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A COMPARATIVE STUDY ON ASSOCIATION OF CAROTID ARTERY INTIMA MEDIA THICKNESS AND OBESITY IN CHILDREN AGED BETWEEN 10 TO 15 YEARS

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ABSTRACT

Introduction: Obesity in childhood is a major risk factor for atherosclerosis and cardiovascular disease in adulthood. Carotid intima media thickness (CIMT) is found to be an excellent marker of pre clinical atherosclerosis.
Objective: To evaluate the association of carotid artery intima media thickness with obesity and fasting lipid profile in children aged between 10 to 15years.
Methods: 130 school children aged between 10 to 15 years from three different schools of Mysuru city were selected, based on convenience sampling. Using WHO BMI charts 2007 Reference, children were classified into two groups, 65 children in the obese group (BMI > 95TH percentile) and another 65 age and sex matched children were taken as non obese control group (BMI 5TH -85TH percentile).CIMT was assessed using Philips HD11XE ultrasound machine and fasting lipid profile was estimated in Randox Imola analyser. Waist hip ratio was also measured in all the subjects.
Results: Both BMI and waist hip ratio were found to be significantly higher in the obese group compared to the non obese group (p <0 .001). Significantly higher CIMT was found in obese children (mean -0.444mm) compared to the non obese control group (mean - 0.391mm).Total cholesterol, triglycerides, LDL and VLDL were found to be significantly higher (p <0.0001) in obese children and HDL cholesterol was significantly lower in the obese group compared to control group.
Conclusion: The Carotid intima media thickness is positively associated with obesity and other associated risk factors like hypercholesterolemia in children. CIMT may be included as a useful tool in screening obese children as a marker of preclinical atherosclerosis and to identify those children at high risk of developing cardiovascular diseases.

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INTRODUCTION

Due to the rapid increase in prevalence of obesity and the serious public health consequences, obesity is commonly considered one of the most serious public health challenges of the early 21st century (Reducing risks, 2005). Significant morbidity and mortality are projected to begin in young adulthood, resulting in more than 100,000 excess cases of CHD by 2035, even with the most modest projection of future obesity (Bibbins- Domingo *et al*., 2007).

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Obesity results in increased deposition of perivascular fat around the heart and its major branches. This increased adipose tissue surrounding the blood vessels causes the overproduction of proinflammatory and profibrotic cytokines, leading to inflammation and atherosclerosis, with a consequent increase in intima-media thickness and decrease in arterial distensibility (Gustafson, 2010). CIMT is defined as the area of tissue starting at the luminal-intimal interface and the media-adventitia interface of coronary artery. Since B-mode (bright-mode) ultrasonography is a safe, noninvasive, and cost-effective to measure CIMT. A recent study more precisely defined CIMT as the double-line pattern visualized by B-mode vascular ultrasound formed by two parallel echogenic lines representing junction of the vessel lumen with intima and media-adventitia interface (Liviakis *et al*., 2010). Hence, study is intended to understand the association of CIMT with obesity, fasting lipid profile, BMI, waist hip ratio and other related risk factors like family history of diabetes hypertension.

METHODOLOGY

A comparative study was done on children between the age group 10 to 15 years studying in 3 different schools of a South Indian city. After taking informed consent from the parents, about 1500 students from the 3 schools were screened for obesity. Children were categorized based on BMI as per WHO BMI charts 2007 reference according to sex and age (Serdula *et al*., 1993). Children with BMI of >95th percentile were considered obese. Based on convenience sampling, 65 obese children and 65 healthy age matched normal children as controls were included in the study. Those children who are diabetic, children who are already on some medication like sympathomimetics, steroids, other drugs known to elevate BP, like caffeine, anti depressants and decongestants, children with previous history of drug intake like anti hypertensive drugs were excluded from the study. The study protocol was approved by the institutional Ethics Committee.

Data including, age of the children, family history of diabetes mellitus, hypertension was obtained from their parents. The height was measured at Frankfurt plane using sliding stadiometer (Johnson and Johnson) with an accuracy of 0.1mm.Weight was recorded using bathroom scale calibrated to 0.5kg accuracy. Waist and hip circumference were measured and waist hip ratio was calculated. Waist circumference / hip circumference > 0.9 was suggestive of central obesity. Based on current data and trends, it is projected that, the current epidemic of adolescent overweight will substantially increase future rates of adult coronary heart disease (CHD) unless other changes intervene. Laboratory investigations like fasting blood lipid profile were estimated in Randox Imola analyser. Normal lipid profile in children was taken as described by Durcan *et al* (1988).Cut off values of >170mg/dl for total cholesterol and<45mg/dl for HDL were taken as abnormal. CIMT in subjects was assessed by high resolution B-MODE ultarsound and later results are collected and tabulated. For CIMT, a high-frequency (12 MHz) vascular linear transducer was used for imaging the carotid arteries.

