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Original Article

Internal Medicine Section

Comparison of Carotid Intima Media Thickness in Children of Patients with and without Premature Coronary Artery Disease

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ABSTRACT

Introduction: Increased Carotid Intima Medial Thickness (CIMT) is associated with cardiovascular risk factors and vascular events like Coronary Artery Disease (CAD) and stroke.

Aim: This study was designed to identify whether CIMT is increased in the children of parents with premature coronary artery disease and compare it with age and sex matched controls who are children of normal individuals. We also tried to compare and correlate the changes in CIMT if any, among the study group with relation to family history of diabetes and hypertension.

Materials and Methods: It was an observational prospective case control study. Twenty five cases (children of parents with premature coronary artery disease) were recruited as per the inclusion and exclusion criteria. Age and sex matched controls were recruited from the paediatric Outpatient Department (OPD). The CIMT was measured using ultrasound Doppler as per the protocol by the Mannheim intima media thickness consensus statement.

Results: Ten children out of 25 controls had CIMT of 0.05 cm and 5 out of 25 cases had CIMT of 0.07 cm. The association between cases and controls was not statistically significant. Even though the CIMT increases after 10 years, there is no statistically significant association between cases and controls in the different age groups. Out of the total 48% of the children among the case group had family history of hypertension whereas 28% in the control group. A 33% of children in the case group with family history of hypertension had CIMT of 0.07 cm; 46% of children in case group without family history of hypertension had CIMT of 0.05 cm. This difference was statistically significant (p=0.005). There was no significant association between family history of diabetes mellitus and CIMT in both groups.

Conclusion: There was significant association between CIMT in children with family history of premature CAD and family history of hypertension when compared with no family history of hypertension with premature CAD. There was no significant association between CIMT of children with and without family history of premature CAD.

Keywords: Cardiovascular risk, Diabetes mellitus, Hypertension

INTRODUCTION

Cardiovascular events are one of the leading causes of morbidity and mortality worldwide. Preventive treatment for patients who are at risk for the development for cardiovascular events depends upon identifying high risk asymptomatic individuals. Studies have also shown that a family history of Coronary Artery Disease (CAD) is itself an independent risk factor for the development of CAD [1]. The association of diabetes, dyslipidemia, hypertension, smoking, central obesity and a positive family history with CAD is well established, and recent studies have also associated these risk factors with premature CAD [2].

Carotid Intima-Medial Thickness (CIMT) is a moderate phenotype for early atherosclerotic disease process [3]. It is an easy to measure, reproducible, non-invasive test and the most important aspect being that it can be used in large-scale population studies [4]. Studies have shown that increased CIMT is associated with cardiovascular risk factors and also very much associated with the presence of atherosclerotic disease process such as ischemic heart disease [5,6]. A number of studies have examined the relationship between CIMT and vascular events like acute coronary syndromes and stroke [7].

Several studies have been done to assess the role of measurement of CIMT to predict the cardio vascular risk. Only a few studies have assessed the CIMT in children to predict the risk for future cardiovascular events [8,9]. Calculating the thickness of the carotid intima media complex in children with parental history of early CAD will give a clue towards the risk of future development of CAD [8,9].

There is no Indian study available regarding the CIMT in children of patients with premature CAD. Hence we did this pilot study. This study assessed the CIMT in children with parental history of premature CAD and the results were compared with age and sex matched controls to find if there was any correlation. It would help to identify at risk individuals very early in their life and help apply primordial prevention strategies on them to decrease the incidence of CAD. Therefore the objective of the study was as follow:

Primary Objective

To identify whether CIMT is increased in the off-springs of patients with premature CAD and compare it with age and sex matched controls who are off springs of normal individuals.

Secondary Objective

To compare and correlate the changes in CIMT if any, among the study group with relation to family history of diabetes and hypertension.

MATERIALS AND METHODS

This study was carried out in PSG Institute of Medical Sciences and Research, Coimbatore after getting the institutional ethical committee clearance. It was an observational, prospective case control study. The cases were recruited from inpatients from general medicine and cardiology wards as per the inclusion and exclusion criteria. Controls were recruited from the paediatric outpatient

department. The sample size was 25 cases, and age and sex matched 25 controls. The duration of the study was one year. The CIMT was measured for all cases and controls as per the Mannheim intima-media thickness consensus statement [10].

Inclusion Criteria

1. Children of patients having premature CAD (CAD < 45 years in males and < 55 years in females) who presented with acute coronary syndrome.

