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Asian Pacific Journal of Tropical Biomedicine

journal homepage: www.elsevier.com/locate/apjtb

Document heading doi: 10.1016/S2221-1691(15)30154-4

Do parental coronary heart disease risk factors (non-modifiable) effect their young ones?

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ARTICLE INFO

Article history:
Received 6 Oct 2014
Received in revised form 20 Oct 2014
Accepted 6 Nov 2014
Available online 11 Nov 2014

Keywords:
Non-modifiable cardiovascular risk factors
Lipid profile
Obesity
Nepalese
Basal metabolic index
Atherogenesis

ABSTRACT

Objective: To study the differences between the lipid profiles of the subjects whose parents are having known non-modifiable risk factors such as obesity, hypertension (HTN), myocardial infarction and diabetes, and compare them with the lipid profiles of the subjects whose parents are not having those risk factors.

Methods: A total of 402 subjects were recruited to this study. A detailed questionnaire which included information on the past medical history, height, weight, blood pressure, physical activity, smoke, alcohol, family history of coronary heart disease, HTN, diabetics and obesity. Basic demographic data and dietary habits were completed by all participants. Blood samples were obtained from all subjects after 14 h. Lipid profiles were analyzed using automated analyzer. The results were analyzed using SPSS software packages.

Results: The mean body mass index of the population was well below the cut-off value of obesity (>24.5 kg/m^2) and high risk of future cardiovascular disorder (CVD) events in this age group. The mean levels of total cholesterol (TC), triglycerides (TG) and TC/high density lipoprotein (HDL) were less than the risk levels indicative of future CVD events according to the ATP III cut-off values. However the mean HDL level in our population was slightly greater than the cut-off value while the mean low density lipoprotein level was almost similar to the risk level. Differences were observed when the subjects without history of maternal obesity were compared with subjects with history of maternal obesity. The greater percentage of subjects who are having risk levels of body mass index, TC, low density lipoprotein, TG, and TC/HDL indicated that maternal obesity contributed to the greater susceptibility of developing CVD risk in their offspring.

Conclusions: Advancing age may result in changes that could be atherogenic in the future. Such atherogenic changes have already initiated when the subjects are about 21 years old. The incidence of atherogenic changes is far greater when mothers who are having any of the risk factors such as obesity, diabetes, HTN and myocardial infarction than that fathers who are having similar risk factors.

1. Introduction

Coronary heart disease (CHD) is still the leading cause of morbidity in the general population[1]. In 2008, five out of the top ten causes for mortality worldwide were non-communicable diseases (NCDs), which have figured out to be seven out of ten by the year 2030 and majority resides in the developing countries. It is projected that, by the year 2030, about 76% of the deaths in the world would be due to NCDs[2]. India topped the world with 1.5 million cardiovascular disease (CVD) related diseases deaths in 2002.

According to the World Health Organization, CVD is the leading cause of death in India now, accounting for 29% of all deaths in 2005 with almost 100 million people affected. India is set to become the heart disease capital of the world[3]. Almost 2 000 people die of strokes every day. This alarming increase implies a future increase in the financial burden associated with this disease and raises the possibility that age-adjusted death rates from coronary artery

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Foundation Project: Supported by Confederation of Epidemiological Associations registered under Govt of Kerala (Grant No. 30-955/2012 CEA).

disease would be increased[4].

Even the worldwide obesity levels have drastically increased over the couple of decades. As the recent World Health Organization estimates over one billion and nearly 300 million adults are overweight and obese respectively[5]. In many developed countries, the prevalence of obesity has reached epidemic levels and is associated with NCDs including diabetes, hypertension (HTN), dyslipidemia and CHD[6]. In South Asia, the major health problems were infectious diseases and under-nutrition, and very little attention was paid to obesity by healthcare workers, policy makers or researchers[7]. However, attention is being paid with the rapid emergence of the obesity epidemic in South Asian countries now.

The term risk factor includes modifiable life styles and biochemical and physiological characteristics as well as non modifiable personal characteristics such as age, gender and family history of early-onset of CVD found in healthy individuals, which are independently related to the subsequent occurrence of CHD. The effects of risk factors in adults are additive, *i.e.* the greater the number of high risk factors present, the greater the risk of CVD[8].