Subjects were examined in the supine position, with the head turned 45° away from the side being scanned. Two segments are identified on each side: the distal 1 cm of the common carotid artery and the bifurcation itself. Measurements are taken at the far wall. A recent study, more precisely defined CIMT as the double-line pattern visualized by B-mode vascular ultrasound formed by two parallel echogenic lines representing junction of the vessel lumen with intima and media-adventitia interface (Liviakis *et al*., 2010). The transducer was kept at distal 1 cm of the common carotid artery. Appropriate statistical methods were applied and the data was analyzed.

RESULTS

Out of 130 school children in the age group of 10-15 years, 65 children in the obese group and 65 age and sex matched children were in the control group. Of the 130 children, 65 were male and 65 were female.

Table 1. Age distribution

Age (years)	Frequency	Percent
10.00	20	15.5
11.00	14	10.9
12.00	32	24.0
13.00	28	21.7
14.00	23	17.8
15.00	13	10.1

Out of 130 children, 24 children had a family history of type 2 diabetes mellitus, 9 (6.9%) Children had a family history of hypertension and 29 children had a family history of either diabetes mellitus or hypertension. Five children had a family history of both diabetes mellitus and hypertension. There was no significant correlation between mean CIMT values observed and family history of diabetes mellitus or hypertension & there was no significant correlation of CIMT with female and male children. Both BMI and waist hip ratio were found to be significantly higher in the obese group when compared to the non-obese group (p <0 .001). Correlation analysis of CIMT revealed, positive association with BMI (p<0.01, r = 0.502) & Poor correlation with waist hip ratio (p <0.01, r = 0.383). Positive association with Total Cholesterol (p <0.01, r = 0.534), Triglycerides (p <0.01, r = 0.463), LDL (p <0.01, r = 0.463), VLDL (p <0.01, r = 0.463), whereas correlation of CIMT with HDL revealed negative correlation (p .572, r= -.050). Carotid ultrasonographic data revealed significantly higher CIMT in obese children when compared to the non-obese control group.

The mean CIMT in male obese children (0.0451cm, SD 0.00366) was higher compared to obese female (0.0439cm, SD 0.00677). There was no significant difference in non-obese male, 0.0390cm (SD 0.00271) and female, 0.0391cm (SD 0.00388) group. Fasting lipid profile was measured in both obese and non-obese children. Total cholesterol, triglycerides, LDL and VLDL were found to be significantly higher (p <0.0001), in obese children, when compared to the non-obese children.HDL cholesterol was significantly lower in the obese group when compared to the non-obese children. In the obese group, the mean cholesterol level was 168.91, triglycerides 108.78, HDL 44.98, LDL 102.26, and VLDL 21.95.In the non-obese group, the mean cholesterol level was 148.2, triglycerides 80.83, HDL 51.18, LDL 80.82, and VLDL 15.91.

DISCUSSION

The atherosclerotic process begins in childhood and develops inconspicuously over adulthood. The WHO describes obesity as ‘one of today’s most blatantly visible yet most neglected public health care problems’(Lobstein *et al*., 2004). Saraswathi *et al*, in their study, noted the prevalence of childhood obesity up to 5% to 17% the in rural and urban areas of south Indian children (Saraswathi, 2011). However overweight is rising in almost all countries, with prevalence rates, growing fastest in lower-middle-income countries (http://www.who.int/ nmh/ publications/ncd_report2010/en/ Accessed). In the past few years, prevalence of obesity in urban youth has reached striking levels in India as a result of which children are exposed to health risks (Pandit, 2014). Many decades before cardiovascular complications, that could lead to myocardial infarction or stroke, which usually, occurs in middle and late age, the first signs of atherosclerosis, include lipid deposits, resulting in fatty streaks in the intima of systemic arteries (Ross, 1993).

Table 2. Correlations of CIMT with BMI, Waist hip ratio and lipid levels

		CIMT	BMI	WHR	CHOLESTEROL mg/dl	TG	HDL	LDL	VLDL
CIMT	Pearson Correlation, r	1.0	0.502**	0.383**	0.534**	0.463**	0.050	0.486**	0.445**
	p	0.0	0.0	0.0	0.0	0.0	0.572	0.0	0.0
	N	130	130	130	130	130	130	130	130

