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Lipid Pentad Index: A novel bioindex for evaluation of lipid risk factors for atherosclerosis in young adolescents and children of premature coronary artery disease patients in India

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Abstract

Objective: To evaluate the role of non-conventional lipid risk factors like Lipoprotein(a) [Lp(a)], Apolipoprotein A-I (Apo A-I) and Apolipoprotein B-100 (Apo B-100) and other conventional lipid profile parameters in children and adolescents of premature coronary artery disease (CAD) patients in India; and thereby explain the highest occurrence of premature CAD in this population.

Methods: Forty-five children and adolescents of premature CAD patients (cases, mean age 12.08±3.71 years) and forty-five age and sex matched children and adolescents of healthy parents without any history or clinical evidence suggestive of CAD were studied (controls, mean age 12.14±3.91 years).

Results: We found a significant increase in mean levels of Lp(a), Apo B-100, Total cholesterol (TC), Low Density Lipoprotein-Cholesterol (LDL-C) and Triglyceride (TG) in cases than controls. In contrast, Apo A-I and High Density Lipoprotein-Cholesterol (HDL-C) values decreased. Lipid Tetrad Index (LTI) and Atherogenic Index in Indian children and adolescents were also calculated. Kolmogorov *D* statistic and cumulative probability plot suggest that the new Lipid Pentad Index (LPI) defined by us is able to discriminate case and control populations more precisely than the existing LTI and Atherogenic Index.

Conclusions: The new proposed LPI appears to be a better indicator of lipid risk factors in children and adolescents of premature CAD patients from India, than the prior LTI and Atherogenic Index.

Keywords: Apolipoproteins; Lipoprotein(a); Lipid Pentad Index; Atherogenic Index; Lipid Tetrad Index; Premature CAD; Children; Adolescents

Introduction

The prevalence of CAD in Indians has been rising steadily over the last 40 years and is very high in both migrant Asian Indians as well as among the people of the Indian subcontinent [1]. A very important cardinal feature of CAD in Indians is its marked prematurity and severity [2]. High rate of CAD in Indians is attributed to nature (genetic predisposition) and nurture (environment) [3]. The CAD risk is magnified several folds by the presence of other factors like diabetes, hypertension, smoking and abnormal lipid profile [4]. Many studies have documented the conventional dyslipidemia in patients of CAD and their children [5–7]. But these traditional lipid risk factors explain only partly the higher prevalence of CAD in Indians and that too in the middle age, because dyslipidemia is usually not expressed until then [8]. Hence there is a strong need to identify the other risk factors preferably early in life to explain the occurrence of severe and premature CAD in Indians.

Genetic predisposition of CAD is reported to be mediated, besides many other factors, by higher levels of lipoprotein (a) [Lp(a)] [9]. It renders Indians genetically susceptible to CAD from early childhood [10]. It is fully expressed in first year of life and its high levels have the same predictive value as the family history of premature CAD [8]. Several studies undertaken to understand this phenomenon have confirmed higher Lp(a) levels in CAD patients than in the controls [11,12]. Lp(a) has been found to be a better marker of CAD than the conventional lipids, and is considered to be an independent risk factor for premature CAD [11]. On the basis of the Adult Treatment Panel (ATP) III

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guidelines, Lp(a) is currently classified as an emerging lipid risk factor for cardiovascular disease [13].

Further, the alteration of blood levels of Apo A-I and Apo B-100 in CAD patients has been found to be better discriminator than HDL-C and LDL-C levels themselves [14,15]. This is primarily due to an active exchange of lipid components between LDL and HDL. Therefore the amount of cholesterol within LDL and HDL molecules can vary widely both in size and composition leading to change of LDL and HDL. Apo A-I and Apo B-100 on the other hand remain with HDL and LDL permanently without any change [16].

