.8±1.2	93.2±1.0***
Waist to hip ratio	0.8±0.01	0.9±0.1**
Waist to height ratio	0.4±0.01	0.6±0.01**
Percent body fat (%)	24.0±1.1	44.6±0.5***
Children with high adiposity (%)	37.1	98.2
Daily activity pattern		
Sleep[a]	480 (60)	480 (60)
Personal work[a]	30 (30)	30 (30)
Classroom hours[a]	420 (65)	420 (120)
Television viewing[a]	60 (60)	120 (120)*
Reading[a]	60 (45)	60 (60)
Walking	60 (45)*	30 (45)
Sports/exercise	60 (50)*	30 (40)
Moderate physical activity (min)[a]	60 (60)*	37 (48)
Classification as per CDC guidelines (%)		
Activity for at least 60 min	61.2	36.4
30-60 min	23.9	37.6
Less than 30 min	14.9	26.0

All the values are expressed as mean±SE; Significance level was set at 0.05.;* indicates $P<0.05$; *** indicated $P<0.001$. Moderate physical activity: Time spent in physical activity like walking/jogging, sports, playing outdoor games, physical training in school etc. [a]Since the daily activity data was non-normally distributed, values are expressed as median and inter-quartile range (IR) CDC: Centers for disease control obese children ($P > 0.1$). Time spent in TV viewing was considered as inactivity, median time spent in television viewing was around 2 h 95CI (107-130) in overweight/obese which is suggestive of their sedentary behavior as compared to 1 h 95CI (77-102) in normal weight children. Median moderate activity (walking/jogging and sports and exercise) was significantly higher in normal weight than overweight/obese children ($P < 0.05$) [Table 1]. Moreover, when the time spent in exercise was classified further as per CDC guidelines;[23] it was observed that only 36% overweight/obese children reported exercise for at least 60 min daily whereas; 61% normal weight children reported exercise for at least 60 min [Table 1].

Table 2 gives arterial parameters of the study population for the normal weight and overweight/obese children. Significantly; higher systolic and diastolic blood pressure was observed in overweight/obese children than normal weight children ($P < 0.05$). Mean arterial parameters *viz*; carotid intima media thickness, stiffness index, elasticity modulus and pulse wave velocity were significantly higher while arterial compliance was significantly lower in overweight/obese children than normal weight children ($P < 0.05$) indicating CV risk in overweight children.

Association of arterial parameters with adiposity and physical activity

Correlation analyses revealed positive association of body fat percentage with PWV ($r = 0.46$), stiffness index (β) ($r = 0.21$) and Ep ($r = 0.43$) ($P < 0.05$) whereas, AC showed a negative association with body fat percentage ($r = -0.25$) envisaging higher risk of atherosclerosis in children with high body fat percentage. Moderate physical activity was inversely associated with PWV ($r = -0.2$), β ($r = -0.13$), Ep ($r = -0.12$) and positively with AC ($r = 0.12$) which are markers of arterial stiffness ($P < 0.05$). Similar correlations for light activity or inactivity could not be achieved. Significant positive correlation was obtained for PWV and Ep with other adiposity measures *viz*, BMI and waist circumference ($r = 0.5$) ($P < 0.05$) and negative correlation of AC with BMI and waist circumference ($r = -0.25$) ($P < 0.05$) demonstrating the importance of central adiposity and BMI in evaluating the risk of increased stiffness. Waist to height ratio also showed positive association with PWV and Ep ($r = 0.4$) ($P < 0.05$) and negative with AC ($r = -0.20$) ($P < 0.05$) however, similar associations with waist to hip ratio could not be achieved. Additionally, change in PWV was examined across tertiles of moderate physical activity and body fat percentage [Figure 1]. PWV significantly increased with increasing body fat percentage for each tertile of moderate physical activity. Also PWV decreased significantly with increasing moderate physical activity in each tertile of body fat percentage, thus illustrating increased risk of stiffness (PWV) with lack of moderate physical activity. To avoid the effect of co-linearity between waist circumference, BMI and body fat, separate multivariate regression analysis was carried out with PWV as dependent variable with physical activity and any one of the 3 variables, *viz*.; waist circumference or body fat or BMI as independent variables. Analysis revealed, physical activity along with all the 3 measures of adiposity, i.e. waist circumference, BMI and body fat were significantly associated with stiffness (PWV) after adjusting for age (Adjusted R^2 = 0.21, 0.24, 0.22 respectively) ($P < 0.05$).

The cutoff value of waist circumference Z-score yielding optimal sensitivity and specificity for predicting the risk of high PWV was found to be −0.43 for boys and -0.44 for girls. Area under the curve (AUC) was 0.60 (95% CI: (0.44, 0.69)) for boys and 0.78 (95% CI: 0.67, 0.87) for girls. Sensitivity was 78% and 87% and specificity was 51% and 70% for boys and girls respectively, [Figures 2 and 3] indicating correct classification of children above and below the waist circumference cutoff with respect to their presence or absence of high PWV.

