IMPORTANCE OF CAROTID INTIMA MEDIA THICKNESS IN CHILDHOOD OBESITY

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ABSTRACT

BACKGROUND
Obesity is increasing at a rapid pace in developing countries because of life style transition. Carotid intima media thickness is a marker of coronary heart disease in adults.

Aim of this study is to find out the correlation of carotid intima media thickness with the usual measures of childhood obesity like waist circumference, waist-hip ratio and also with abdominal fat indices and lipid profile

MATERIALS AND METHODS
75 obese children and 50 age and sex matched controls between 5-12 years attending Paediatric Endocrinology Clinic in Government Medical College, Kozhikode, Kerala were included. Abdominal fat thickness and fatty liver were measured by abdominal ultrasound and intima media thickness of both carotid arteries were measured at 2 cm before the bifurcation of common carotid artery. Statistical analysis was performed by using SPSS version 18.

RESULTS
Abdominal fat indices and carotid intima media thickness were higher in obese children compared to controls. Carotid intima media thickness had positive correlation with waist circumference, abdominal fat indices, systolic pressure, fasting blood sugar and total cholesterol in obese children

CONCLUSION
Carotid intima media thickness is a definitive screening method for evaluating cardiovascular risk in obese children.

KEYWORDS
Childhood Obesity, Carotid Intima Media Thickness, Waist Circumference, Waist-Hip Ratio.

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BACKGROUND
Childhood obesity affects both developed and developing countries and all socio-economic groups irrespective of age, sex and ethnicity. Over 22 million under 5 children are obese and one child out of ten are overweight.(1) In India, all the available studies indicate that prevalence of overweight in Indian children between ages 5-17 is 10%.(2) The present pandemic of childhood obesity is due to life style changes. Obesity is an independent risk factor for coronary artery disease and Type 2 diabetes.(3)

Body Mass Index (BMI) is recognised as the gold standard in diagnosing and categorising childhood obesity. But it is a less sensitive index of fatness since it is a measure of excessive weight relative to height, rather than excess body fat.(4) Pattern of fat distribution influences cardiovascular risk. Abdominal obesity predicts cardiovascular risk better than BMI. Hence, waist circumference has a better association with the risk for coronary heart disease.(5)

Carotid intima media thickness provides an indirect method of assessing coronary heart disease.(5,6) Obese children develop endothelial dysfunction with deposition of fatty streaks and fibrous plaques and they are at a greater risk of developing coronary heart disease during adult life.(7)
Even though the health consequences of obesity are seen in adulthood, it could start earlier in childhood and track into adulthood. Children may be asymptomatic, yet they should be followed closely for preventing early coronary heart disorders, diabetes and other complications.(8)

Aim of the Study
To find out the correlation of carotid intima media thickness with usual measures of childhood obesity like waist circumference, waist-hip ratio and also with abdominal fat indices and lipid profile.

MATERIALS AND METHODS
Subjects
75 obese children and 50 age and sex matched controls between 5-12 years attending Paediatric Endocrinology Clinic in Government Medical College, Kozhikode, Kerala were included in this study.

Study Setting
Paediatric Endocrinology Clinic in the Institute of Maternal and Child Health, Government Medical College, Kozhikode, Kerala.

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Study Period
January 2014 – December 2015.

Inclusion Criteria
Children between 5 -12 years who had body mass index (BMI) above 95th percentile in IAP BMI growth charts for age and sex constituted the obese group. Age and sex matched children attending the institute for minor illness constituted the control group.

Exclusion Criteria
Children with secondary obesity and very sick obese children were excluded from this study.

Methodology

Anthropometric Measurements
Height and weight were recorded and body mass index (BMI) was calculated in kg/m^2. The waist circumference was measured at the expiratory phase on the horizontal plane between the lowest margin of the 12th rib and the mid portion of the superior iliac crest to the nearest 0.1 cm with a non-stretchable tape. Hip circumference was measured from the most protruding part of the hip to the nearest 0.1 cm with a non-stretchable tape.

Blood Pressure
Blood pressure was measured in sitting position in the right arm with a mercury sphygmomanometer. A cuff of width that encircles 40-50% of the upper arm was used. All subjects having a systolic and/or diastolic blood pressure higher than 95th percentile for age, sex and height were classified as having hypertension.

Carotid Artery Ultrasound
A longitudinal view of the distal common carotid artery was obtained from the suprasternal notch using a 7.5 MHz sector transducer in supine position. The intima media thickness measurements were made in both carotid arteries at 2 cm before bifurcation. All measurements were done with the help of experienced radiologist.

