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Original Research Article

The study of lipid profile and other cardiovascular risk factors in children born to parents having premature ischemic heart disease

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ABSTRACT

Background: Most of the studies on cardiovascular risk factors are concentrated on adults. But atherosclerotic process begins in childhood and is influenced by genetics, diet and life style. Hence, present study was undertaken. The objectives of the study were to study lipid profile and other cardiovascular risk factors like hypertensive status, BMI(Body mass index) in children aged between 5years and 18 years born to parents having premature IHD(Ischemic heart disease), to study diet and life style factors in study group having family history of IHD, to study the sociodemographic profile of dyslipidemia.
Methods: There were 200 cases of premature IHD were selected. Their children(n=200) in the age group of 5 to 18 years were selected and analysed for cardiovascular risk factors. They were compared with 200 normal children without any family history of IHD.
Results: On comparison of mean lipid profile between cases and controls HDL cholesterol was very low amongst cases (p=0.001). The mean values of triglycerides and VLDL were very high amongst cases (p=0.001). The mean atherogenic index (AI) was high amongst cases (p=0.001). Prehypertension or hypertension was seen amongst 8.5% cases (p=0.004). Amongst the cases 19.5% had excess junk food intake (p=0.001). 51.5% of cases had sedentary life style (p=0.001).
Conclusions: Children in our area born to parents with premature IHD have significant incidence of dyslipidaemia. There is an increased incidence of other cardiovascular risk factors like hypertension, excess junk food intake, sedentary life style in these children.

Keywords: Cardiovascular risk factors, Dyslipidaemia, Premature IHD

INTRODUCTION

Ischemic heart disease (IHD) in Indians has been shown to be premature, occurs at an early age and is more aggressive, extensive and malignant. 52.2% of deaths due to cardiovascular diseases occur below the age of 70 years in India as compared with only 22.8% in the developed world.[1] Primary prevention of IHD is important as approximately 1/4 to 1/3 of first myocardial infarction results in death.

Recent evidence, both pathologic and epidemiologic points to an association between individual genetic makeup, environmental factors and premature development of atherosclerotic disease. Atherosclerotic process begins in childhood and is influenced by

genetics, diet and life style. The changes in arteries that precede formation of intimal plaques are present in life as early as 3-9 years of age and the established risk factors are applicable to children as well as adults. In addition, familial aggregation of risk factors and of premature atherosclerotic disease is often noted.[2-4] The present mortality and morbidity rates are the consequence of previous exposure to behavioral risk factors and biological factors. Behavioral risk factors are inappropriate nutrition, insufficient physical activity, increased tobacco consumption etc. and biological risk factors are overweight (obesity), high blood pressure, dyslipidemia, and diabetes mellitus.

There is growing conviction that the only way to significantly alter the cause of atherosclerosis is to attack the constitutional and environmental precursors long before the overt symptoms become manifest.[5] There are studies which show that there is considerable reduction in risk of IHD with diet, life style modification. Thus, intervention must begin early in life to prevent or delay the onset of atherosclerotic disease.

It is seen that South Indians are more prone for IHD because of their life style and also high carbohydrate consumption.[6] Fewer studies compared the risk status in lower income group. Thus, there is a need to study cardiovascular risk status in South India and also including lower income subjects, hence the present study was undertaken, keeping in mind that intervention early in life prevents or delays the onset of IHD.

METHODS

A total of 200 cases of premature IHD were selected after obtaining their written consent, from intensive coronary care unit of Sri Jayadeva Institute of Cardiology, Mysore, Karnataka, India. Their IHD status was taken into account by their history, medical case sheets, laboratory data. Data was collected based on a predesigned questionnaire. Then their children were included for the study.

Inclusion criteria of parents

- Age <55 years males diagnosed with IHD,
- <65 years females diagnosed with IHD.

Exclusion criteria of 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, certain diuretics, beta blockers etc., leading to hyperlipidemia.

Inclusion criteria of children

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

Exclusion criteria of children

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

Comparison group

There were 200 children selected from normal siblings of children attending outpatient department of pediatrics who are not suffering from cardio vascular disease. Not having any family history of IHD.

