

## Original Research Article

# Cardiovascular risk factors and their association with carotid intima media thickness in children in Western India

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## ABSTRACT

**Background:** Cardiovascular disease occurs in early in Indians risk factors of which may start from childhood. Objective was to identify CV risk factors in children and study their association with carotid intima media thickness.

**Methods:** In this cross-sectional study, we studied children aged 4 to 14 years visiting our institute for routine health check-up. Data was collected on demographics, clinical and biochemical parameters. All patient underwent electrocardiographic, 2-D echocardiography examination. Carotid intima media thickness (CMT) was observed by carotid ultrasound.

**Results:** In 378 children enrolled in the study, mean age was  $9.1 \pm 2.6$  years with 74.6% being males. Mean body mass index was  $18.7 \pm 3.9$  kg/m<sup>2</sup>. Among various CV risk factors, dyslipidemia (46.6%) was most common followed by family history of premature CV disease (9.5%), hypertension (4.49%), obesity (3.17%), smoking (1.05%). High dietary fat intake was seen in 22.2% cases. CMT showed significant association with age ( $p=0.027$ ), BMI ( $p=0.031$ ), systolic ( $p=0.026$ ) and diastolic ( $p=0.036$ ) blood pressure, high-density lipoprotein cholesterol levels ( $p=0.001$ ), and low-density lipoprotein cholesterol ( $p=0.047$ ). No association with fat intake or total calorie intake was observed.

**Conclusions:** Dyslipidemia along other risk factors can be present as CV risk factor from early childhood. Screening of children for such risk factors to mitigate the risk of atherosclerotic CV disease in adulthood.

**Keywords:** Cardiovascular disease, Children, Carotid intima media thickness, Dyslipidemia, Obesity, Risk

## INTRODUCTION

Cardiovascular diseases (CVD) are the leading cause of death and major contributors to disability adjusted life years lost among Indians.<sup>1</sup> In India, evidence suggest that there has been significant increase in premature mortality because of CVD has increased by 59%, from 23.2 million (1990) to 37 million (2010).<sup>2</sup> Further, India suffers the greatest loss in potentially productive years of life, due to deaths attributable to cardiovascular diseases among people aged 35-64 years.<sup>3</sup> This is a decade earlier than

their counterparts in developed countries.<sup>4</sup> Though there are several reasons for this increased propensity, diabetes, insulin resistance and metabolic syndrome are major contributors to CVD in India.<sup>5</sup> Development of atherosclerotic CVD starts in early childhood as the risk factors and risk behaviours begun in this age.<sup>6</sup> A recent study suggested that obese children aged 5 to 17 years have significant presence of CVD risk factors like insulin resistance, triglycerides, uric acid, fibrinogen, etc. which were significantly higher in these population.<sup>7</sup> However, there is relative lack of evidence on CVD risk factors in

relatively healthy children in India. Hence, we investigated prevalence of risk factors of CAD in very young population (4 to 14 years) of Gujarat and studied their association with preclinical atherosclerosis measured by carotid media thickness (CMT).

## METHODS

This cross-sectional, observational study was conducted in children visiting at a tertiary care hospital in Gujarat. Inclusion criteria was children aged 4-14 years, either gender, visiting the institute for routine health check-up. Children having cardiac disease other than CAD (i.e. RHD, Congenital heart disease, Myocarditis) were excluded.

Patient visiting institute were randomly selected. Detailed clinical history including dietary history, family history and personal history with special reference to smoking, tobacco chewing, alcohol intake was obtained, and detailed clinical examination was carried out. According to NCEP ATP III guidelines, family history of premature CAD was defined as CHD in a first-degree male relative of age <55 years and female relative of age <65 years. Obesity was considered with body mass index (BMI) of >25kg/m<sup>2</sup>.

Hypertension was diagnosed in children if their systolic and diastolic blood pressure was more than 95th percentile for their height and age as defined by the sixth report of the joint national committee on prevention, detection evaluation and treatment of high blood pressure. Fasting lipid profile comprising of total cholesterol (TC), high density lipoprotein cholesterol (HDL), low density lipoprotein cholesterol (LDL), very-low density lipoprotein cholesterol (VLDL), serum triglycerides (TGs) was done in all subjects. Dyslipidemia was defined according ATP III classification when any of the following abnormality was found-TC  $\geq$ 200mg/dl, LDL  $\geq$ 100mg/dl, TGs>150mg/dl, or HDL <40mg/dl. Diabetes was diagnosed if FBS > 125mg/dl according to the American Diabetic Association (ADA) criteria.