Autopsy studies have shown that early coronary atherosclerosis often begins in childhood and adolescence. Further, hypercholesterolaemia in adolescents correlated positively with changes in vasculature predictive of later CVD[9]. There is a tendency to persistence in ranks (tracking) for total serum and β-lipoprotein cholesterol with age[10].

Hypercholesterolemia in childhood is common in westernized countries with high rates of CHD[11]. India is a classical example to illustrate drastic changes that occur in societies during the industrialization and urbanization or the westernization[12]. Thus incidence of chronic diseases due to changes in the dietary patterns and physical activity are on the rise among Indians.

The prevalence of cardiovascular risk factors such as HTN, diabetes and obesity are very high among Indian adults in the age group of 30-65 years old[13]. Furthermore, 12.6% of hypercholesterolemia, 18.4% of body mass index (BMI) (>24 kg/m^2) and 5.8% of diabetic were reported among 975 middle aged males of 35-39 years old[14]. Therefore the effects of parental CVD risk factors on the future risk of CVD in adolescents should be investigated.

The parental obesity influences childhood obesity through a mixture of genetic and environmental mechanisms[15]. Children with obese family members are several folds more likely to be obese than children whose family members are lean, due to the reason that the former has increased preferences for high fat foods but decreased physical activity[16]. Furthermore, adolescents with extreme obesity (BMI>40 kg/m^2) have significantly heavier parents than those with Class I or II obesity (BMI<40 kg/m^2)[17].

A substantial amount of weight gain occurs in the transition from adolescence to young adulthood with strong tracking from adolescence into adulthood[18-21]. It is also suggested that adults who become obese in childhood and remained obese into adulthood are at higher metabolic risk than those with adult-onset obesity[22]. It has been found that maternal obesity was the most significant predictor of obesity during childhood[23]. Thus the combination of having an obese mother and an earlier onset of obesity translates into higher BMI and weight at young adulthood, especially in black children as compared with white children[22,23].

Furthermore, adolescent obesity is associated with increased mortality and morbidity related to a variety of chronic diseases later in life, and reversal of obesity is associated with decreased metabolic risk in adulthood[24,25].

According to the fetal insulin hypothesis, non-insulin-dependent diabetes in parents is associated with lower birth weight among their offsprings[26].

Data on increased risk of non-insulin dependent diabetes for the fathers of children with low birth weight confirm that diabetes in fathers and the birth weight of their offsprings are strongly associated[27]. On the other hand, diabetes in the mother increase the birth weight of offspring, which is likely to reflect immediate effects of the mother's metabolic control, possibly masking genetic effects operating in the opposite direction[24,28].

There are very few studies on the effects of history of parental HTN on young adults. In such a study of 315 black and white students, on the effects of parental HTN on children's BMI and cardiovascular reactivity over time[29], it was concluded that parental HTN independently predicted children's BMI, BMI z score, resting blood pressure, and blood pressure reactivity.

Family history of premature CHD is an independent risk factor for cardiovascular events in the offspring due to an increased susceptibility to atherosclerosis, and an increased tendency for thrombosis or other factors[30].

It is important to elucidate the mechanism on offspring of parents with premature CHD which differs from offspring of parents without premature CHD because it would be beneficial to asymptomatic adults with a positive family history in determining the need for primary preventive therapies[31].

Increased intima-media thickness, which is a heritable trait, is associated with prevalent CHD, peripheral vascular disease and incidents of cardiovascular events[30]. It was reported that CHD family risk score was correlated with mean increased intima-media thickness in whites, but not African-Americans.

In the Framingham offspring study of 1 662 subjects who underwent carotid ultrasonography, it has been found that subclinical atherosclerosis, assessed in the carotid arteries, is more prevalent in individuals with a family history of CHD. Early-onset parental CHD, in particular, identifies offspring with a strong familial predisposition to atherosclerosis. This confirms the concept that premature age of parental disease identifies a subgroup with a strong familial predisposition to vascular disease[30].

It is evident that the intervention to prevent CVD in adulthood may be difficult, particularly in the middle age, of being too late in terms of the atherosclerotic process. Therefore, early intervention, perhaps starting in childhood, may be more appropriate. It is only in the 1980s that adult epidemiological risk factor models have been extended to children.