Data was collected using a pre-designed proforma, which included the following data

- Dietary information (vegetarian/non vegetarian, consumption of junk food etc.),
- Physical activity information in terms of hours of moderate physical activity,
- In these children blood pressure (BP) was documented.

Before recording the blood pressure, procedure was fully explained to the and blood pressure was recorded in sitting position in right arm with cubital fossa at heart level, by auscultatory method using standard mercury sphygmomanometer. The appropriately sized cuff was selected with the bladder width about 40% of the arm circumference at a point midway between olecranon and acromion and bladder length covering at least 80% to 100% of the circumference of the arm. When the cuff was too small, the next larger cuff was used. The first and fifth phases of korotk off sounds were taken as indicative of systolic and diastolic pressure respectively. Three measurements were taken at interval of five minutes each and systolic and diastolic blood pressure were categorized by higher value.

The percentile charts based on gender, age and height provided by IAP (Indian Academy of Pediatrics) were used for classification of blood pressure.[8]

The child was considered

Normotensive: blood pressure less than 90th percentile

Prehypertensive: If blood pressure was greater or equal to 90th percentile or greater or equal to120/80mmHg, B.P. was rechecked at the same visit after one hour. If BP was persistently abnormal even in second screening, BP was

rechecked at one-week interval. If at the fourth screening, BP was persistently elevated to between 90th percentile to 95th percentile or greater or equal to 120/80 mmHg (even if less than 90th percentile), child was considered prehypertensive.

Hypertensive: BP at the end of fourth screening is greater or equal to 95th percentile.

Anthropometric measurements were taken. Height was measured using a stadiometer without footwear with an accuracy of up to 0.5cm. The weight was measured using a weighing scale having an accuracy of up to 0.1kg with children wearing light clothing.

Body mass index (BMI) was calculated using height (in meters), weight (in kg) using the formula Kg/m^2. The children were categorized as normal, underweight, overweight or obese. The percentile charts based on gender; age provided by IAP (Indian academy of Pediatrics) was used for classification of BMI.[9]

Blood sample of about 2ml was drawn from the child and sent to the central laboratory. The blood was drawn after 12hours of fast. Lipid profile was estimated using Auto analyzer kit method. Total cholesterol l(TC), triglycerides (TG), High density lipoprotein (HDL), very low-density lipoprotein (VLDL), Low density lipoprotein (LDL) levels were estimated. Although HDL is a more useful predictor of IHD than TC alone, the ratio of' HDL to TC may be even more predictive which is called as atherogenic index (AI) was also calculated. Atherogenic index has been used as marker of future coronary atherosclerosis. AI >5 was taken as abnormal. The values recommended by American academy of Pediatrics according to age and gender were used for interpretation of lipid values. For TC, TG and LDL values >95th percentile for age were considered as abnormal. For HDL, values <5th percentile were considered as abnormal.[10]

Nutritional intake was assessed by dietary recall method. Junk food intake more than thrice a week was taken as excess junk food intake. The physical activity of the children was assessed and documented by taking history.

WHO recommends at least 30 minutes of cumulative moderate exercise (equivalent to walking briskly) for all ages; plus for children, an additional 20 minutes of vigorous exercise (equivalent to running), three times a week.[11] Those children not satisfying the above criteria were grouped under sedentary lifestyle, those who meet the criteria were grouped under active life style.

Statistical analysis

Lipid levels were expressed as mean ± SD. The data was further categorized according to age group, gender, family history, diet, life style. Difference between groups was compared with an unpaired student t test. Simple linear regression analysis was applied to examine the relationship between two variables. Descriptive statistics such as mean and standard deviation (SD) for continuous variables, and frequency and percentage for categorical variables was determined. Chi-square test and Fischer's test was used to show comparison between 2 groups for categorical variables and unpaired t test for continuous variables having 2 groups respectively. A p value <0.05 was considered statistically significant. The statistical analysis was performed using the SPSS package the SPSS for windows (version 20.0).