**. Correlation is significant at the 0.01 level (2-tailed).
*. Correlation is significant at the 0.05 level (2-tailed).

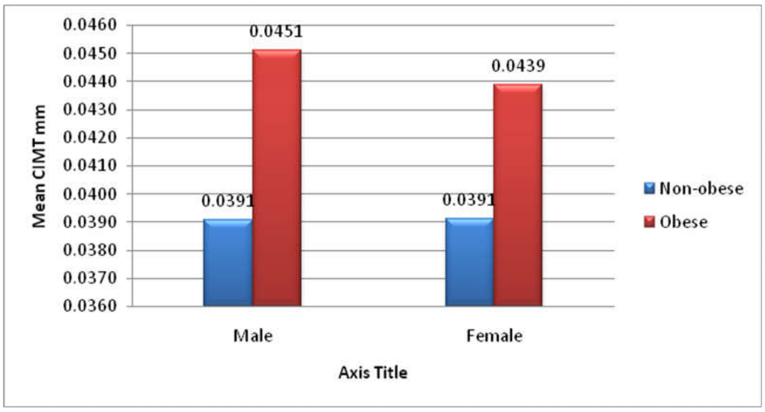

Fig. 1. CIMT value in obese group and non-obese control group

Table 3. Correlations between CIMT, BMI and cholesterol levels in obese children

		BMI	WHR	CHOLESTEROL (mg/dl)	TG	HDL	LDL	VLDL
CIMT	Pearson Correlation	0.252*	0.159	0.443**	0.327**	0.168	0.350**	0.281*
	p	0.043	0.205	0.0001	0.008	0.180	0.004	0.023
	N	65	65	65	65	65	65	65

Correlation analysis of CIMT in obese children revealed POSITIVE association, with BMI ($p < 0.05$, $r = 0.252$).NO SIGNIFICANT association with waist hip ratio ($p > 0.05$). Positive association with total cholesterol ($p < 0.01$, $r = 0.443$), triglycerides ($p < 0.01$, $r = 0.327$), LDL ($p < 0.01$, $r = 0.350$), VLDL ($p < 0.01$, $r = 0.281$). No significant correlation of CIMT with HDL ($p > 0.05$) was observed.

Table 4. Correlations between CIMT, anthropometry and cholesterol levels in non-obese children

		BMI	WHR	CHOLESTEROL (mg/dl)	TG	HDL	LDL	VLDL
CIMT	Pearson Correlation	0.127	0.151	0.300*	0.256*	0.149	0.202	0.262*
	p	0.313	0.230	0.015	0.040	0.237	0.106	0.035
	N	65	65	65	65	65	65	65

Correlation analysis of CIMT in no-obese children revealed no significant association analysis showed positive association with total cholesterol ($p < 0.05$, $r = 0.300$), triglycerides ($p < 0.05$, $r = .256$) and VLDL ($p < 0.05$, $r = 0.262$).

Advanced atherosclerotic lesions arise from these fatty streaks, and their progression during childhood and adolescence is accelerated in the presence of risk factors for adult coronary artery disease, such as elevated LDL, cholesterol, hypertension, and smoking (McGill *et al*., 1997; Berenson, ?). These observations, therefore, emphasize that risk factor control for the long-range prevention of atherosclerosis and its sequelae should begin in childhood (Van Horn, 1997). A lack of accurate diagnostic tests of preclinical atherosclerosis, however, has hampered the ability to detect and monitor such early atherosclerotic lesions.

The development of such noninvasive tests could facilitate the early diagnosis and management of high risk individuals. Studies in adults have shown that the measurement of the thickness of CIMT complex represents an excellent marker of subclinical atherosclerosis (Raitakari, 1999). Autopsy studies in children and adolescents have confirmed the presence of preclinical atherosclerotic lesions and shown their associations with ante mortem vascular risk factors (Salonen, 1991; Bots, 1997). High-resolution B-mode ultrasound measurements of CIMT and stiffness are markers of early, preclinical atherosclerosis.

Previous observations show significantly increased CIMT in children with familial hypercholesterolemia and in children with type 1 diabetes and hypertension (Tonstad *et al*., 1996; Jarvisalo, 2001; Sorof *et al*., 2003). Recent evidence suggests an increased arterial stiffness in children with familial hypercholesterolemia & severe obesity (Aggoun *et al*., 2000) Present study also showed significantly higher CIMT in obese children, when compared to the non-obese control group. However, in the study by Tounian *et al*, there was no evidence of statistically significant difference in CIMT between severely obese children and control subjects (Tounian *et al*., 2001). In the present study, both BMI and waist hip ratio were found to be significantly higher in the obese group, when compared to the non-obese group (p <0 .001). Total cholesterol, triglycerides, LDL and VLDL were found to be significantly higher ($p < 0.0001$) in obese children when compared to the non-obese children. The HDL cholesterol was significantly lower in the obese group when compared to the non-obese children. In the obese group, the mean CIMT of male children was found to be significantly higher compared to females. Yangxiao-zheng *et al*, in their study noted a direct correlation between the CIMT thickness and a positive family history of risk factors like, hypertension and dyslipidemia