All subjects underwent electrocardiogram (ECG), 2D-Echocardiography examination and carotid ultrasonography. Premature atherosclerosis was suggested by increased carotid media thickness (CMT) on carotid ultrasound. Coronary artery disease (CAD) was suspected based on ECG evidence of myocardial infarction (MI) or ischemia (Pathological Q wave, ST-T changes, left bundle branch block (LBBB)), echocardiography evidence of MI (regional wall motion abnormality, septal thinning, apical aneurysm). Patients suspected to have CAD on ECG or 2D- echocardiography underwent evaluation with coronary angiography (CAG). Patient having CAD on CAG were investigated for novel risk factors for CAD like Lp (a) (20-30mg/dl as high and >30mg/dl as very high), serum homocysteine > 15 $\mu$ moles/L, serum fibrinogen > 4g/L, high sensitivity C-

reactive protein (hs-CRP) > 6mg % as positive. Significant CAD was defined as a >50% diameter stenosis in one or one of the vessels. Sub-critical stenosis <50% was classified as non-obstructive CAD. Patients were classified as having left main coronary artery disease, single vessel double vessel, triple vessel, non-critical or normal depending on the extent of disease.

The study was approved from Institutional ethical committee. Consent from parents was obtained in all the cases for enrolment of their children in the study.

## Statistical analysis

The data was entered in to Microsoft excel sheet. Data was analysed using descriptive statistics. Categorical data were presented as frequency and percentages whereas continuous data was presented as mean and standard deviation. Association between various risk factors and CMT was studied using Pearson correlation. P value < 0.05 was considered significant.

## RESULTS

In total 378 patients enrolled in the study, mean age was 9.1years and the maximum number of patients were in the 8-10years age group. Nearly 3/4<sup>th</sup> of the patients were males with male: female ration of 2.8:1. Mean BMI was 18.7 $\pm$ 3.9kg/m<sup>2</sup>. Mean level of CIMT was 0.58 $\pm$ 0.08mm. Mean cholesterol level was 142.1 $\pm$ 58.7mg/dL and mean TG level was 96.8 $\pm$ 52.7mg/dL. Mean HDL was 38.4 $\pm$ 8.8mg/dL whereas mean LDL level was 84.2 $\pm$ 46.9mg/dL. Total calorie intake per day was 736.4 $\pm$ 179.7 Kcal and mean total fat intake was 20.0 $\pm$ 5.4mg/d. The baseline characteristics are shown in Table 1.

Among various cardiovascular risk factors, dyslipidemia was present in 176 (46.56%) subjects and was the most prevalent risk factor observed in the study. Among dyslipidemia, low HDL was most common abnormality found in 162 (42.8%) subjects followed by high LDL in 72 (19%), high triglycerides in 36 (9.5%), high total cholesterol in 6 (1.5%) subjects. Positive family history was present in 36 (9.5%) subjects. Hypertension was found in 17 (4.5%) subjects followed by obesity which was present in 12 (3.17%) subjects. Smoking was present in 4 (1.05%) subjects. Only one (0.21%) was diabetic and was on insulin. High fat diet (>30 % of calories by fat) was taken by 84 (22.2%) subjects (Table 2).

Table 3 describes association of CIMT with various parameters. CIMT was significantly associated with age (p=0.027), systolic and diastolic blood pressure (p=0.026 and 0.036), BMI (p=0.031). Also, a significant association with HDL cholesterol level (p=0.001), LDL cholesterol level (p=0.047), LDL/HDL ratio (p=0.006), TC/HDL ratio (p=0.023) was found. There was no significant association of CMT with total calories intake, fat percentage and total grams of fat per day. Two

subjects having abnormal ECG and 2D Echo underwent coronary angiography. CAG in the first subject revealed coronary artery disease (LMCA disease + RCA disease).