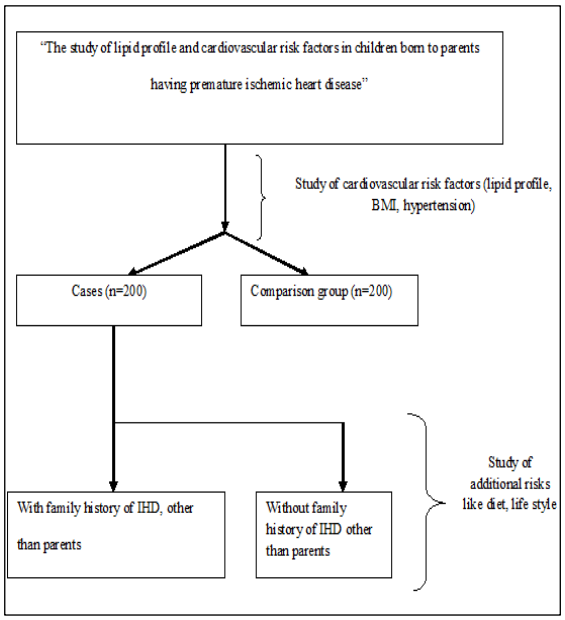

Figure 1: Pattern of study.

RESULTS

The present study included 200 children born to parents with premature ischemic heart disease and 200 children without any family history of ischemic heart disease as the comparison group. In the present study amongst the cases there were 130 males and 70 females (Male: Female =1.8:1) as compared to 103 males and 97 females amongst controls. (Male: Female=1.06:1). The age and the gender distribution are shown in (Table 1).

The distribution of males and females was not statistically significant (males, p=0.058, females, p=0.12). All our cases and controls belonged to lower class and lower middle class. The incidence of dyslipidemia amongst cases and controls is shown in (Table 2).

On comparison of mean lipid profile between cases and controls HDL cholesterol was very low amongst cases as compared to controls which was statistically highly significant. Similarly, the triglycerides and VLDL were very high amongst cases as compared to controls which were statistically highly significant. The atherogenic index was high among cases as compared to controls

which was also statistically significant. However, there was no statistically significant difference between cases and controls as far as total cholesterol and LDL cholesterol were concerned. The comparison of mean lipid profile between cases and controls is shown in (Table 3).

Table 1: Age and gender distribution of cases and controls.

Gender				Group		Total
				Cases	Controls	
Male	Ages	5-9 years	Count	3	0	3
			%	2.3	0.0	1.3
		10-14 years	Count	11	3	14
			%	8.5	2.9	6.0
		15-18 years	Count	116	100	216
			%	89.2	97.1	92.7
	Total		Count	130	103	233
			%	100.0	100.0	100.0
Female	Ages	5-9 years	Count	1	1	2
			%	1.4	1.0	1.2
		10-14 years	Count	10	5	15
			%	14.3	5.2	9.0
		15-18 years	Count	59	91	150
			%	84.3	93.8	89.8
	Total		Count	70	97	167
			%	100.0	100.0	100.0
Total	Ages	5-9 years	Count	4	1	5
			%	2.0	0.5	1.2
		10-14 years	Count	21	8	29
			%	10.5	4.0	7.2
		15-18 years	Count	175	191	366
			%	87.5	95.5	91.5
	Total		Count	200	200	400
			%	100.0	100.0	100.0

Table 2: The incidence of dyslipidemia amongst cases and controls.

Parameter	Cases no. (percent)	Controls no. (percent)
Dyslipidemia	125 (62.5)	76 (38)
More than one dyslipidemia	75 (37.5)	26 (13)

Table 3: Comparison of mean lipid profile between cases and controls.

Lipid profile	Group	Number	Mean	SD	P value
HDL	Cases	200	34.2676	12.68064	
	Controls	200	43.2424	11.41364	0.001
TG	Cases	200	148.6105	107.01871	
	Controls	200	105.0430	49.78163	0.001
TC	Cases	200	140.5625	45.54008	
	Controls	200	146.8640	25.79076	0.089
LDL_	Cases	200	81.4614	38.95839	
	Controls	200	86.6515	22.88590	0.105
TC/HDL	Cases	200	4.9495	3.62581	
	Controls	200	3.7635	2.20204	0.001
VLDL	Cases	200	24.6844	17.46888	
	Controls	200	17.2000	11.62003	0.001

On comparison of actual values of lipid profile, there was statistically significant pathologically low level of HDL amongst cases as compared to controls(p=0.001) as shown in (Table 4).