Abdominal Ultrasound for Abdominal Fat Thickness and Fatty Liver
Measurements were made using a 5 MHz sector transducer. Subcutaneous fat thickness was measured from skin to anterior abdominal muscle. Visceral fat thickness from posterior abdominal muscle to abdominal anterior wall of aorta and pre-peritoneal fat thickness from the subcutaneous layer to the peritoneum. Fatty liver is graded as Grade 0- no fatty liver, Grade 1 –mild, Grade 2- moderate and Grade 3- severe.

Biochemical Analysis
Fasting blood samples were obtained from all subjects and controls for measuring the levels of glucose, total cholesterol (TC), triglycerides (TG), low density lipoprotein cholesterol (LDL-C), and high density lipoprotein cholesterol (HDL-C). Serum glucose was measured by enzymatic spectrophotometric glucose oxidase method. Lipid parameters were determined by enzymatic methods using commercial kits.

Statistical Methods
Statistical analysis was performed using SPSS Version 18. Three statistical methods were used in this study. Chi-square test for gender distribution. Student's t test for age, anthropometric parameters, clinical parameters, carotid intima media thickness, abdominal fat indices and biochemical parameters. The Pearson correlation coefficient for correlation between the carotid intima media thickness with age, anthropometric parameters, blood pressure, abdominal fat indices and biochemical parameters.

RESULTS
75 obese children and 50 age and sex matched controls were enrolled for the study. In the obese group, youngest child was 5 years old and oldest child was having 12 years of age. 38 children were boys.

Anthropometric Data
Waist circumference (WC) and Waist-Hip ratio (WHR) were significantly higher in obese group. Mean BMI was 24.50. Waist circumference ranged from 63–103 cm with a mean value of 77 cm. The mean WHR in these children was 0.93. Anthropometric measurements of control group were well below the obese group with mean BMI of 14.78, WC of 45.72 and WHR of 0.88.

Blood Pressure
Both systolic blood pressure and diastolic blood pressure were significantly higher in obese children. 13 obese children had hypertension of which 6 had systolic hypertension, 3 had diastolic hypertension and 4 had both systolic and diastolic hypertension.

Parameters	Obese Group		Control		P value
	Mean	Standard Deviation	Mean	Standard Deviation	
Body mass index	24.50	3.11	14.78	1.98	< 0.001
Waist circumference	77.09	8.33	45.72	4.57	< 0.001
Waist-Hip ratio	0.93	0.03	0.88	0.01	< 0.001
Systolic blood pressure	107.2	11.8	95.2	6.7	< 0.001
Diastolic blood pressure	69.9	8.7	64.8	7.1	< 0.009

Table 1. Comparison of Anthropometric Measurements and Blood Pressure

Parameters	Right Carotid Intima Media Thickness		Left Carotid Intima Media Thickness	
	Pearson Correlation	P Value	Pearson Correlation	P Value
Waist circumference	0.291	0.011	0.65	0.578
Waist-Hip ratio	0.166	0.154	0.184	0.114
Systolic blood pressure	0.296	0.010	0.081	0.492
Diastolic blood pressure	0.101	0.392	0.107	0.362

Table 2. Correlation between Anthropometric Parameters and Blood Pressure with Carotid Intima Media Thickness in Obese Children

Carotid Ultrasonological Data

Both right and left carotid intima media thickness (cIMT) were measured. Significantly higher carotid intima media thickness was found in obese children compared to the control group. The mean right cIMT in obese children was 0.485 mm and the maximum thickness was 0.9 mm. On the left side, mean cIMT was 0.465 mm with a maximum thickness of 0.7 mm. In the control group, mean right cIMT was found to be 0.340 mm and left cIMT was 0.320 mm.

Abdominal Ultrasonological Data

In the abdomen, parameters measured were subcutaneous fat thickness (SFT), visceral fat thickness (VFT), pre-peritoneal fat thickness (PPFT) and fatty liver grading. There were statistically significant higher values of subcutaneous, visceral and pre-peritoneal fat thickness in obese children when compared to control group. 44% of obese children had fatty liver, but no fatty liver was seen in the control group. In obese children, subcutaneous fat thickness ranged from 28 mm to 33 mm, visceral fat thickness ranged from 8 mm to 63 mm, and pre-peritoneal fat thickness ranged from 11 mm to 58 mm. In non-obese children, subcutaneous fat thickness ranged from 6 mm to 14 mm, visceral fat thickness ranged from 19 mm to 35 mm, and pre-peritoneal fat thickness ranged from 12 mm to 21 mm.