**Table 1: Baseline characteristics in study population.**

Parameter	Observation (n=378)
Age (years)	9.1±2.6
<b>Age groups</b>	
4 to 7 (%)	114 (30.1)
8 to 10 (%)	156 (41.2)
11 to 14 (%)	108 (28.7)
<b>Sex (%)</b>	
Male	282 (74.6)
Female	96 (25.4)
M: F ratio	2.8
BMI (Kg/m <sup>2</sup> )	18.7±3.9
SBP (mmHg)	115.2±12.7
DBP (mmHg)	66.4±8.2
CIMT (mm)	0.58±0.08
<b>Laboratory parameters</b>	
Fasting blood sugar (mg/dL)	83.5±16.5
TC (mg/dL)	142.1±58.7
TGs (mg/dL)	96.8±52.7
HDL (mg/dL)	38.4±8.8
LDL (mg/dL)	84.2±46.9
VLDL (mg/dL)	19.3±10.5
LDL/HDL ratio	2.3±1.5
TC/HDL ratio	3.8±1.9
<b>Fat and calorie intake</b>	
Total calorie intake per day (Kcal)	736.4±179.7
Total fat intake per day (gm)	20.0±5.4

**Table 2: Risk factors for coronary artery disease in study population.**

Risk Factors	N (%)
Dyslipidemia	176 (46.6)
High TC	6 (1.5)
High TG	36 (9.5)
Low HDL	162 (42.8)
High LDL	72 (19.0)
Family history of cardiovascular disease	36 (9.5)
Hypertension	17 (4.49)
Obesity	12 (3.17)
Smoking	4 (1.05)
Diabetes	1 (0.26)
High fat diet	84 (22.2)

**DISCUSSION**

Cardiovascular disease burden in India is significant in adults. There have much concerns about development CVD in young ages. It has been suggested that the risk factors and risk behaviours initiate and accelerate from childhood.<sup>6</sup> In this study, we included children of age 4 to

14 years of age with mean age of 9.06 years. In one similar case control study, mean age was observed was 11.1 years in cases.<sup>7</sup>

**Table 3: Relation of CIMT with different parameters.**

Variables	F value	P value
Age	2.757	0.027
BMI	3.509	0.031
Systolic BP	4.235	0.026
Diastolic BP	2.912	0.036
FBS	1.112	0.364
TC	1.602	0.174
TG	0.746	0.593
HDL	5.126	0.001
LDL	2.164	0.047
VLDL	0.743	0.594
LDL/HDL	3.679	0.006
TC/HDL	2.845	0.023
Total calories intake/day	0.717	0.614
Percentage of calories by fat	0.248	0.939
Total grams of fat/days	0.704	0.623

Among various risk factor in this study, Dyslipidemia was the most prevalent risk factor for CAD and was present in 46.6% subjects. Particularly low HDL level 43% was most the prominent finding, followed by high LDL level that was found in 19% subjects. One similar study from Jaipur in 237 school children aged 13-17 years reported Borderline hypercholesterolemia (170-199mg/dl) in 33% and definite hypercholesterolemia was in 6.8%.<sup>8</sup> Gupta et al, from Delhi defined dyslipidemia using >95% percentile values using the same cohort. In males and females, high total cholesterol was in 14% and 15%, high LDL cholesterol was in 12% and 13%, high triglycerides in 14% and 16% and low HDL cholesterol was in 5%.<sup>9</sup> Another study from Gulati et al, suggests that low HDL was found in 25% subjects, high total cholesterol in 10%, high LDL cholesterol in 15%, and high triglycerides in 22.5%.<sup>10</sup> This suggests that the prevalence of low HDL is a very significant risk factor in Gujarati children probably due to their genetic predisposition and dietary habits.

Other risk factors identified included high fat diet (22%), positive family history (9.5%), hypertension (4.5%), obesity (3.17%), smoking (1.05%), diabetes (0.21%) that were observed in this study. Study from Chandrasekhar et al. reported risk factors like dyslipidemia, oxidative stress, insulin resistance and endothelial dysfunction in children aged 5 to 17 years who were obese.<sup>7</sup>

Mean CIMT was significantly higher (0.58mm) suggestive of initiation of preclinical atherosclerosis at this early age in Gujarati children. In study of young Gujarati children, low HDL cholesterol and raised LDL cholesterol were the strongest current predictors of higher carotid intima media thickness; age, obesity, high blood pressure and smoking were other significant risk factor

for higher CMT. Case control studies of children and young adults demonstrate that familial hypercholesterolemia and borderline hypertension are associated with greater IMT.<sup>11-13</sup> The young Finns study wherein children aged 3 to 18 years were re-examined 21 years later in their adulthood reported that risk factors like high levels of LDL, SBP, BMI, cigarette smoking studied in 12 to 18 years of age were directly related to CMT in adulthood.<sup>14</sup> Therefore, exposure to CV risk factors in early life may lead to atherosclerosis in arteries in adulthood.