Table 4: HDL cholesterol values between cases and controls.

HDL values in mg/dl			Group		Total
			Cases	Controls	
HDLC	< 30	Count	62	21	83
		%	0.5	0.0	0.2
	30-70	Count	138	178	316
		%	1.5	0.0	0.8
	>70	Count	0	1	1
		%	98.0	100.0%	99.0
Total		Count	200	200	400
		%	100.0	100.0	100.0

P=0.001

More number of cases had pathologically high values of triglycerides as compared to controls which was statistically significant(p=0.001). This is also depicted in (Figure 2).

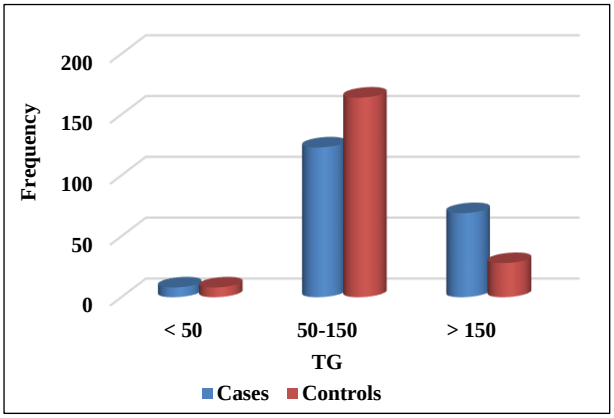

Figure 2: Comparison of triglyceride values between cases and controls.

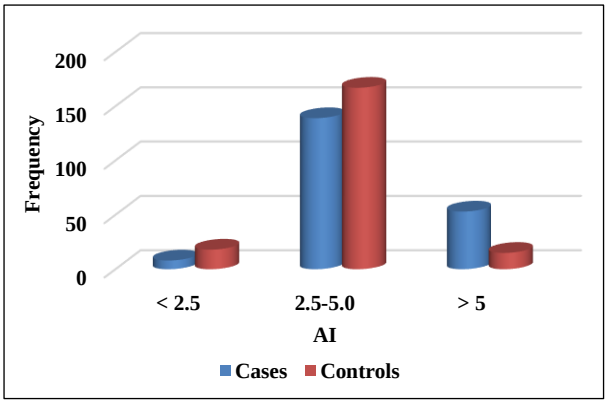

Figure 3: Comparison of atherogenic index (TC/HDL) values between cases and controls.

Though a greater number of cases had pathologically high total cholesterol as compared to controls, it was not statistically significant (p=0.083). More number of cases had a very high atherogenic index which was statistically highly significant (p=0.001). The same is shown in (Figure 3).

Though a greater number of cases had pathologically high LDL cholesterol as compared to controls, it was not statistically significant (p=0.36). More number of cases had a pathologically high values of VLDL as compared to controls (p=0.001). The same is shown in the (Table 5).

Table 5: Comparison of VLDL cholesterol values between cases and controls.

VLDL cholesterol in mg/dl			Group		Total
			Cases	Controls	
VLDLc	<50	Count	181	196	377
		%	90.5%	98.0%	94.2%
	>50	Count	19	4	23
		%	9.5%	2.0%	5.8%
Total		Count	200	200	400
		%	100.0%	100.0%	100.0%

The pattern of dyslipidemia was studied across three different age groups namely- 5-9 years, 10-14 years and 15-18 years. The mean HDL cholesterol was significantly lower across all the three age groups amongst cases as compared to controls which was statistically significant (p=0.01).The mean triglyceride was significantly more across all age groups amongst cases than controls which were statistically significant(p=0.007).There was no statistically significant difference of mean total cholesterol levels across various age groups between cases and controls (p=0.165).There was no statistically significant difference in mean LDL cholesterol levels between cases and controls across all age groups (0.169).The atherogenic index (TC/HDL) was high among cases across all age groups which was statistically significant(p=0.004).The mean VLDL values were higher across all age groups among cases as compared to controls which was statistically significant(p=0.001).