Although Lp(a), Apo A-I and Apo B-100 have been evaluated in several studies involving CAD patients, very few studies have reported alterations in serum levels of Lp(a), Apo A-I and Apo B-100 in children of premature CAD patients worldwide [6,17]. To the best of our knowledge, only one study from India has analyzed Lp(a) levels in first degree relatives of patients with premature CAD [5] and no such study exists on Apo A-I and Apo B-100 levels in Indian children. Hence, we decided to analyze the serum levels of Lp(a), Apo A-I and Apo B-100 along with conventional lipids like total cholesterol, triglycerides, HDL-C and LDL-C in children and adolescents of patients of premature CAD. Also we calculated the value of Lipid Tetrad Index [3] postulated by Enas as indicator of dyslipidemia. This index, though known in many ethnic population, was not known in Indian children and adolescents so far. We have also evaluated the Atherogenic Index [18,19] in cases and controls, which is again not reported as yet in Indian children and adolescents.

Based on our findings, we have proposed a new bioindex-Lipid Pentad Index (LPI) to explain the lipid risk profile in children and adolescents of premature CAD patients in native India. LPI reflects the total burden arising out of alteration in traditional lipid profile as well as emerging lipid risk factors like Lp(a), Apo A-I and Apo B-100. Our study reveals that LPI proposed by us is better than the existing indices.

Materials and methods

Study design and subjects

This case control study was carried out in the Departments of Biochemistry and Medicine of Maulana Azad Medical College and associated LNJP hospital, New Delhi, India. A total of 90 subjects from 3–19 years of age of both sexes were studied.

Our case group comprised of 45 healthy children and adolescents of known patients of premature coronary artery disease (cases of acute MI and stable or unstable angina) admitted to medical emergency and coronary care unit of LNJP Hospital, New Delhi, India. Thirty-nine of these patients are fathers, while 6 are mothers of our case group subjects. Diagnosis of these parents of our case group was established by clinical history of typical chest pain, clinical examination, typical enzyme patterns, cardiac markers and diagnostic ECG changes, followed by stress echocardiography and angiography.

Premature CAD for the parents is defined as coronary artery disease occurring before the age of 45 years in men and 55 years in women [20].

Forty-five age and sex matched healthy children and adolescents of healthy parents without any history or clinical evidence of CAD were chosen as control group from general population.

Details of clinical history, physical examination, routine laboratory investigations and life-style risk factors were recorded in both case and control groups.

The case and control groups had mean age of 12.08± 3.71 years and 12.14±3.91 years, respectively. Male to female ratio in cases and control groups was 5:4 and 23:22, respectively.

In this study, all subjects as well as their parents were excluded, if they had clinical or laboratory evidence of liver and kidney diseases, acute and chronic infections, diabetes mellitus, thyroid disorders and history of use of drugs like oral contraceptive, anticonvulsants and retinoic acid etc.

The blood samples of all the subjects were collected after an overnight fasting. The serum was separated and stored at −70°C until analysis.

Ethical consideration

Prior to the study, informed consent was taken from all the subjects or from the parents in case of minors. An institutional committee had approved the study protocol.

Laboratory methods

Total serum cholesterol and triglycerides were estimated by enzymatic method using commercially available kits (Merck Ltd., Mumbai, India). HDL-Cholesterol was estimated by the precipitation method in which cholesterol is estimated in the supernatant containing HDL-C by cholesterol oxidase enzymatic method (Accurex Biomedical Pvt. Ltd., Mumbai India). LDL-C was calculated using Friedwald's formula. Lp(a), Apo A-I and Apo B-100 in serum were estimated using immunoturibidimetry kits (Clonital, Carvico, Italy for Lp(a) and Randox Laboratories Ltd., Antrim, UK for Apo A-I and Apo B-100) on the Olympus AU400 autoanalyzer (Olympus, Hamburg, Germany).