Such an approach is based on the following rationale:

1. The foundations of CHD are laid in infancy and early childhood with post mortem studies as evidence for such lesions.

2. Strong association is between ante-mortem risk factors and post mortem observations in young individuals.

3. Individuals at the upper end of distribution with respect to a given risk factor tend to maintain that position relative to their parents and family. This phenomenon is referred as tracking.

Therefore it has been suggested that children and adolescence who are at the highest risk for the development of accelerated atherosclerosis should be identified by examining cholesterol screening on the condition that they have a parent with a history of myocardial infarction (MI), obesity, diabetes, HTN, and also angina pectoris, peripheral vascular disease, cerebrovascular disease or sudden death.

In addition, cholesterol screening may be considered in children and adolescents whose parental history is unobtainable, particularly if other cardiovascular risk factors are present.

Thus our study was designed to study the differences between the lipid profiles of the subjects who are having parents with known non-modifiable risk factors such as obesity, HTN, MI, and diabetes, and compare them with subjects whose parents are not having those risk factors.

2. Materials and methods

2.1. Materials

A total of 402 medical students of the Manipal College of Medical Sciences, Kathmandu University were recruited to this study after informed consent, of them 167 subjects (41.5%) were females and 235 subjects (58.5%) were males. All subjects were freshmen and represented of Nepal and India.

2.2. Data collection

2.2.1. Questionnaire

A detailed questionnaire, which included information of the past medical history, height, weight, blood pressure, physical activity, smoking, alcohol, family history of CHD, HTN, diabetics, obesity, basic demographic data and dietary habits was completed by all participants.

2.2.2. Blood samples

Blood samples were obtained from all subjects after 14 h. Venepuncture was done in a sitting position and 10 mL samples of blood were obtained. All samples were allowed to clot. Serum was separated and maintained at 4 °C until analyzed. All analyses were commenced within 3 h after collection.

2.3. Laboratory methods

Total cholesterol (TC) concentration was estimated by enzymatic techniques (CHOD-PAP method, Boehringer Mannheim) and high density lipoprotein (HDL) concentration by phosphotungstic acid magnesium reagents (Boehringer Mannheim) and low density lipoprotein cholesterol (LDL-C) by using the Friedewald formula. Plasma triglycerides (TG) was estimated by the GPO-PAP method (Boehringer Mannheim). All analyses were performed on Erba XL-300 autoanalyzer. External and internal quality control procedures were used to ensure the levels of precision and accuracy required for the TC and lipoprotein cholesterol analyses. The external quality control procedures-Randox International Quality Assessment Scheme from Randox Laboratories Co. Ltd., United Kingdom were used.

2.4. Statistical analysis

The results were analyzed using SPSS software packages. The aim of the statistical analysis was to establish the differences between the lipid profile parameters of the young people with respect to the presence or absence of history of parental risk factors. Family history of CHD was evaluated from the information given in the questionnaire.

3. Results

The distribution of anthropometric parameters of the subjects was obtained. Among the 402 young subjects, only 1.5% of them were non-vegetarians.

The mean body weight, height and BMI of the subjects were (52.00±9.75) kg, (161.00±9.30) cm and (20.11±2.91) kg/m^2, respectively. The mean BMI of the population studied was well below the cut-off value of obesity (>24.5 kg/m^2) which had higher risk of future CVD events in this age group.

Table 1 shows the results of the biochemical parameters of the subjects. The mean levels of TC, TG and TC/HDL were less than the risk levels indicative of future CVD events according to the ATP III cut-off values[38]. Though the values were within the normal range, they were also very closer to the cut-off values. However, the mean HDL level in our population was slightly greater than the cut-off value while the mean LDL level was almost similar as the risk level.

Table 1
The biochemical parameters of the subjects.

Parameter	Mean±SD	Cut-off levels as per NCEP ATP-III
TC (mg/dL)	190.00±35.60	>200
TG (mg/dL)	100.00±40.50	>150
HDL-C (mg/dL)	51.51±4.90	<50
LDL-C (mg/dL)	119.00±31.85	>110
TC/HDL	3.71±0.64	>4

HDL-C: HDL cholesterol. *n*=402.

Table 2 shows the frequency of subjects with risk levels. These frequency values indicated that though a very low proportion (8.2%) of subjects were with risk values as indicated by anthropometric parameter of BMI, all the biochemical parameters indicated much

more severe situation as far as the development of future CVD events were concerned.

Table 2
Frequency of subjects with risk levels (*n*=402).