To facilitate application of the waist Z score cutoffs, residual standard deviation of gender-specific regression of waist circumference on age was used. ROC cutoffs of waist Z scores for boys and girls were then converted into age

Table 2: Arterial parameters of the study population

Characteristic	Normal weight children (*n*=72)	Overweight/ obese children (*n*=178)
Systolic blood pressure (mmHg)	100±1.5	121±1.3***
Diastolic blood pressure (mmHg)	65.1±1.1	76.7±0.8***
C-intima media thickness (mm)	0.31±0.01	0.34±0.01*
β (stiffness index)	3.4±0.1	3.6±0.1*
Elasticity modulus (Kpa)	36.8±1.3	46.8±1.3*
Pulse wave velocity (v/s)	3.7±0.01	4.2±0.01*
Arterial compliance (mm^2/kpa)	1.3±0.01	1.2±0.01

All the values are expressed as mean±SE; Significance level was set at 0.05. *indicated $P<0.05$

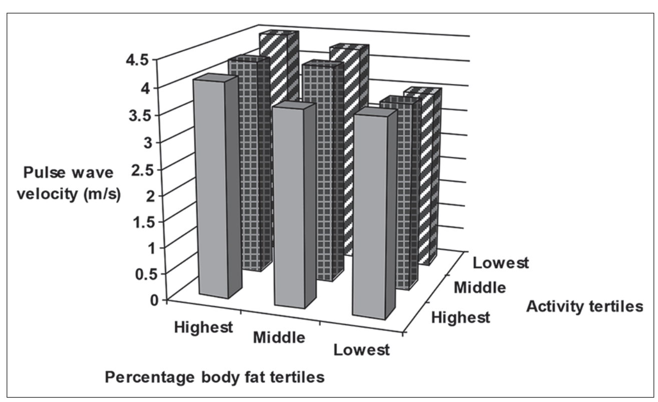

Figure 1: PWV by tertiles of body fat and moderate physical activity

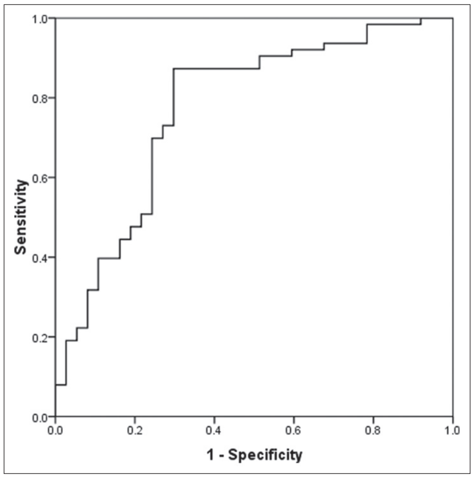

Figure 2: ROC curve of waist Z score for girls with PWV. Sensitivity 87%, specificity 70%, area under the curve 0.78 (95% CI: 0.67, 0.87)

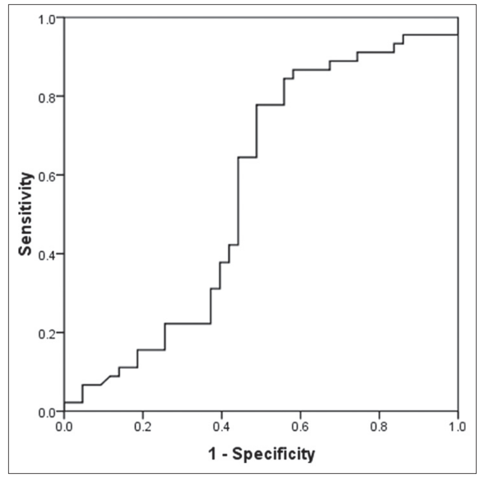

Figure 3: ROC curve of waist Z score for boys with PWV. Sensitivity 78%, specificity 51%, area under the curve is 0.60 (95% CI: 0.44, 0.69)

Table 3: Comparison of interpolated cutoffs of waist circumference with the existing 90th percentiles according to age and sex: NHANES-III

Age groups	Boys		Girls	
	Waist circumference cutoffs*	Interpolated cutoffs	Waist circumference cutoffs*	Interpolated cutoffs
6	66.1	60.5	62.5	56.8
7	69	63.4	68.4	62.7
8	70.9	65.3	69	63.3
9	78	72.4	80.8	75.2
10	80	74.4	79	73.3
11	84.2	78.6	80.9	75.2
12	85.9	80.3	81.2	75.5
13	90	84.4	89.5	83.8
14	96	90.4	91.9	86.2
15	95.9	90.3	89	83.3
16	90.2	84.6	92.1	86.5
17	98	92.4	94.6	88.9
18	97.6	92.0	92.8	87.2

*Waist circumference cutoffs for 90th centile (NHANES-III)

specific waist circumference cutoffs using the 90th percentile of waist circumference from NHANES-III[24] [Table 3].