Statistical analysis

The data were analyzed using statistical software packages Minitab (Minitab Inc., PA) and Prism (Graphpad Software, San Diego, CA). Statistics of all parameters were computed by classifying on the basis of age and gender. The significance of each individual lipid parameter was determined by *t*-test, which is applicable for data with normal distribution. However in our study the data of all the lipid parameters for the case and control groups were normally or log-normally distributed. This was further confirmed by the probability plots of each lipid parameter. It was concluded that considering case and control groups together, we could use lognormal distributions for TG, Lp(a) and Apo B, whereas normal distributions could be applied for TC, LDL-C, HDL-C and Apo A-I. It is also known that natural logarithm of a log-normally distributed variable is normally distributed. Consequently, we applied the *t*-statistics on their

respective natural logarithms for TG, Lp(a) and Apo B-100. On the other hand, for TC, LDL-C, HDL-C and Apo A-I, *t*-statistics was applied on the raw data itself. Furthermore, we also applied *F* test on each pair of case and control groups for all the lipid parameters. This test determines whether the variance between the case and control groups was significantly different. It was indeed found that for some of the lipid parameters, namely HDL-C, LDL-C, Lp(a) and Apo B-100, there was significant difference in variance of case and control groups. For these parameters then, we applied a modified *t*-test with Welch's correction. Mann–Whitney U test, though gave similar conclusions, was not used because it is a non parametric test (as it does not use any form of distribution of the underlying data) and has limited value in terms of conclusions.

Correlation between different parameters was obtained by calculating correlation coefficients, which theoretically lie between +1 to −1.

Using the data, we have defined a new Lipid Pentad Index (LPI) and plotted the empirical (and also the corresponding best-fitted lognormal form of) cumulative distribution functions in various figures. From these plots, one can find out the difference in the range of values of this and other existing indices, between case and control groups, irrespective of their life-style and other environmental risks. Further, when we plot the cumulative fraction of the case group on the same graph as the control cumulative fraction, the Kolmogorov–Smirnov (KS) test gives the maximum vertical deviation between the two curves as the *D* statistic [21]. Therefore, the larger the value of *D*, the greater is the separation between the case and control groups.

Results

Among the conventional risk factors, it was noted that blood sugar and body mass index (BMI) were within the normal range according to available guidelines [22]. However, they were significantly higher in cases than in controls (Table 1). Only two cases had blood pressure values above the normal range and 11 cases had positive history of smoking, while 29 cases had history of passive smoking at home.

The data of various serum lipid parameters (Table 2) show that the levels of Total Cholesterol (TC), Triglycerides (TG), Low density Lipoprotein-Cholesterol (LDL-C), Apolipoprotein B-100 (Apo B-100) and Lipoprotein (a) [Lp (a)] are significantly higher in cases than in controls. On the other hand, the levels of High Density Lipoprotein-=Cholesterol (HDL-C) and Apolipoprotein A-I (Apo A-I) are significantly lower in cases than in controls. However, according to the absolute norms of lipid parameters [23], low HDL-C and high Lp(a) were found in only 46% and 42% of total cases, respectively. It was further seen that age and gender had no significant effect on any of the lipid parameters in either case or control subjects. Age classified data show that there is no definite trend in change of any of the lipid parameters with regard to age. Similarly, active or passive smoking had no effect on any of the parameters.

Table 1
Conventional risk factors: children of premature CAD patients versus controls

Risk factors	Cases (n=45) (mean±SD)	Controls (n=45) (mean±SD)	p value
BMI (kg/m^2)	19.1±3.28	17.5±2.99	0.0202 (S)
SBP (mm Hg)	108.1±10.35	102.5±8.23	0.0062 (S)
SBP (Pa)	14376±1376	13631±1094	0.0062 (S)
DBP (mm Hg)	60.58±9.83	51.16±6.32	<0.0001 (S)
DBP (Pa)	8057±1308	6804±840.2	<0.0001 (S)
Blood sugar (mg/dL)	78.49±6.76	67.38±5.60	<0.0001 (S)
Blood sugar (mmol/L)	4.36±0.38	3.73±0.31	<0.0001 (S)

Where S=significant, BMI=body mass index, SBP=systolic blood pressure, DBP=diastolic blood pressure.