Parameter	Risk level*	Abnormal values of subjects
BMI (kg/m^2)	>24.5	33 (8.20%)
TC (mg/dL)	>200	142 (35.30%)
	200-239	102 (25.40%)
	>239	40 (9.95%)
TG (mg/dL)	>150	50 (12.40%)
LDL-C (mg/dL)	>110	250 (62.20%)
	>200	16 (4.00%)
	>130	135 (33.60%)
HDL-C (mg/dL)	<50	153 (38.10%)
TC/HDL	>4	80 (20.00%)

*: Risk levels as indicated by ATP III.

The data were then analyzed to see the relationship between the presence or absence of obesity in mother and variation in anthropometric and biochemical parameters of the subjects (Table 3).

Following differences were observed when the subjects without history of maternal obesity were compared with subjects with history of maternal obesity. Both groups of subjects had similar levels of BMI values which indicated no differences of anthropometry. However, TC, LDL-C, TC/HDL values of the subjects with a history of maternal obesity were significantly higher than the levels of the subjects without history of maternal obesity. HDL-C levels were also similar in two groups of subjects (Table 3).

Table 3
The effects of maternal obesity on the lipid pattern of the young adolescents.

Parameter	Non obese (*n*=357)	Obese (*n*=45)	Significance
Body weight (kg)	51.83±9.66	53.93±10.37	Ns
BMI (kg/m^2)	20.05±2.94	20.60±2.68	Ns
TC (mg/dL)	189.00±34.78	203.00±39.84	*P*<0.009 0
TG (mg/dL)	99.40±40.30	105.51±41.68	Ns
HDL-C (mg/dL)	51.38±4.86	52.56±5.23	Ns
LDL-C (mg/dl)	117.00±31.26	1 370.00±34.29	*P*<0.008 0
TC/HDL	3.67±0.63	3.97±0.67	*P*<0.02 7

Ns: Not significant.

The data in Table 4 also confirmed the fact that greater percentage of subjects are having risk levels of BMI, TC, LDL , TG, and TC/HDL indicating that maternal obesity contributes to the greater susceptibility of developing CVD risk in their offspring.

Table 4
Frequency of subjects reaching risk levels with respect to maternal obesity.

Parameter	Non Obese (*n*=357)	Obese (*n*=45)
BMI>24.5 kg/m^2	28 (7.8%)	5 (11.1%)
TC>200 mg/dL	120 (33.6%)	22 (48.9%)
LDL>110 mg/dL	215 (60.2%)	35 (77.8%)
TG>150 mg/dL	40 (11.2%)	10 (22.2%)
HDL<50 mg/dL	135 (37.8%)	18 (40.0%)
TC/HDL>4	68 (19.0%)	12 (26.7%)

When the subjects with a history of paternal obesity were compared with those without history of paternal obesity, only BMI and the LDL levels were significantly greater in the subjects with a history of paternal obesity. This indicated that contribution of paternal obesity in creating atherogenic picture in the offspring was weaker than that of the history of maternal obesity.

Frequency of abnormal values in the presence of paternal obesity was given in the Table 5. The frequency of subjects with a risk level of BMI was greater when paternal obesity (15.8%) was present when compared to the presence of maternal obesity (11.1%). Except for that, frequencies of subjects with abnormal values of TC, LDL, TG were significantly greater in the presence of maternal obesity than that of paternal obesity (Tables 3, 5, 6).

Table 5
Frequency of abnormal values in the presence of paternal obesity.

Parameter	Non obese (*n*=373)	Obese (*n*=29)	Significance
Body weight (kg)	52.10±9.78	53.16±9.28	Ns
BMI (kg/m^2)	20.07±2.88	21.05±3.52	*P*<0.036
TC (mg/dL)	190.00±35.33	200.00±37.00	Ns
TG (mg/dL)	101.00±41.01	90.32±25.80	Ns
HDL (mg/dL)	51.49±4.93	51.95±4.43	Ns
LDL (mg/dL)	118.00±31.70	132.00±34.00	*P*<0.028
TC/HDL	3.69±0.63	3.83±0.69	Ns

Ns: Not significant.

Table 6
Frequency of subjects reaching risk levels with respect to paternal obesity.

