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Original Research Article

A study of lipid profile and carotid artery and abdominal aorta intima-media thickness in children with parental history of premature ischemic heart disease

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ABSTRACT

Background: Children born to parents with ischemic heart disease (IHD) can have dyslipidemia, a marker for IHD, detectable in early childhood and track to adulthood. Dyslipidemia along with factors like BMI, diet, sedentary activity increases risk of child developing IHD in adulthood. Early detection with non-invasive methods such as B mode ultrasound to measure carotid artery and abdominal aorta intima-media thickness can help in modification of these risk factors by suitable interventional strategies. The objectives of this study was to study the lipid profile and carotid artery and abdominal aorta intima-media thickness among children in the age group 5-18 years born to parents with history of premature IHD.

Methods: 23 children of parents with premature IHD and aged matched 28 controls without any family history of IHD were analyzed for cardiovascular risk factors: lipid profile and carotid and abdominal aorta intima-media thickness. The carotid intima-media thickness and abdominal aorta intima-media thickness was found by using B mode ultrasound.

Results: Mean abdominal aorta intima-media thickness was significantly higher among children with parental history of premature IHD than in those without it. Abdominal aorta intima-media thickness also showed significant positive correlation with total cholesterol. Carotid intima-media thickness showed positive correlation with the waist circumference. Mean total cholesterol levels (TC), low density lipoprotein cholesterol (LDL) and triglycerides (TG) were higher in children with family history as compared to children without family history but it was not statistically significant.

Conclusions: Abdominal aortic IMT is significantly more among children with parental history of premature ischemic heart disease compared to children without parental history of premature ischemic heart disease. Abdominal aortic intima-media thickness has significant association with total cholesterol while carotid intima-media thickness is significantly associated with waist circumference.

Keywords: Abdominal aorta, Atherosclerosis, IMT, Ultrasound

INTRODUCTION

Atherosclerosis is a slow, progressive disease of arteries that starts in childhood and usually manifests itself clinically much later.[1] Hyperlipidemia is considered to be one of the major risk factor in the causation of atherosclerosis.[2-4] Over the past decade, high-resolution B-mode ultrasonography has proved to be a valid and reliable method in detecting initial structural atherosclerotic changes in the arterial wall. Increased thickness of intima and media of the carotid artery has been found in subjects with risk factors for cardiovascular

disease and is a powerful predictor of the presence of coronary atherosclerosis and its clinical sequelae.[5-7] Development of non-invasive methods has allowed us to assess in vivo abnormalities in vascular structure and function. In particular, carotid intima-media thickness (cIMT) is used as a measure of subclinical atherosclerosis. The presence of asymptomatic vascular changes in adolescents and young adults and the association of these changes with a parental history of premature myocardial infarction have potential implications for clinical practice. The examination of arterial-wall structure and function in young persons with the use of non-invasive ultrasonographic methods may provide important information on early changes in the course of developing atherosclerosis, especially in persons at high risk for cardiovascular disease. Ultrasonography has been used to demonstrate an increase in common cIMT in children and adolescents with hypercholesterolaemia.

Objectives of this study were to study the lipid profile in children aged between 5-18 years with a parental history of premature ischemic heart disease as compared to controls without parental history of premature ischemic heart disease and to study carotid artery (cIMT) and abdominal aorta intima-media thickness in children between 5-18 years of age with parental history of premature ischemic heart disease as compared to controls without parental history of premature ischemic heart disease and to study correlation between lipid profile and cIMT.

METHODS

This study was carried out in the Pediatrics Department of Cheluvamba Hospital attached to Mysore Medical College and Research Institute, Mysore for a period of two months from June to July 2015. Sampling method used was purposive sampling.

The present study was a comparative study conducted at Cheluvamba Hospital, which is a tertiary level teaching hospital connected to Mysore Medical College and Research Institute (MMCRI), Mysore, Karnataka.