Table 2
Conventional and SI units of lipid parameters of cases and controls

Parameters	Case (n=45) (mean±SD)	Control (n=45) (mean±SD)	p value
Total cholesterol			
(mg/dL)	151.11±16.81	113.4±13.15	<0.0001 (S)
(mmol/L)	3.91±0.44	2.94±0.34	<0.0001 (S)
Triglycerides			
(mg/dL)	83.98±14.02	64.47±9.92	<0.0001 (S)
(mmol/L	0.95±0.16	0.73±0.11	<0.0001 (S)
LDL-C			
(mg/dL)	97.36±14.03	60.02±12.41	<0.0001 (S)
(mmol/L)	2.52±0.36	1.55±0.32	<0.0001 (S)
HDL-C			
(mg/dL)	36.96±5.40	40.49±3.88	0.0006 (S)
(mmol/L)	0.96±0.14	1.05±0.10	0.0006 (S)
Apolipoprotein A-I			
(mg/dL)	109.6±10.45	115.9±9.43	0.0035 (S)
(g/L)	1.10±0.10	1.16±0.09	0.0035 (S)
Apolipoprotein B-100			
(mg/dL)	80.80±18.77	55.53±8.18	<0.0001 (S)
(g/L)	0.81±0.19	0.56±0.08	<0.0001 (S)
Lipoprotein (a)			
(mg/dL)	36.45±19.50	15.82±5.26	<0.0001 (S)
(mg/L)	364.5±195	158.2±52.6	<0.0001 (S)

Where S=significant, LDL-C=low density lipoprotein-cholesterol, HDL-C=high density lipoprotein-cholesterol.

Ratios between the different lipid parameters were also compared between the two groups. The LDL-C/HDL-C ratio in cases was significantly more than in controls (2.69±0.55 versus 1.50±0.38; $p<0.0001$). Similarly, Total cholesterol/HDL-C ratio (4.15±0.62 versus 2.82±0.42; $p<0.0001$) and Apo B-100/Apo A-I ratio (0.74±0.16 versus 0.48±0.07; $p<0.0001$) were significantly higher in cases than in controls.

Furthermore, Apo B-100/Apo A-I ratio was found to be a better indicator of atherosclerosis than LDL-C/HDL-C ratio by the cumulative distribution function (CDF) plot analysis (method described later). We find from LDL-C/HDL-C plots that 65% of cases can be wrongly classified as control (Fig. 1). Whereas, from Apo B-100/Apo A-I, only 46% of the cases can be wrongly classified as controls (Fig. 1).

Most lipid parameters do not reveal any strong positive or negative correlation among them, except between TC and LDL-C levels, where there is a strong positive correlation [$r=0.91$, $p<0.0001$ (S)]. In this paper, (S) stands for significant and (NS) stands for non-significant.

Total cholesterol, LDL cholesterol and Apo B-100 values were corrected because of compositional contributions, according

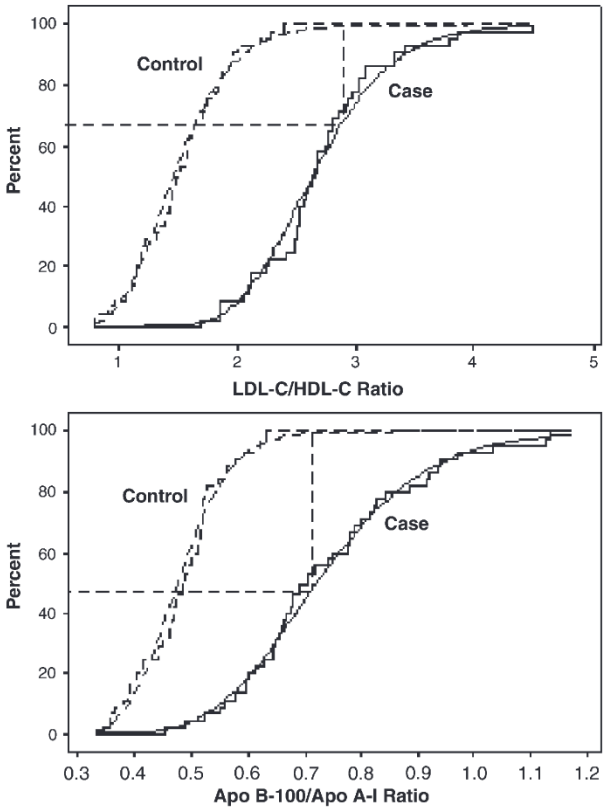

Fig. 1. Cumulative distribution function (CDF) plots of LDL-C/HDL-C ratio and Apo B-100/Apo A-I ratio in control and case groups. Stair case curves are empirical CDFs from measured data and smooth curves are corresponding lognormal CDF fit of the data.