Parameter	Non obese (*n*=383)	Obese (*n*=19)
BMI>24.5 kg/m^2	30 (7.8%)	3 (15.8%)
TC>200 mg/dL	135 (35.2%)	7 (36.8%)
LDL>110 mg/dL	237 (61.8%)	13 (68.4%)
TG>150 mg/dL	47 (12.3%)	2 (10.5%)
HDL<50 mg/dL	140 (36.4%)	13 (68.4 %)
TC/HDL> 4	75 (19.6%)	5 (26.3%)

Our data also indicated that LDL levels were significantly elevated in the subjects when both mother (*P*<0.008 0) and father were obese (*P*<0.028) when compared to the LDL levels of the subjects whose parents were not obese. Though there were greater values of TC/HDL when both parents were obese, only the levels in subjects with a history of maternal obesity were significant (*P*<0.027).

The distribution of lipid parameters of the subjects were assessed with respect to the presence or absence of diabetes in parents and data are given in Table 7. The body weight of the subjects with a history of maternal diabetes was significantly greater than that of the subjects without diabetes (*P*<0.025). Furthermore, the levels of BMI, TC, TG and TC/HDL of the subjects with a history of maternal diabetes were all significantly greater than that of the subjects without a history of maternal diabetes (Table 7).

Table 7
The distribution of lipid parameters of the subjects with respect to the presence or absence of maternal diabetes.

Parameter	Non diabetic (*n*=372)	Diabetic (*n*=30)	Significance
Body weight (kg)	51.760±9.760	55.970±8.890	*P*<0.025
BMI (kg/m^2)	20.030±2.950	21.140±2.210	*P*<0.049
TC (mg/dL)	187.000±36.180	198.530±28.410	*P*<0.028
TG (mg/dL)	99.000±40.040	117.000±44.530	*P*<0.036
HDL (mg/dL)	51.490±4.910	51.770±4.950	Ns
LDL (mg/dL)	119.000±32.480	124.000±22.980	Ns
TC/HDL	3.704±0.640	3.905±0.550	*P*<0.028

Ns: Not significant.

These frequency data revealed the most unexpected observation. Though the mean levels of TC were significantly greater in the

subjects with a history of maternal diabetes (Table 7), the number of subjects with risk levels were less in the subjects with a history of maternal obesity than that of the subjects without a history of maternal diabetes. This was because of the TC and LDL levels in greater proportion of the subjects (*i.e.* 7/9 exceeds 290 level for TC and 10/16 exceeds 200 level for LDL), which resulted in greater mean values for TC and LDL (Table 8).

Table 8
Frequency of abnormal values with respect to the maternal diabetes.

Parameter	Non diabetic (*n*=372)	Diabetic (*n*=30)
BMI>24.5 kg/m^2	29 (7.8%)	4 (13.3%)
TC>200 mg/dL	133 (35.8%)	9 (30.0%)
LDL>110 mg/dL	234 (62.9%)	16 (53.3%)
TG>150 mg/dL	46 (12.3%)	4 (13.3%)
HDL<50 mg/dL	142 (38.2 %)	10 (33.3%)
TC/HDL> 4	73 (19.6%)	7 (23.3%)

The body weight of the subjects with a history of paternal diabetes was significantly greater than that of the subjects without diabetes (P<0.028) (Table 9). Furthermore, the levels of BMI, TC, TG of the subjects with a history of paternal diabetes were all significantly greater than that of the subjects without a history of diabetes. This was also observed in the subjects with a history of maternal diabetes. In addition, paternal obesity was associated with significantly increased level of LDL.

Table 9
The distribution of lipid parameters of the subjects with respect to the presence or absence of paternal diabetes.

Parameter	Non diabetic (*n*=354)	Diabetic (*n*=48)	Significance
Body weight (kg)	51.60±9.34	55.48±11.95	P<0.028
BMI (kg/m^2)	19.95±2.87	21.27±2.97	P<0.003
TC (mg/dL)	189.00±36.00	206.00±32.09	P<0.028
TG (mg/dL)	100.00±40.11	112.00±43.29	P<0.038
HDL (mg/dL)	51.40±5.05	52.29±3.57	Ns
LDL (mg/dL)	108.00±32.22	124.00±28.86	P<0.036
TC/HDL	3.69±0.64	3.76±0.60	Ns

Ns: Not significant.