Cases

23 cases of IHD were selected after obtaining their written consent, from ICCU (Intensive Coronary Care Unit) of Cardiac Department attached to Mysore Medical College and Research Institute. Their IHD (Ischemic Heart Disease) status was taken into account by history, medical case sheets and laboratory data. Data was collected based on a predesigned questionnaire. Their children were included for the study.

Inclusion criteria for parents

- <55 years males and <65 years females diagnosed with IHD.

Exclusion criteria for parents

- Suffering from other incidental cardiac conditions like associated congenital heart disease or cardiomyopathy etc.
- Other endocrine diseases, renal disease leading to hyperlipidemia.
- History of drug intake like corticosteroids, diuretics, beta blockers etc. leading to hyperlipidemia.

Inclusion criteria for children

- Age 5 years to 18 years
- Parents suffering from premature IHD.

Exclusion criteria for children

- Having any other cardiovascular disorder (congenital or acquired) other endocrine diseases, renal disease leading to hyperlipidemia.
- History of drug intake like corticosteroids, diuretics, beta blockers etc, leading to hyperlipidemia.

Controls

28 controls were selected from normal siblings of children attending Outpatient Department of Pediatrics who are

- Not suffering from cardio vascular diseases.
- Not having any family history of IHD.

Methodology and techniques

1. Data was collected using a preformed proforma, which included the following data.

For parents

- General profile
- Clinical history

For children

- General profile
- Clinical history

2. Anthropometric measurements height and weight were taken, and BMI was calculated and interpreted using WHO charts.
3. Blood sample were drawn from the child and was sent for the central laboratory, biochemistry, KR hospital for lipid profile.

The blood was drawn after 12 hours of fasting. Lipid profile was done by estimating total cholesterol, triglycerides, HDL (high density lipoprotein), using photometer. LDL (low density lipoprotein) level was obtained by calculation using the Friedewald's formula.

Atherosclerotic index (AI) is calculated using the formula AI = total cholesterol / HDL. Cholesterol levels were compared using NCEP guidelines.[8]

Acceptable levels of total cholesterol is <170 mg/dl and LDL cholesterol is <110 mg/dl, both <75th percentile. Borderline levels of total cholesterol is 170-199 mg/dl and LDL cholesterol is 110-129 mg/dl, both 75-95th centile. High levels of total cholesterol is ≥ 200 mg/dl and LDL cholesterol is ≥130 mg/dl both >95th centile. Normal levels of triglycerides and HDL is <150mg% and >35mg % respectively. Normal atherosclerotic index is <5 and high is >5.

All these children were subjected to ultrasonography to assess carotid artery and abdominal aorta intima media thickness. It was performed with ultrasound unit (ESAOTE My Lab 40) equipped with 3-6.6 MHz curvilinear transducer and 7-12 MHz linear transducer. Scans were performed by a single radiologist with experience in vascular sonography. The study protocol involved scanning of the far wall of common carotid arteries in the distal 1.0 cm. The crest at the origin of the bifurcation was used as anatomical landmark to identify the segment to be visualised.

The abdominal aorta was first identified in the upper abdomen using a 7.5-MHz pediatric phased array transducer, and it was then followed distally until the aortic bifurcation was reached. For the assessment of aIMT, the image was focused on the far wall (dorsal arterial wall of the most distal 15 mm of the abdominal aorta) and gain settings were used to optimize image quality. Images 15 mm in width were magnified using a resolution box function. Two images of the best quality were chosen for analysis in each study subject. IMT was measured using ultrasonic calipers.

Statistical analysis

The statistical analysis was performed using the SPSS (version 17.0). Lipid levels were expressed as the mean±SD. The data was further categorized according to age group, gender, family history, diet, life style. Pearson's chi square test was applied in comparisons of independent and dependent proportions.

Difference between groups were compared with an unpaired Students' t test. Simple linear regression analysis was applied to examine the relationship between two variables. A p value <0.05 was considered statistically significant.

RESULTS

The average (SD) age of the study group was (12.54±3.6) years, with a range from 05 to 18 years, with 31.37% in the age group of 10 years or less than 10 years. Among the study subjects 34 (66.7%) were male and 17 (33%) were females. Of the total number of males, cases constituted 12 (35.29%) while controls were 22 (64.71%) on the other hand among females 11 (64.71%) were cases and 6 (35.29%) were controls.