to the following equations; only for the purpose of calculating correlation coefficient of these three parameters with Lp(a) [24].

$$\text{Corrected Total Cholesterol} = \text{Total Cholesterol} - [0.3 \times \text{Lp(a)}]$$

$$\text{Corrected LDL Cholesterol} = \text{LDL Cholesterol} - [0.3 \times \text{Lp(a)}]$$

$$\text{Corrected Apolipoprotein B} = \text{Apolipoprotein B} - [0.16 \times \text{Lp(a)}]$$

However, Lp(a) shows no correlation with corrected values of TC [$r=0.15$, $p=0.3132$ (NS)], LDL-C ($r=0.15$, $p=0.3329$ (NS)] and Apo B [$r=0.20$, $p=0.1850$ (NS)].

Lp(a) is seen to have weak positive correlation only with TG [$r=0.39$, $p=0.0075$ (S)]. Similarly Apo B shows weak positive correlation with TC [$r=0.46$, $p=0.0014$ (S)] and LDL-C [$r=0.41$, $p=0.0053$ (S)], Apo A-I also displays very weak correlation with other parameters.

Lipid Tetrad Index (LTI) and Atherogenic Index

We have calculated the Lipid Tetrad Index (LTI) [3], defined by Enas as follows,

$$\text{LTI} = [\text{TC} \times \text{TG} \times \text{Lp(a)}]/\text{HDL-C}$$

Our results show that LTI values are more than fourfold higher in cases than in controls (Table 3). The LTI values were so far unknown in Indian children and adolescents and our study has been able to give some projections on this. Similarly, we have also evaluated Atherogenic Index as logarithm of the ratio of molar concentration (mmol/l) of triglycerides to HDL-cholesterol i.e., (Log [TG/HDL-C]) [18,19]. The value of Atherogenic Index is also significantly higher in cases than controls from our data (Table 3).

Table 3
Lipid Tetrad Index, Atherogenic Index and Lipid Pentad Index in children of premature CAD patients

Parameter	Cases ($n=45$) (mean±SD)	Control ($n=45$) (mean±SD)	p value
Lipid Tetrad Index			
(conventional units)	$1.4\times10^4\pm1.1\times10^4$	$0.29\times10^4\pm0.13\times10^4$	<0.0001 (S)
(SI units)	1550±1219	332.7±151.4	<0.0001 (S)
Atherogenic Index			
(SI units)	−0.005±0.09	−0.162±0.08	<0.0001 (S)
Lipid Pentad Index			
(Conventional units)	$3.9\times10^5\pm3.4\times10^5$	$0.58\times10^5\pm0.31\times10^5$	<0.0001 (S)
(SI units)	1136±1001	169.9±90.07	<0.0001 (S)

Where S=significant.

New bioindex-Lipid Pentad Index (LPI)

Since Apo B-100/Apo A-I ratio is better than the LDL-C/HDL-C ratio, we have defined a new index (Lipid Pentad Index, LPI) incorporating this ratio into the known Lipid Tetrad Index. Thus, in the present work, we define,

$$\text{LPI} = [\text{TC} \times \text{TG} \times \text{Lp(a)} \times \text{Apo B} - 100]/\text{Apo A} - \text{I}$$

Our calculation shows that LPI too is significantly higher in cases than in controls (Table 3). Large standard deviation is due to underlying variation of mean normal values of individual parameters over the range of age of our cases (3–19 years) and controls (3–19 years). Thus LTI, Atherogenic Index and LPI all have statistically significant differences between cases and controls.