The number of subjects with risk level of BMI was very much greater (25.0%) in the group with a history of paternal diabetes when compared to the number of subjects without paternal diabetes (5.9%). The frequency of subjects with abnormal levels of TC, LDL, and TG in the history of paternal diabetes was greater than the frequency of subjects without paternal diabetes (Table 10).

Table 10
Frequency of abnormal values with respect to the paternal diabetes.

Parameter	Non diabetic (*n*=354)	Diabetic (*n*=48)
BMI>24.5 kg/m^2	21 (5.9%)	12 (25.0%)
TC>200 mg/dL	119 (33.6%)	23 (47.9%)
LDL>110 mg/dL	218 (61.6%)	32 (66.7%)
TG>150 mg/dL	38 (10.7%)	12 (25.0%)
HDL< 50 mg/dL	139 (39.3%)	14 (29.2%)
TC/HDL>4	68 (19.2%)	12 (25.0%)

The distribution of lipid parameters of the subjects were assessed with respect to the presence or absence of a history of maternal HTN and data were given in Table 11.

The body weight, BMI, HDL and TC/HDL of the subjects with a history of maternal HTN were no significantly different from that of the subjects without a history of HTN (Table 11). However, TC, LDL, TG levels of the subjects with a history of maternal HTN was significantly greater than that of the subjects without a history of HTN. The frequency of subjects with abnormal parameters when the maternal HTN was present was given in the Table 12.

Table 11
The distribution of lipid parameters of the first assessment with respect to the presence or absence of maternal HTN.

Parameter	Non HTN (*n*=353)	HTN (*n*=49)	Significance
Body weight (kg)	51.74±9.55	53.32±10.84	Ns
BMI (kg/m^2)	20.02±2.93	20.58±2.54	Ns
TC (mg/dL)	185.90±32.53	202.11±29.43	P<0.001
HDL (mg/dL)	51.29±4.95	51.69±4.48	Ns
LDL(mg/dL)	115.40±27.93	123.40±25.31	P<0.045
TG (mg/dL)	100.72±42.44	114.46±43.56	P<0.045
TC/HDL	3.61±0.55	3.76±0.57	Ns

Ns: Not significant.

Table 12
Frequency of abnormal values with respect to the maternal HTN.

Parameter	Maternal HTN absent (*n*=353)	Maternal HTN present (*n*=49)
BMI: >24.5 kg/m^2	21 (6.0%)	12 (24.5%)
TC: >200 mg/dL	126 (35.7%)	16 (32.7%)
LDL: >110 mg/dL	220 (62.3%)	30 (61.2%)
TG: >150 mg/dL	40 (11.3%)	10 (20.4%)
HDL: <50 mg/dL	125 (35.4%)	28 (57.1%)
TC/HDL: >4	53 (15.0%)	27 (55.1%)

The number of subjects with risk levels of BMI, TG, HDL and TC/HDL was higher in subjects with a history of maternal HTN. Very similar to frequencies were observed for TC and LDL as shown in Table 13.

Table 13
The distribution of lipid parameters of the subjects with respect to the presence or absence of paternal HTN.

Parameter	Non HTN (*n*=351)	HTN (*n*=51)	Significance
Body weight (kg)	52.31±9.65	52.09±10.07	Ns
BMI (kg/m^2)	20.17±2.92	19.54±2.70	Ns
TC (mg/dL)	186.60±32.78	197.39±29.46	P<0.028
HDL (mg/dL)	51.33±5.00	52.27±4.17	Ns
LDL (mg /dL)	115.61±27.87	142.27±4.17	P<0.001
TG (mg/dL)	101.39±42.59	99.01±42.35	Ns
TC/HDL	3.62±0.56	3.64±0.49	Ns

Ns: Not significant.

The frequency of abnormal values with and without paternal HTN was given in Table 14. It indicated that all parameters were higher in subjects whose father were hypertensive.

Table 14
Frequency of abnormal values with respect to the paternal HTN.

Parameter	Non Hypertensive (*n*=351)	Hypertensive (*n*=51)
BMI: >24.5 kg/m^2	10 (2.8%)	23 (45.1%)
TC: >200 mg/dL	118 (33.6%)	24 (47.1%)
LDL: >110 mg/dL	123 (35.0%)	27 (52.9%)
TG: >150 mg/dL	26 (7.4%)	24 (47.1%)
HDL: <50 mg/dL	125 (35.6%)	28 (54.9%)
TC/HDL: >4	50 (14.2%)	30 (58.8%)

Then the relationships of the incidence of maternal and paternal MI on the lipid parameters of the subjects were assessed and results were given in Tables 15 and 16.