Table 1: Comparison between the lumen and distal wall intima media thickness of Common carotid artery among cases and controls.

Parameter	Subject	Mean (in mm)	Standard Deviation (in mm)	P value
RCCA-Lumen	Case	5.14	1.07	0.564
	Control	5.28	0.49	
RCCA-Distal wall	Case	0.49	0.10	0.823
	Control	0.48	0.05	
LCCA-Lumen	Case	5.39	0.34	0.345
	Control	5.29	0.36	
LCCA-Distal wall	Case	0.51	0.04	0.183
	Control	0.49	0.05	

Among the cases the right common carotid artery distal wall thickness had a higher Mean (0.49±0.08) compared to their counterparts in controls (0.48±0.05) subsequently the controls had higher mean of lumen diameter for right common carotid artery, but both were not statistically significant. Children of the two sexes did not significantly differ for other parameters.

Table 2: Comparison of abdominal aorta lumen diameter and distal wall thickness among cases and controls.

	Subjects	Mean (mm)	Standard Deviation (mm)	P value
AA-Distal wall	Case	0.74	0.10	0.009
	Control	0.66	0.08	
AA-Lumen	Case	9.60	1.13	0.040
	Control	8.84	1.44	

Table 3: Comparison between waist circumference, total cholesterol and high-density lipoprotein with intima media thicknesses of right carotid, left carotid and abdominal aorta.

	Cases (mg/dl)	Controls (mg/dl)	P value
Total cholesterol	152.52±16.87	151.39±15.04	0.804
Triglyceride	132.17±16.16	129.71±13.34	0.562
HDL	44.26± 4.41	45.96±4.99	0.202
LDL	82.83± 14.51	80.75±13.33	0.298

The mean abdominal aorta intima media thickness of cases and controls were compared and it was found to be significantly higher among the cases 0.74±0.10mm than controls 0.66±0.08mm with p value 0.009.The mean was higher among the females 0.68±0.06mm compared to males among the cases 0.66±0.43mm but this was not statistically significant (p >0.05).

Present study study showed that cases had a significant positive correlation between the distal wall intima-media thickness of the right common carotid artery and waist circumference. There was correlation noted between the total cholesterol levels with that of abdominal aorta distal wall intima-media thickness.

Table 4: Comparison of lipid profile.

	Boys (mg/dl)	Girls (mg/dl)
Total cholesterol	152.52±16.11	148.36±17.44
Triglyceride	132.17±16.24	130.18±16.64
HDL	44.26±4.96	45.09±3.86
LDL	82.46±14.26	80.16±13.02
Atherosclerotic index	3.46±0.44	3.32±0.4

The analysis of lipid profile of children revealed that mean levels of total cholesterol (TC), low density lipoprotein (LDL) and triglycerides (TG) were higher while high density lipoprotein (HDL) was lower in children of affected individuals as compared to controls but was not statistically significant. Of the 23 cases dyslipidemic cases accounted for 66% (n = 7) compared to 16% (n = 3) in controls.

Table 5: Comparison of cases and controls with respect to gender variation in lipid profile.

	Boys (mg/dl)	Girls (mg/dl)
Total cholesterol	152.52±16.11	148.36±17.44
Triglyceride	132.17±16.24	130.18±16.64
HDL	44.26±4.96	45.09±3.86
LDL	82.46±14.26	80.16±13.02
Atherosclerotic index	3.46±0.44	3.32±0.4

In the cases, the boys had higher mean values of total cholesterol, triglyceride, LDL than the girls, the mean vales of HDL of boys lower than the girls and the mean of atherosclerotic index was higher among boys compared to girls. The values were not statistically significant.

DISCUSSION

Many studies have documented the relationship between elevated lipid levels and higher risk of ischemic heart disease. Cardiovascular risk factors identified in childhood have been previously linked to adult atherosclerosis in the Muscatine study, Bogalusa study, Hopkins J study etc.[9,10] The subclinical atherosclerosis among children and young adults can be detected by non-invasive technique such as ultrasound.