Fig. 2 shows the histograms of LPI in control and case subjects and gives an idea about the range of this new index in these population categories. The data could be fitted to lognormal

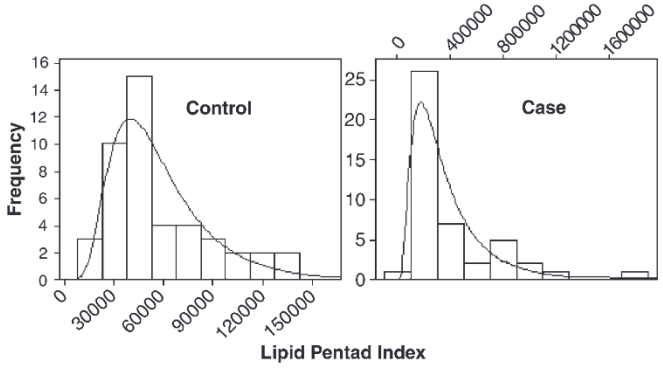

Fig. 2. Histogram of measured LPI data and corresponding lognormal fit in control and case groups.

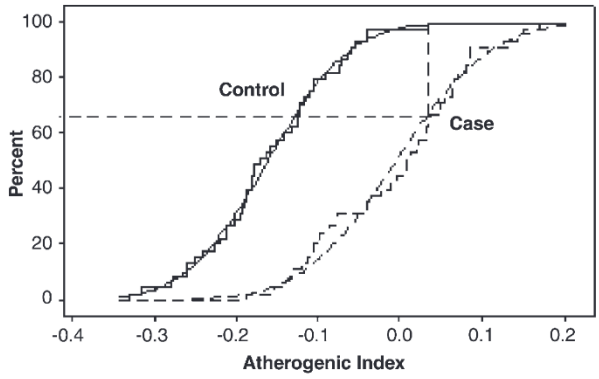

Fig. 3. Cumulative distribution function (CDF) plots of Atherogenic Index in control and case groups. Stair case curves are empirical CDFs from measured data and smooth curves are corresponding lognormal CDF fit of the data.

distributions as shown by the continuous curves. This is expected since LPI is defined to be the product of several variables, which themselves are log-normally or normally distributed.

From an analysis of the CDF plots of Atherogenic Index, LTI and LPI in controls and cases (Figs. 3–5), we have evaluated the percentage of cases that can be wrongly classified as controls for each index. In each figure, we have followed two simple steps to get this percentage. First, from the control curve, we have identified the point having a y-axis value of 100%. We then read off the x-axis value of this point. Let us call the latter X. Next, we noted down the y-axis value of the point (having x-axis value of X) on the case curve. Let us call it Y. Y is then the percentage of interest to us. Dotted lines in Fig. 1 and Figs. 3–5 have been drawn as a guide to the eye to facilitate reading of the X and Y values. The value of Y gives us the percentage of cases which can be wrongly classified as controls. From the CDFs of Atherogenic Index, we find that around 68% of cases can be wrongly classified as control (Fig. 3), whereas for LTI, it is 40% (Fig. 4). The corresponding overlap between case and control groups for LPI is 25% of the case population only (Fig. 5). This implies that a maximum of 25% of the population of the case group can be mistakenly classified to be in the control group, while using the LPI. But for LTI, the corresponding value is as high as 40% population of the case group.

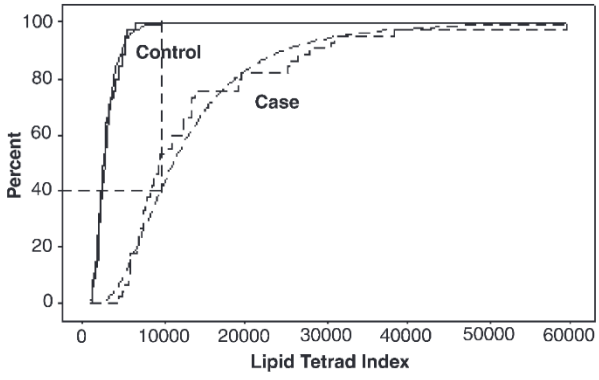

Fig. 4. Cumulative distribution function (CDF) plots of LTI in control and case groups. Stair case curves are empirical CDFs from measured data and smooth curves are corresponding lognormal CDF fit of the data.