Discussion

Present study, results imply that high adiposity (in terms of higher body fat and higher waist circumference) and low physical activity levels are associated with increased arterial stiffening in Indian children and adolescents. PWV increases with increasing body fat percentage for each tertile of moderate physical activity. Waist circumference was found to be a sensitive predictor of increased stiffness in children. In a similar study done on 10-year old children it was found that radial-femoral PWV was related to fat energy percentage and physical activity but not associated with body fat.[9] In another study, on 970 healthy children, PWV measured between the brachium and ankle using a plethysmographic method was associated with increased age, BP, and heart rate but not BMI.[25] These discrepancies in the results between studies may be attributable to differences in the methods used for the assessment of PWV. Our findings suggest an association between decreased physical activity and higher body fat percentage and higher arterial stiffness which is on par with a cross-sectional study[26] with respect to increasing PWV where, Sakuragi *et al.*, have demonstrated an influence of cardio-respiratory fitness on PWV after adjusting for body fat in healthy pre-pubescent children. The influence of obesity and physical activity on arterial stiffness has also been reported in adults.[27] Kupari *et al.*,[28] have also found a significant correlation between arterial distensibility and physical activity ($r^2 = 0.45$). Physical activity levels were evaluated and examined for association with metabolic syndrome by Pan and Pratt.[29] Pan and Pratt have shown that the tertile with the lowest levels of physical activity had the highest prevalence of metabolic syndrome and the tertile with the highest levels of physical activity showed the lowest prevalence of metabolic syndrome, but the differences were not significant.[29] Another cross-sectional study in 9-15 yr old school children in Denmark revealed decreasing odds ratio for clustered cardiovascular risk with ascending quintiles of physical activity.[30] Thus, the present study results revealing increasing stiffness with increasing tertile of body fat and decreasing tertile of physical activity are in line with the above finings. Although, the underlying mechanisms by which increased adiposity promotes arterial stiffening cannot be determined using cross-sectional data, several possibilities exists like increased BMI and adiposity are accompanied by increases in heart rate[31] blood pressure,[32] and intermediary cardiovascular metabolic risk factors such as insulin resistance[33] and dyslipidemia.[34] Physical inactivity may be associated with both an increase in adiposity and increased arterial stiffness. Arterial stiffness is determined by the properties of the arterial wall matrix and by vascular smooth muscle tone, and may be changed by an alteration in vascular smooth muscle tone caused by exercise.[35] Waist circumference is a better surrogate for body fat assessment and also one of the components in metabolic syndrome; it has been identified as a risk factor for CVD in many studies.[11,12] Therefore, the efficacy of waist circumference in predicting the risk of arterial stiffness was identified using ROC analysis. The standardized residual (Z-score) of waist circumference was used as a test variable in ROC curve analyses in order to account for the effect of age and gender. Higher sensitivity obtained for waist circumference using ROC analyses envisages waist circumference as putative marker of the risk of increased arterial stiffness (PWV).

Further, it was observed that the proposed cutoff values for waist circumference were lower at all ages and for both the genders in comparison with those proposed by the NHANES-III. These lower cutoffs are in line with lower cut-offs for BMI to define overweight and obesity for Asian adults and children (23 and 28 vs 25 and 30).[36,37] Also, in Asian the risk association with diabetes and cardiovascular diseases occurs at lower levels of BMI when compared with the white population.[38] This is attributed to body fat distribution; Asian Indians tend to have more visceral adipose tissue, causing higher insulin resistance, despite having lean BMI.[14] Thus, suggesting the importance of age-specific WC cutoffs in Indian children. Waist to height ratio was found to be significantly associated with pulse wave velocity and elasticity elucidating the importance of waist to height ratio in predicting increasing risk of arterial stiffness. Average waist to height ratio in the present study is on par with Swiss children (0.47 ± 0.04)[39] and also in agreement with the cutoff of 0.5 proposed by one Indian study.[40] A cross-sectional study in Chinese children also has explored the optimal waist circumference value for predicting the cardiovascular risk. The findings suggest sensitivity and specificity ranging from 67% to 83% which is on par with the present study.[41] However, further studies on larger data sets need to be performed to elucidate the most appropriate cutoffs for Indian children and adolescents. Also, with the lowered cutoffs proposed in the present study, validation is required. Based on these findings, it can be concluded that, children with high adiposity and low physical activity are at higher risk of developing premature cardiovascular problems. Waist circumference has been identified as a valuable predictor of cardiovascular risk in children. The development of waist circumference percentiles and cut-offs in Indian children is necessary because of ethnic differences in body composition.

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