(Yang Xiao-zheng *et al*., 2007). In the present study, there was no significant correlation between CIMT and children with a positive history of diabetes mellitus or hypertension. Yang Xiao-Zheng *et al* defined the CIMT as thickened, when it was ≥ 0.45 mm in children younger than 10 years or it was ≥ 0.55 mm in children between10 to18 years. Arcangelo Iannuzzi *et al*, in Naples, Italy, selected 100 obese children and 47 age matched controls, aged 6 to 14 years and studied their CIMT and found that mean CIMT in obese children was 0.55 mm (95% CI, 0.54–0.57) and in healthy control subjects was 0.48 mm (0.46 - 0.51, *P* - 0.001) (Arcangelo Iannuzzi, 2004). They concluded that, obese children have significantly increased CIMT and stiffness compared with healthy control children and similar observation was noted in the present study. Olli T. Raitakari *et al* conducted the cardiovascular risk in young adults at 5 centers in Finland where in 2229 white adults aged 24 to 39 years were examined in childhood and adolescent at 3 years and 18 years (Raitakari *et al*., 2003). They concluded that risk factor profile assessed in 12 -18 year old adolescents, predicts adult common carotid artery intima media thickness. These findings suggest that exposure to cardiovascular risk factors (systolic and diastolic blood pressure, elevated BMI, smoking, elevated levels of LDL cholesterol, HDL cholesterol and triglycerides), early in life induce changes in arteries that contribute to the development of atherosclerosis. In a study by Jie Fang *et al*, in China, a total of 86 obese Chinese children and 22 controls were enrolled from July 2008 to March 2009 (Jie Fang *et al*., 2010). The aim was to investigate risk factors which impact on common CIMT. They found that CIMT in obese children and adolescents were significantly increased as compared with non-obese children of similar age and sex. The present study also revealed positive association of CIMT in obese children. Patricia H Davis *et al*, found that childhood risk factors including total cholesterol for both sexes and BMI only for women, predicted CIMT (Patricia, 2001). Risk factors measured as early as ages 8 to 11 years are predictive of carotid CIMT. Meyer *et al*. in his study assessed the vascular status of 32 obese children and 20 controls by measurements of E-selectin, thrombomodulin, vwf (von willebrand factor), flow mediated vasodilatation and CIMT (Meyer, 2006). The study revealed increased CIMT in obese children when compared to control group.

However in a study by Pandit *et al*, in Pune, India, 44 overweight, 95 obese (6-17 years) and 69 healthy age matched normal children were enrolled and CIMT was assessed. In this study, overweight and obese children did not show any significant difference in CIMT when compared with normal children (Pandit, 2011). In Hong Kong, K S Woo *et al*, conducted a study to evaluate the reversibility of obesity related arterial dysfunction and CIMT by dietary and/or exercise intervention programs (Woo, 2004). In this study, 82 overweight children with BMI 25, in the age group of 9 to 12 years, were randomly assigned to dietary modification only or diet plus a supervised structured exercise program for 6 weeks and followed for 1 year. The prospectively defined primary end points were ultrasound-derived arterial endothelial function (endothelium-dependent dilation) of the brachial artery and CIMT of common carotid artery. At 6 weeks, both interventions were associated with decreased waist-hip ratio (*P*=0.02) and cholesterol level (*P*=0.05) as well as improved arterial endothelial function. Diet and exercise together were associated with a significantly greater improvement in endothelial function than di*et al*one (*P*=0.01). At the end of 1 year, there was significant decrease in the thickening of the carotid wall (*P*=0.001) as well as persistent improvements in body fat content and lipid profiles in the group continuing an exercise program. Vascular function was significantly better in the children continuing exercise (n=22) compared with children who withdrew from the exercise program (n=19) (*P*=0.05). The authors concluded that obesity related vascular dysfunction in otherwise healthy young children is partially reversible with di*et al*one or particularly diet combined with exercise training at 6 weeks, with sustained improvements at 1 year in those persisting with diet plus regular exercise. Thus the present study revealed that the major predictors of cardiovascular disease like the BMI and hypercholesterolemia is found to be associated with an increase in CIMT in children. Carotid ultrasound may be used as a simple noninvasive screening tool in evaluating cardiovascular risk in obese children.

Conclusion

In our study the carotid intima media thickness (CIMT) was significantly high in obese children when compared to the non-obese children. The CIMT also showed moderate positive correlation with BMI, total cholesterol, triglycerides, LDL and VLDL in obese group. Obese male children had significantly high CIMT than the females. Thus CIMT may be included as a useful tool in screening obese and overweight children as a marker of preclinical atherosclerosis and to identify those children at high risk of developing cardiovascular diseases. Carotid ultrasound may be used as a simple non-invasive screening tool in evaluating cardiovascular risk in obese children.

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