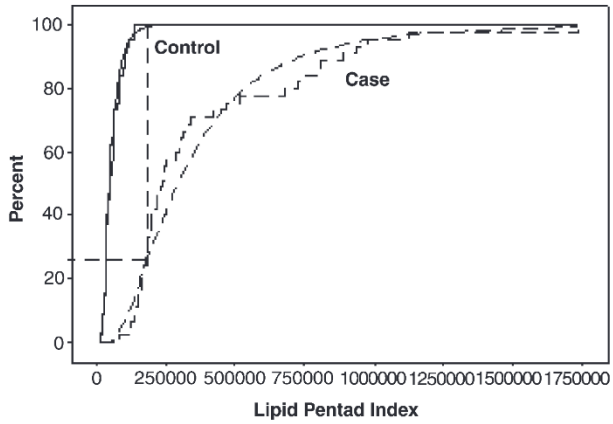

Fig. 5. Cumulative distribution function (CDF) plots of LPI in control and case groups. Stair case curves are empirical CDFs from measured data and smooth curves are corresponding lognormal CDF fit of the data.

We further calculated the Kolmogorov statistic (D) [21], which is a measure of the separation between any two CDFs. We obtain, $D_{LPI}=0.76$ and $D_{LTI}=0.70$, from the smooth lognormal fits to the CDFs in Figs. 4 and 5, respectively. This proves $D_{LPI}>D_{LTI}$ and confirms that the separation of the case and control CDFs is more for LPI, than it is for LTI. The D statistic is also highly significant for both LPI and LTI (for both indices $p<0.0001$).

Discussion

In the present study, the emphasis has been on identifying the newer non-traditional lipid risk factors early in life and in defining the total burden of lipid risks more precisely in children and adolescents of premature CAD patients in India.

We find that these children and adolescents had significantly higher levels of Lp (a), Apo B-100, TC, TG and LDL-C than their age matched controls, but lower Apo A-I and HDL-C than the latter. Age and gender had no significant effect on any of these lipid parameters in either cases or controls. Moreover, Apo B-100/Apo A-I ratio proved to be a better indicator of coronary risks than conventional LDL-C/HDL-C ratio. With regard to usual lipid profile, our data are consistent with previous studies [5,6].

We believe that the above data have clinical relevance for several reasons. Firstly, our data support the findings of prior studies involving Lp(a) levels in blood [17]. To the best of our knowledge, only one study from India has analyzed Lp(a) levels in first-degree relatives of patients with premature CAD [5]. Our data for Lp(a) are consistent with their observations. Since Lp(a) is inherited as a quantitative genetic trait [25] and we have found significantly higher level in cases than the recommended normal levels of Lp(a), it renders Indians genetically susceptible from early childhood [10]. Age classified data of our study show no definite trend with Lp(a) levels, which is supported by the observations that Lp(a) levels, unlike other lipid measures, do not vary with the age of the subject [26]. It is well known that Lp (a) is fully expressed in the first year of life [8]. Hence, its tracking from early childhood could be more useful than other lipids.