Exclusion Criteria

1. Morbidly obese children (BMI >97th percentile),
2. Children < 5 years and ≥ 18years.

STATISTICAL ANALYSIS

The statistical software used for the analysis of the data was SPSS version 19. Chi-Square test was used to calculate p-value. Microsoft Word and Excel have been used to generate figures and table

RESULTS

Comparison of CIMT between Cases and Controls: A 40% (10 children out of 25) of controls had a CIMT of 0.05 cm while 6 out of 25 children in cases had a CIMT of 0.06 cm and 5 out of 25 children in the cases group had a CIMT of 0.07 cm. The relation between CIMT for cases and controls were however not significant [Table/Fig-1].

CIMT (cm)		Cases	Controls	Total	p-value*
0.04	No.	4	5	9	0.710
	%	44.4%	55.6%	100.0%	
0.05	No.	7	10	17	
	%	41.2%	58.8%	100.0%	
0.06	No.	6	6	12	
	%	50.0%	50.0%	100.0%	
0.07	No.	5	3	8	
	%	62.5%	37.5%	100.0%	
0.08	No.	3	1	4	
	%	75.0%	25.0%	100.0%	
Total	No.	25	25	50	
	%	50.0%	50.0%	100.0%	

[Table/Fig-1]: Comparison of CIMT – cases and controls.
*Chi-square test

Comparison of CIMT in Different Age Groups among Cases and Controls: The study population (both cases and controls) were divided into three groups. Those between 5 to 10 years were one group, 10 to 15 years second group and more than 15 years belonged to the third group. CIMT was compared age wise for both cases and controls. In control, group 1 (age 5 to 10years) had 3 numbers whereas group 2 (age 10 to 15 years) and group 3 (age more than 15 years) had 11 numbers each.

Among the cases, 33% in the case group 1 (5-10 years) had a CIMT of 0.05cm, 0.06cm and 0.07cm respectively. In the group 2 (10 to 15 years), 44% had a CIMT of 0.05cm and 11% had a CIMT of 0.08cm. In the group 3 (> 15 years), 30% and 15% had a CIMT of 0.07cm and 0.08cm respectively [Table/Fig-2].

Among the control population 67% of the children in the group 1 (5 to 10 years) had a CIMT of 0.04cm. 64% of the children in the group 3 (15 years and above) had a CIMT of 0.05cm [Table/Fig-2].

However, for both the case as well as the control population there was no statistically significant relationship between the CIMT and the age [Table/Fig-2].

Relation between CIMT and Family History of Diabetes Mellitus: A 56% of the population in both cases and controls had a family history of diabetes mellitus. There was no significant relation between family history of diabetes mellitus and CIMT both for cases and controls [Table/Fig-3].

Relation between Family History of Hypertension and CIMT: A 48% of the children among the case group had a positive family history for hypertension and 52% had no family history of hypertension. A 28% of the total children in the control group had a family history of hypertension while the rest had no family history of hypertension [Table/Fig-4].

Majority of the patients in the cases with family history of hypertension had a CIMT of 0.07 cm while most of the children in the cases with no family history hypertension had a CIMT of 0.05 cm and the difference was statistically significant [Table/Fig-4]. Majority of children without family history of hypertension in the control group had a CIMT of 0.05 cm [Table/Fig-4], and the difference is statistically significant (p-value 0.05).

Age (Years)			Carotid Intima Medial Thickness(cm) 0.04	0.05	0.06	0.07	0.08	Total	p-value*
Cases	5-10	No.	0	1	1	1	0	3	0.672
		%	.0%	33.3%	33.3%	33.3%	.0%	100.0%	
	10-15	No.	2	4	2	0	1	9	
		%	22.2%	44.4%	22.2%	.0%	11.1%	100.0%	
	>15	No.	2	2	3	4	2	13	
		%	15.4%	15.4%	23.1%	30.8%	15.4%	100.0%	
	Total	No.	4	7	6	5	3	25	
		%	16.0%	28.0%	24.0%	20.0%	12.0%	100.0%	
Controls	5-10	No.	2	0	1	0	0	3	0.185
		%	66.7%	.0%	33.3%	.0%	.0%	100.0%	
	10-15	No.	3	3	2	2	1	11	
		%	27.3%	27.3%	18.2%	18.2%	9.1%	100.0%	
	>15	No.	0	7	3	1	0	11	
		%	.0%	63.6%	27.3%	9.1%	.0%	100.0%	
	Total	No.	5	10	6	3	1	25	
		%	20.0%	40.0%	24.0%	12.0%	4.0%	100.0%	

[Table/Fig-2]: Comparison of CIMT in different age groups among cases and controls.
*Chi-square test