In this study the mean abdominal aorta intima media thickness of cases and controls were compared, and it was found to be significantly higher among the cases than controls. Jarvisalo MJ et al in their study conducted in showed similar results.[11] Because atherosclerosis begins first in the intima of the aorta, these data suggest that the aIMT might provide the best currently available non-invasive marker of preclinical atherosclerosis in children. Not many studies have been done to determine the aortic wall thickness in children, and the reports on adult subjects are few. In adults, aIMT in the thoracic region has been measured using transoesophageal ultrasound, which yields better image quality than transcutaneous imaging.

In the present study we found that cases had a higher mean of intima media thickness of carotid artery (cIMT) compared to controls in all age groups, however this was not statistically significant. No significant variation in sex was noticed. In the Framingham heart study done on 1662 subjects, a positive family history of IHD was associated with increased carotid IMT.[12] Similarly, Gaeta et al reported that the offspring of patients hospitalized with premature acute myocardial infarct have increased carotid IMT.[13]

In this study though, there is higher mean value of intima-media thickness of carotid artery among cases there is little significant correlation. In a Finnish study, the severity of carotid atherosclerosis, was not associated with family history of ischemic heart disease. Reasons to explain the differential association of parental history with carotid plaques and CCA IMT are methodology used to assess the intima-media thickness, especially on the site of measurement, that some genetic factors might be specifically involved in plaque formation but not in diffuse intima-media thickening.[14,15] Genetic inheritance and the environmental factors associated with variation of carotid intima media thickness have not been fully understood and further studies in this are needed.

Among the 23 cases, we observed dyslipidemia in (26%) subjects which is lower than observed by Gupta et al (44%).[16] Present study revealed that children of IHD patients had a higher mean of dyslipidemia compared to controls. This observation is consistent with study by Gulati et al and other studies.[17] We also found decreased means of HDL-C and increased atherosclerotic index among cases but was not statistically significant (p>0.05). Khalil et al, in a study from India compared offspring of patients with proven ischemic heart disease (n = 50) and healthy parents (n = 50).[18,19] There was no difference in the lipid profile of children of both the groups. Several studies have shown that childhood rank orders of cholesterol are maintained over time, a phenomenon known as tracking.[18]

High TG levels have been associated with increased levels of small dense LDL which are considered to be highly atherogenic.[20] Increased prevalence of low HDL has been reported earlier by Enas et al who found that only 4% of Asian Indian men and 5% Asian Indian women had optimal HDL levels.[21]

The Tromso heart study says that high HDL-C levels are protective against IHD at all ages.[22] Gordon et al suggested that HDL-C is a stronger predictor of IHD than total cholesterol and LDL-C.[21] Although HDL-C is a more useful predictor of IHD than TC alone, the ratio of HDL-C to TC may be even more predictive.[23] The TC/HDLC (atherogenic index) has been used as markers of coronary atherosclerosis but has received limited attention in pediatric literature.[20]

Thus children whose cholesterol levels are high tend in general to have high levels during adulthood and early diagnosis of dyslipidemia in children provides an opportunity for long-term primary amelioration of risk factors, if introduced at an early age.

The boys had prevalence of dyslipidemia more than the girls in our study, similar to data by Gupta et al and a Turkish study.[16,25] The Bogalusa heart study, Framingham heart study and many other studies have also shown the fact that males are more affected.[12] Further studies are needed to better understand the development of cardiovascular protection during adolescence.

Limitations in the present study were the small number of subjects included in this study and the hospital-based nature of study sample. Moreover, we acknowledge that we did not evaluate several risk factors for cardiovascular disease such as glucose metabolism, pro-thrombotic and inflammatory markers.

CONCLUSION

Abdominal aortic IMT is significantly more among children with parental history of premature ischemic heart disease compared to children without parental history of premature ischemic heart disease. Abdominal Aortic intima-media thickness has significant association with total cholesterol while carotid intima-media thickness is significantly associated with waist circumference.

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