With regard to Apo B-100 and Apo A-I levels, our findings are similar to earlier reports from other countries [6,17]. However, in Indian population, our findings of these apoprotein levels in children and adolescents of premature CAD patients as well as healthy controls are novel because no such study has been reported from India to the best of our knowledge. Apo B-100 and Apo A-I are also reported to be better discriminators of CAD patients than LDL-cholesterol or HDL-cholesterol [14,15]. The reason behind this is that there is an active exchange of lipid components between LDL and HDL. Therefore the amount of cholesterol within LDL and HDL molecules can vary widely both in size and composition leading to change of LDL and HDL. Apo A-I and Apo B-100 on the other hand remain with HDL and LDL permanently without any change [16]. It is suggested that due to the different roles played by apolipoproteins in lipid metabolism, the metabolic fate of a lipoprotein is regulated more by its protein rather than its lipid content. This being the case, our finding of Apo B-100/Apo A-I ratio as a better discriminator than LDL-C/HDL-C is quite in agreement with this fact. In our analysis on measuring the data with cumulative distribution function, we find that, for LDL-C/HDL-C, 65% of case patients can be wrongly classified as control. Whereas, for Apo B-100/Apo A-I, only 46% of the case patients can be wrongly classified as controls. So Apo B-100/Apo A-I is better than LDL-C/HDL-C.

Atherogenic Index [Log (TG/HDL-C)] correlates with cholesterol esterification rates in Apo B-lipoprotein-depleted plasma (FERHDL) and lipoprotein particle size [18]. With regard to Atherogenic Index, our study is consistent with the mean values of the prior study [18,19]. The values of Atherogenic Index in Indian children were so far not reported. Our study has given that for the first time in Indian children and adolescents (Table 3).

LTI has been previously used to define the overall atherogenic risk arising out of dyslipidemia [3]. It is known in adult populations of various ethnicity and geographical locations including Indians. It explains the markedly different rates of CAD among people of different ethnicity and geographical regions, than individual risk factor or their ratios. Its value varies from approximately 4300 in the Japanese population, who have a low incidence of CAD, up to a maximum of approximately 24000 in Asian Indians in US, who have a high incidence of CAD. The mean LTI value in native Indians is reported to be 12899 in male and 10814 in female [3]. But the values of LTI in Indian children were so far unknown. We have found this value in healthy control children. There is more than fourfold rise of this value in case children of our study (Table 3). In view of altered levels of individual lipid parameters in cases than in the controls, this increased LTI value is quite justified. Again it is a novel finding from our study, which could be further exploited in future.

As Lp(a) is a powerful coronary risk factor and Apo B-100/Apo A-I is a strong indicator of coronary risks, we thought it logical to include Lp(a) level and the ratio of Apo B-100/Apo A-I into a mathematical index to express the total dyslipidemia in Indian children of premature CAD patients. With this consideration, we defined a new index called Lipid Pentad Index (LPI), in order to explain the risk profile in children of native Indians and examined if it is better than Atherogenic Index and LTI. Kolmogorov *D* statistic and cumulative probability plots of our data does indicate that LPI is able to discriminate between case and control populations more precisely than the existing LTI. Thus, according to Atherogenic Index, 68% of cases overlap with the controls, whereas 40% of case population overlap with the control group in LTI data. Compared to these two existing indices, when classified according to LPI, only 25% of case population overlap with control, thereby making LPI a better discriminator of cardiovascular risks in children of premature CAD patients.

However, our study does have some limitations that merit consideration. Our sample size is relatively small. To this end, we have fitted a lognormal distribution to our measured LPI data, which gives us a smoother distribution and hence a better statistical conclusion from cumulative probability plots. However, the new index (LPI) proposed by us has to be further tested in larger population of all age groups. In spite of these shortcomings, we feel that LPI expresses the dyslipidemia in a more comprehensive manner, taking into account newer lipid risk factors. It may therefore be used in further studies to establish its usefulness. Another limitation is that we evaluated serum levels only once and thus have not established our findings as predictors of prospective CAD in these children. Here we feel that a follow up study of these children is needed to strengthen our claim of LPI to be a better predictor.

In summary, we conclude that children of premature coronary artery disease patients have significant incidence of dyslipidemia characterized by high Lp(a) and Apo B-100 levels and low Apo A-I levels besides the conventional lipid profile abnormalities compared to age matched controls. A new bioindex (Lipid Pentad Index) reflects the total burden arising out of dyslipidemias that probably renders Indians more susceptible to CAD. Therefore, all children of premature CAD patients, independent of sex and age group, should be screened for dyslipidemia, so that healthy life style measures including dietary modifications can be instituted as a first step towards a healthy future.

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