Two subjects having abnormal ECG and 2D Echo underwent coronary angiography. CAG in the first subject revealed coronary artery disease (LMCA disease + RCA disease). The lipid profile in this subject was suggestive of Homozygous Hypercholesterolemia and a marked raised Lp (a) level. CAG in the other subject revealed coronary artery disease (RCA disease) and on further investigation the subject was found to have increased triglyceride secondary to nephrotic syndrome, both of the subjects were having significantly increased CMT (1.1mm Vs mean 0.58mm). The atherogenic dyslipidemia found in Indians has two main components - low HDL levels and hypertriglyceridemia; of these two, low HDL levels are present in young Gujarati children.<sup>15</sup>

## CONCLUSION

The findings of the study suggest that CVD risk factors may be present from early age. Children should be screened for presence of such risk factors. Screening of dyslipidemia and other potential risk factors at an early age can help identify the high-risk individuals to initiate appropriate strategies to prevent development of CV disease.

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## REFERENCES

- Murray CJL, Lopez AD, eds. Global burden of disease. Harvard, MS: Harvard School of Public Health, 1996;1.
- Prabhakaran D, Jeemon P, Roy A. Cardiovascular diseases in India: current epidemiology and future directions. *Circulation.* 2016;133:1605-20.
- Leeder S, Raymond S, Greenberg H, Liu H, Esson K. A race against time. The challenge of cardiovascular disease in developing economics. New York: Columbia University, 2004.
- Prabhakaran D, Yusuf S, Mehta S, Pogue J, Avezum A, Budaj A, et al. Two-year outcomes in patients admitted with non-ST elevation acute coronary syndrome: results of the OASIS registry 1 and 2. *Indian Heart J.* 2005;57:217-25.
- Reddy KS, Yusuf S. Emerging epidemic of cardiovascular disease in developing countries. *Circulation.* 1998;1997:596-601.
- Raj M. Cardiovascular health in children and adolescents. *Kerala Heart J.* 2014;4:22-28.
- Chandrasekhar T, Suchitra MM, Pallavi M, Srinivasa Rao PVLN, Sachan A. Risk Factors for Cardiovascular Disease in Obese Children. *Indian Pediatrics.* 2017;54:752-6.
- Gupta R, Goyle A, Kashyap S, Agarwal M, Consul B, Jain BK. Prevalence of atherosclerosis risk factors in adolescent school children. *Indian Heart J.* 1998;50:511-5.
- Gupta N, Shah P, Goel K, Misra A, Rastogi K, Vikram NK, et al. Imbalanced dietary profile, anthropometry and lipids in urban Asian Indian adolescents and young adults. *J Am Colloid Nutr.* 2010;29:81-91.
- Gulati S, Saxena A. Lipid profile in children of patients with premature coronary artery disease. *Indian Pediatrics.* 2003;40:556-60.
- Tonstad S, Joakimsen O, Stensland-Bugge E, Leren TP, Ose L, Russell D, et al. Risk factors related to carotid, intima media thickness and plaque in children with familial hypercholesterolemia and control subjects. *Arterioscler Thromb Vase Biol.* 1996;16:984-991.
- Rubba P, Mercuri M, Faccenda F, annuzzi A, Irace C, Strisciuglio P, et al. Premature carotid atherosclerosis; does it occur in both familial hypercholesterolemia and homocystinuria? Ultrasound assessment of arterial intima-media thickness and blood flow velocity. *Stroke.* 1994;25:943-50.
- Pauletto P, Palatini P, Da Ros S, Pagliara V, Santipolo N, Baccillieri S, et al. Factors underlying the increase in carotid intima-media thickness in borderline hypertensives. *Arterioscler Thromb Base Biol.* 1999;19:1231-7.
- Raitakari OT, Juonala M, Kähönen M, Taittonen L, Laitinen T, Mäki-Torkko N, et al. Cardiovascular risk factors in childhood and carotid artery intima-media thickness in adulthood: the Cardiovascular Risk in Young Finns Study. *JAMA.* 2003;290:2277-83.
- Joshi SR, Anjana RM, Deepa M, Pradeepa R, Bhansali A, Dhandania VK, et al. Prevalence of dyslipidemia in urban and rural India: the ICMR-INDIAB study. *PLoS one.* 2014; 9(5):e96808.

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