The pattern of dyslipidemia was studied across both the genders. There was no statistically significant difference in the HDL values between boys and girls across all age groups. Hypertriglyceridemia was more amongst males in the 10-18 years age group in cases as compared to controls which was statistically significant(p=0.001). TC was high among boys in the 10-18 years age group amongst cases as compared to controls which was statistically significant(p=0.016).The atherogenic index was high amongst boys in cases from 10 years onwards and in girls from 15 years onwards as compared to controls which was statistically significant(p=0.001). LDL cholesterol was not significantly high among cases across all age groups and across all genders. There was no statistically significant difference in VLDL levels across all age groups in both the genders.

More number of cases had prehypertension and hypertension as compared to controls which was statistically significant(p=0.004). This is also shown in (Table 6).

Table 6: Comparison of blood pressure amongst cases and controls.

			Group		Total
			Cases	Controls	
BP	Normal	Count	183	197	380
		%	91.5%	98.5%	95.0%
	Pre-HTN	Count	12	3	15
		%	6.0%	1.5%	3.8%
	HTN	Count	5	0	5
		%	2.5%	0.0%	1.2%
Total		Count	200	200	400
		%	100.0%	100.0%	100.0%

Though a greater number of cases were obese/overweight, it was not statistically significant when compared to controls(p=0.07). More number of cases consumed excess junk food as compared to controls which was statistically significant(39 Vs 15,p=0.001). More number of cases had sedentary life style as compared to controls which was statistically significant (103 Vs 30, p=0.001). Among 200 cases 41 cases (20.5%) had family history of ischemic heart disease apart from parents. There was no statistically significant higher lipid profile amongst cases with multiple family history. However, 14.6% of those with multiple family history were either overweight or obese as compared to 3.1% of cases without multiple family history which was statistically significant (p=0.016).

DISCUSSION

In the present study a greater number of cases had dyslipidemia than controls. But the prevalence of dyslipidemia amongst controls was also 38%. This is because of the western cut-offs used for the diagnosis of dyslipidemia. The values of lipid profile observed in present study in Indian children were lower than their Western counterparts, similar to the results observed by Khalil A et al.[12] In a study done by Nijaguna N et al, on study of lipid profile among adolescent school children in Bangalore using NCEP standards found prevalence of dyslipidemia to the extent of 62.27% and concluded that there should be appropriate cut-offs for Indian children.[13] Hence, there is a need to establish nomograms for lipid levels for Indian children.

Present study revealed that children of premature ischemic heart disease patients have significant incidence of dyslipidemia compared to age matched controls. This observation is consistent with study by Gulati S et al, and Saxena A et al, and other studies.[14,15] In a study by Blumenthal S et al, of the 72 children whose fathers had myocardial infarction,13.8% had cholesterol levels greater than 230 mg% whereas there was no significant difference between mean triglyceride levels.[16] In contrast, Khalil A et al, in a study from India compared offspring of patients with proven coronary artery disease (n = 50) and healthy parents (n = 50). There was no difference in the lipid profile of children of both the groups.[17] In the present study, the mean HDL cholesterol was significantly lower across all the three age groups amongst cases as compared to controls. The Tromso heart study says that high HDL-C levels are protective against IHD at all ages.[18] Gordon D et al, and Rifkind BM et al, suggested that HDL-C is a stronger predictor of IHD than total cholesterol and LDL-C.[19]

The boys had prevalence of dyslipidemia more than the girls in present study, similar to data by Gupta R et al, and a Turkish study.[20,21] The Bogalusa heart study, Framingham heart study and many other studies have also shown the fact that males are more affected.[22,23] However, another Indian study by Kumar S et al, in 2003 has shown that mean cholesterol and triglyceride values were higher amongst girls compared to boys. HDL-cholesterol values were lower amongst Indian boys compared to girls.[24] During adolescence, body-mass index and waist size increased in both sexes. As expected during puberty, changes in body composition differed sharply between sexes, with the percentage of body fat decreasing in boys and increasing in girls, may be hormones might be influencing early in age, estrogen may be protective, or testosterone may be harmful. Further studies are needed to better understand the development of cardiovascular protection during adolescence.