Family history of diabetes mellitus			Carotid Intima Medial Thickness(cm) 0.04	0.05	0.06	0.07	0.08	Total	p-value*
Cases	Yes	No.	1	5	2	4	2	14	0.802
		%	7.1%	35.7%	14.3%	28.6%	14.3%	100.0%	
	No	No.	3	2	4	1	1	11	
		%	27.3%	18.2%	36.4%	9.1%	9.1%	100.0%	
	Total	No.	4	7	6	5	3	25	
		%	16.0%	28.0%	24.0%	20.0%	12.0%	100.0%	
Controls	Yes	No.	3	4	5	2	0	14	0.129
		%	21.4%	28.6%	35.7%	14.3%	.0%	100.0%	
	No	No.	2	6	1	1	1	11	
		%	18.2%	54.5%	9.1%	9.1%	9.1%	100.0%	
	Total	No.	5	10	6	3	1	25	
		%	20.0%	40.0%	24.0%	12.0%	4.0%	100.0%	

[Table/Fig-3]: Comparison of family history of diabetes mellitus and CIMT.
*Chi-square test.

DISCUSSION

In our study, even though more number of children in the case group had higher CIMT as compared with the controls (62% and 75% of the children in the study population with a CIMT of 0.07 cm and 0.08 cm respectively were from the case group and 56% and

Family history of hypertension			Carotid Intima Medial Thickness(cm)					Total	p-value*
			0.04	0.05	0.06	0.07	0.08		
Cases	Yes	No.	1	1	3	4	3	12	0.049
		%	8.3%	8.3%	25.0%	33.3%	25.0%	100.0%	
	No	No.	3	6	3	1	0	13	
		%	23.1%	46.2%	23.1%	7.7%	.0%	100.0%	
	Total	No.	4	7	6	5	3	25	
		%	16.0%	28.0%	24.0%	20.0%	12.0%	100.0%	
Controls	Yes	No.	0	3	1	2	1	7	0.129
		%	.0%	42.9%	14.3%	28.6%	14.3%	100.0%	
	No	No.	5	7	5	1	0	18	
		%	27.8%	38.9%	27.8%	5.6%	.0%	100.0%	
	Total	No.	5	10	6	3	1	25	
		%	20.0%	40.0%	24.0%	12.0%	4.0%	100.0%	

[Table/Fig-4]: Comparison of family history of hypertension and CIMT.
*Chi-square test

59% of the children in the study population with a CIMT of 0.04 cm and 0.05 cm were from the control group) it was not statistically significant. This was in contrast to the study done by Barra S et al., who had a similar sample size yet had significant relationship between CIMT in cases (positive parental history of myocardial infarction) than in controls [8]. Another similar study by Cuomo et al., with higher sample size (114 children-adolescents with positive family history of diabetes with age and sex matched controls) found that there was an association between positive family history of CAD and increased CIMT and this association was independent of lipids, lipoproteins and several other traditional risk factors [9].

When we analysed the CIMT of cases and controls after dividing them into 3 groups, the association between age group and the CIMT was not statistically significant. In our study we found children with parental history of premature CAD along with parental history of hypertension had increased CIMT compared to those children without family history of hypertension but with parental history of premature CAD. Hence, a positive family history of hypertension could have an additive effect with positive family history of premature CAD on the CIMT. In the study by Barra S et al., they compared children with positive family history of hypertension and negative family history of CAD and children with positive family history of CAD and negative family history of SHT with children who had negative family history for both hypertension and CAD. They concluded saying that children with positive parental history of CAD has significant relation to increased CIMT than those with positive family history of hypertension and family history of hypertension did not have any additive effect on the increased CIMT.

In our study, children with positive parental history of diabetes and premature CAD were compared with children with negative family history of CAD and diabetes mellitus. There was no significant association with increased CIMT with family history of diabetes mellitus for both cases and controls. This is in contrast with a study done by Carlos et al., which showed positive co-relation; but this study was done on adult population [11]. In an another study done by Vijay Cheluvaraj NV et al., in young adult population, family history of diabetes mellitus was significantly associated with CIMT [12]. It could be due to that CIMT increases as the off springs with family history of diabetes mellitus become older.

LIMITATION

The major limitation of the study was the sample size. We need a larger study to confirm our findings.

CONCLUSION

There was significant association between CIMT in children and positive family history of both hypertension and premature CAD when compared with children without family history of hypertension but with premature CAD. There was no significant correlation between CIMT of children with or without parental history of premature coronary artery disease. There was no significant relation between CIMT and family history of diabetes mellitus between cases and controls.

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