Parameter	Obese Group		Control		P value
	Mean (mm)	Standard Deviation	Mean (mm)	Standard Deviation	
Right cIMT	0.485	0.12	0.340	0.05	<0.001
Left cIMT	0.467	0.09	0.320	0.40	<0.001
Subcutaneous fat thickness	19.1	4.6	10.1	2	<0.001
Visceral fat thickness	31.7	11.9	24.5	3.9	0.004
Preperitoneal fat thickness	25.6	15.9	8.1	2.4	<0.001
Fatty liver	0.45	0.527	0	0	<0.001

Table 3. Comparison of Carotid and Abdominal Ultrasonological Data

Parameters	Right Carotid Intima Media Thickness		Left Carotid Intima Media Thickness	
	Pearson Correlation	P value	Pearson Correlation	P value
Subcutaneous fat thickness	0.254	0.028	0.209	0.072
Visceral fat thickness	0.325	0.004	0.362	0.001
Pre peritoneal fat thickness	0.348	0.002	0.155	0.185
Fatty liver	0.305	0.008	0.166	0.155

Table 4. Correlation between Abdominal Fat Indices with Carotid Intima Media Thickness in Obese Children

Laboratory Data

Fasting blood sugar was found to be higher in the obese children, even though the values were in the normal range. Total cholesterol, LDL cholesterol, and triglycerides were significantly higher in obese children. HDL cholesterol was significantly lower in this group.

To assess the relationship between anthropometric indices, blood pressure, abdominal fat indices and laboratory values on carotid intima media thickness, the Pearson product –moment correlation coefficient was used

Among the anthropometric indices, waist circumference showed a significant correlation with right cIMT. Systolic blood pressure had significant correlation with right cIMT while diastolic blood pressure did not show any correlation with cIMT. Among fat indices, visceral fat thickness had significant correlation with cIMT of both sides, while superficial fat thickness and pre-peritoneal fat thickness had good correlation with right cIMT. Fatty liver was significantly correlated with right cIMT. Among laboratory parameters, fasting blood sugar and total cholesterol values were having significant correlation with left cIMT

Parameter	Obese Group		Control		P Value
	Mean	Standard Deviation	Mean	Standard Deviation	
Fasting blood glucose (mg/dL)	79	10	73.1	5.4	0.007
Total cholesterol (mg/dL)	180.4	27.7	137.4	9.5	< 0.001
LDL–cholesterol (mg/dL)	110.4	23.1	72.4	9.7	< 0.001
Triglycerides (mg/dL)	122	48.8	72.5	8	< 0.001
HDL-cholesterol (mg/dL)	45.6	8.3	50.3	3	0.007

Table 5. Comparison of Laboratory Data

Parameters	Right Carotid Intima Media Thickness		Left Carotid Intima Media Thickness	
	Pearson Correlation	P value	Pearson Correlation	P value
Fasting blood glucose	0.148	0.204	0.256	0.027
Total cholesterol	0.196	0.092	0.236	0.042
LDL - cholesterol	0.128	0.272	0.203	0.081
Triglycerides	0.209	0.072	0.087	0.045
HDL - cholesterol	0.052	0.656	0.121	0.300

Table 6. Correlation between Laboratory Parameters and Carotid Intima Media Thickness in Obese Children

DISCUSSION

The emerging pandemic of obesity, cardiovascular disease and diabetes is causing serious public health concern and contributes to 2.6 million deaths every year.[9] Obesity pandemic has significantly escalated the health care costs in the last 2 decades.[10] Obesity is an independent risk factor for cardiovascular disease and is associated with increased risks of early deaths and morbidity.[11,12]

In the present study, waist circumference was found to be significantly higher in the obese group. Waist circumference also showed a significant correlation with right carotid intima media thickness (cIMT), which is a marker of future cardiovascular risk.[13] Sava SC et al had shown that waist circumference has strong associations with the risk for coronary heart disease.[14] Panjikkaran ST[15] et al and Rebecca Kuriyan et al[16] had measured waist circumference in Indian school going children and had developed age and gender specific waist circumference reference data.[17]

The Waist-Hip ratio (WHR) is an index of regional adipose tissue distribution. In the present study, a significantly high WHR was seen in obese children, but it had no correlation with carotid intima media thickness. Pouliot et al demonstrated that WHR determines the regional distribution of adipose tissue, and is relatively independent of the degree of obesity.[18]

Obesity is a prominent risk factor in the development of hypertension[19] In the present study, both systolic blood pressure and diastolic blood pressure were significantly high in obese children.[20] Systolic blood pressure had significant correlation with carotid intima media thickness. A Turkish study noted systolic hypertension in 11.6% and diastolic hypertension in 19.6% in obese children.[21] In the present study, systolic hypertension was positively related to waist circumference which underscores the importance of maintaining an ideal waist circumference for preventing an elevated blood pressure.[22]

Carotid intima media thickness (cIMT) is associated with the risk of early development of atherosclerosis.[23] It can be measured in a simple, cheap and non-invasive way by using an ultrasound. Hence, it can be used in large scale population studies.[24] In 2001 Tounian et al reported that severe obesity in children was associated with impaired carotid distensibility.[25,26] Similar results were recorded in the studies of Lannuzzi A et al and Woo et al.[27] The present study also demonstrated increase in cIMT in obese children when compared with age and sex matched control group.