In the present study, a greater number of cases consumed excess junk food as compared to controls which was statistically significant. Dholpuria R et al, study showed that high prevalence of hypercholesterolemia was related mainly to dietary habits of the study children.[25] Diet with high fat and calorie intake and lack of physical activity would be the major culprits of dyslipidemia in our population. Dietary intervention is a key component of primordial prevention of dyslipidemia. Reduced intake of saturated fat and cholesterol in the diet has been shown in numerous studies to be associated with lower total and low-density lipoprotein cholesterol. Overall control of calories and restriction of added sugar also are important in the prevention of hypertriglyceridemia. References have shown that our diets are rich in saturated fats. Besides it also involves overcooking of food which results in destruction of nutrients like folate, deep frying and refrying in the same oil leading to trans-fatty acids formation which probably contributes to increase of dyslipidemia in our population. The influence of diet on dyslipidemia was best seen in the Canadian study wherein 3 groups: a control group, a group that was administered statin and a group with dietary modification was included.[26] The lipid levels were checked at baseline and again after 4 weeks. A drastic reduction in lipid levels was observed in statin and dietary modified groups

as compared to control group. However, between the statin and dietary modification group they did not very much. This means therapeutic intervention i.e. statin and dietary interventions seems to have the same effect, and the latter seems to be a more viable option.

In the present study, more children with multiple family history were either overweight or obese. This result is similar to those observed by Saxena A et al, Parmar IB et al.[14,27]

Csabi G et al, found that 76.7% of the obese children had one, two or three cardiovascular risk factors.[28] Chu NF et al, reported the prevalence of two or more cardiovascular risk factors four to five times greater in obese than in non-obese children.[29]

BMI shows a strong tracking effect from childhood into young adulthood. Waist-to-hip ratio has been positively correlated with serum cholesterol and LDL-C as early as 4 years of age. In particular, the BMI tracking correlations in the muscatine study from childhood to early adulthood ranged from0.58 to 0.91, and most obese children became obese adults.[30] This tracking effect is accompanied by an increase in adult cardiovascular risk. A 40-year follow-up in Stockholm, Sweden, showed a significant relation between overweight in adolescence and adult premature death and cardiovascular disease.[31] Similarly, an evaluation of adults who were enrolled as children in the Harvard growth study in the 1920s showed that increased adult morbidity and mortality from coronary heart disease were related to overweight in adolescence.[32] The Framingham study followed a cohort of individuals for 26 years and showed that each 1-SD increment in relative weight was associated with a 15% increase in the risk of cardiovascular events in men and a 22% increase in women. In 2 separate Bogalusa cohorts evaluated after an 8-year period of observation, increases in weight were accompanied by adverse changes in lipids and lipoproteins. Young adults (mean age, 22 years) in the beaver county lipid study had positive and significant correlations between BMI and LDL-C and triglycerides. Conversely, weight loss reduces risk in overweight individuals.[33] Sedentary life style leads on to obesity has been reported by many studies. Singh et al reported that 54.4% of the boys and 69.3% of girls replied as not being engaged in sports at school or at home and among them 52.8% were obese.[34]

The study by Berkey CS et al, has shown that children will benefit by increasing their physical activity and by reducing time watching TV or videos and playing video games, and this is beneficial even children who are obese prior35. Elgar et al study has also shown that sedentary behavior and physical activity in early adolescence both influenced body mass index in late adolescence.[36]These problems of overweight and cardiac risk factors begin at an early age, not just in teenage or adult years. The physician and parent should rather deal with these issues before the habits are set.

CONCLUSION

We conclude that children in our area born to parents with premature IHD have significant incidence of dyslipidaemia compared to controls. There is an increased incidence of risk factors like increased BMI, excess junk food intake, sedentary life style in these children.

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