Recently, many studies throw light to the importance of cIMT in children also, for predicting future cardiovascular risk.[28] But standard cut-off values in children are lacking. Limited studies are available and most of them are from developed countries.[29] These include studies from Belgium, Austria, Spain, Italy and Portugal.[30,31] The present study found a significantly higher cIMT in obese children.

The main limitation of published studies was the heterogeneity of ultrasound measurement protocols which could partially explain the wide ranges of cIMT values obtained. The present study measured intima media thickness in both carotid arteries at about 2 cm before bifurcation.

The present study also found that cIMT was positively correlated with waist circumference, systolic blood pressure, abdominal fat indices, fasting blood sugar and total cholesterol. Hence all major predictors for cardiovascular disease are found to be associated with an increase in cIMT in children. It is therefore useful to include carotid ultrasound assessment in screening evaluation of overweight children to identify those at high cardiovascular risk.

Abdominal visceral fat begins to accumulate in early childhood.[32,33] In the present study, there was a statistically significant higher values of subcutaneous, visceral and pre-peritoneal fat thickness in obese children even in the pre-pubertal age group.[34,35,36]

Prevalence of fatty liver increased progressively from children with normal weight to overweight and obese children, affecting almost 50% of obese children.[37,38] Fatty liver is considered to be the hepatic expression of metabolic syndrome.[39,40,41] In the present study, 42.7% of obese children had Grade 1 fatty liver and 1.3% had Grade 2 fatty liver while no fatty liver was seen in the control group. Caserta et al found an overall prevalence of fatty liver in 12.5% of overweight children.[36]

In the present study, we found that fasting blood sugar was significantly higher in obese children even though the values were in the normal range. Total cholesterol, LDL cholesterol, and triglycerides were significantly higher in the obese children. HDL cholesterol was significantly lower in this group.[42,43] A positive correlation between pre-peritoneal fat thickness had positive correlation with total cholesterol values. Present study showed that increase in total body fat leads to fat deposition in both subcutaneous and visceral areas. Goran et al reported that body fat in general is the predominant factor influencing insulin sensitivity.[44,45,46]

Study	Country	Year of Study	Subjects		Age Group	Carotid Intima Media Thickness Mean (Range) Obese	Control
			Obese	Control			
Iannuzi A et al[47]	Belgium	2004	100	47	6-14	0.55(0.54-0.57)	0.48 (0.46-0.51)
Woo KS et al[27]	China	2004	36	36	9-12	0.49 (0.45- 0.53)	0.45 (0.37-0.53)
Jourdan EW et al[47]	Germany	2005	0	247	10-20	-	0.39(0.38-0.40)
Kapiotis S et al[47]	Austria	2006	127	24	8-16	0.37(0.33-0.41)	0.34 (0.31-0.37)
Beauloye V et al[47]	Italy	2007	104	93	10-13	0.47 (0.39-0.55)	0.43(0.35-0.51)
Nunez F et al [46]	Italy	2010	65	34	8-16	No difference in cIMT	
A Leite et al	Portugal	2012	50	50	10-18	0.472	0.461
Present study	India	2016	75	50	5-12	0.485 (0.3-0.9)- Rt 0.465 (0.3-0.7) Lt	0.340 (0.3-0.4) Rt 0.320(0.3-0.4) Lt

Table 7. Studies showing Carotid Intima Media Thickness Measurements in Obese Children

CONCLUSION

Waist circumference and waist-hip ratio are significantly higher in obese children. These children have significantly higher fasting blood sugar, total cholesterol, LDL cholesterol, triglycerides and lower HDL compared to normal children. They have significantly high abdominal fat indices like subcutaneous fat thickness, visceral fat thickness, pre-peritoneal fat thickness and fatty liver. Carotid intima media thickness (cIMT) is significantly higher in obese children. cIMT is positively correlated with waist circumference, abdominal fat indices, systolic blood pressure, fasting blood sugar and total cholesterol. Among abdominal fat indices, visceral fat thickness has high correlation with cIMT in obese children. Waist circumference has significant association with carotid intima media thickness.

Hence, carotid ultrasound assessment is a definitive screening method in evaluating cardiovascular risk in obese children. Since waist circumference is having a significant correlation with cIMT, this simple diagnostic tool is a good predictor of atherosclerotic disease in children with obesity.

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Contributions

All authors involved in case taking and interviewing the subjects and their parents. VK was involved in data collection, analysis and writing and reviewing the manuscript.

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