Table 15

The relationship of the incidence of maternal MI on the lipid parameters of the subjects.

Parameter	Non MI (n=386)	MI (n=16)	Significance
Body weight (kg)	52.05±9.81	53.17±4.54	Ns
BMI (kg/m^2)	20.11±2.93	20.50±0.84	Ns
TC (mg/dL)	190.00±35.25	223.17±4.99	P<0.01
TG (mg/dL)	99.50±39.75	138.00±70.89	P<0.001
HDL (mg/dL)	55.46±4.92	51.00±2.66	P<0.001
LDL (mg/dL)	108.20±31.66	132.17±44.44	P<0.028
TC/HDL	3.69±0.63	3.94±1.19	Ns

Ns: Not significant.

Table 16

The relationship of the incidence of paternal MI on the lipid parameters of the subjects.

Parameter	Non MI (n=382)	MI (n=20)	Significance
Body weight (kg)	52.07±9.72	52.94±10.92	Ns
BMI (kg/m^2)	20.11±2.88	20.27±3.77	Ns
TC (mg/dL)	189.00±34.78	216.71±49.95	P<0.012
TG (mg/dL)	100.03±40.19	102.00±31.3	Ns
HDL (mg/dL)	51.49±4.96	52.00±3.59	Ns
LDL (mg/dL)	117.94±30.78	137.02±30.17	P<0.045
TC/HDL	3.69±0.62	3.97±0.93	Ns

Ns: Not significant.

No significant difference was observed for mean values of body weight, BMI and TC/HDL between the two groups. Significantly greater values were observed in TC and TG levels of the subjects with a history of maternal MI. However, significantly lower levels were observed in HDL of the subjects with a history of maternal MI.

No significant difference was observed for mean values of body weight, BMI and TC/HDL between the two groups. However, TC and LDL levels were significantly higher in subjects with paternal MI. Further, a significant reduction of HDL (P<0.001) and significant elevation of TG was observed in subjects who had a history of maternal MI. However, frequency analyses and the effects of parental MI on the frequency of subjects with or without a history of parental MI were not analyzed due to the fewer number of cases.

4. Discussion

There are very little data available regarding lipid profiles of young adolescents, especially in developing countries. Our study was an attempt to determine whether apparently healthy adolescent students who have family histories of cardiovascular risk factors, could result to undesirable anthropometric indices and lipid profiles which may increase their predisposition to CVD in their adult life. Our study population represented from Nepal, thus any observation reached here could easily be extrapolated to predict the relationships in the general population.

There is no acceptable and suggestive cut-off value of obesity in adolescent males. It may vary with age and also be affected by racial differences. The cut-off value for each group was obtained by calculating the BMI using the median height for each age group and weight corresponding to the 90th percentile in the NCHS standards[32].

The subjects that were studied in our group were younger (19-21 years of age) than the subjects (20-25 years of age) reported previously[33]. Thus we would expect our subjects to show some of the anthropometric and biochemical parameters to approach risk levels with the advancement in age. The mean BMI of our subjects [(20.11±2.91) kg/m^2] was well below the cut-off value (24.5 kg/m^2) indicative of the risk level of future CVD events. The value of BMI obtained in the current study is almost similar to the values (21.32±2.68 kg/m^2) observed in the (sub group) age group of 20-25 years from Nepal[33]. Furthermore, they also observed 15.70% of the subject's BMI values exceeded 24.5 kg/m^2 in the age group of 20-25 years. When we used the same cut–off level for the subjects in our study, 33 subjects (8.0%) had BMI values greater than the cut-off value. This indicates the increase in prevalence of obesity between age groups of 20-25 years and 19-21 years. It was reported that the prevalence of obesity among Nepalese men and women were 59.1% and 61.8%, respectively, though they used a lower cut-off (22 kg/m^2) in a study conducted by Sharma[34]. It was also reported that the prevalence of overweight was among 9% of the subjects in a study conducted in young adolescent females (n=1 303, 18-26 years of age) from Baroda, India[35]. Moreover, it was reported that obesity among 12.6% of the participants under study had Grade I and Grade II obesity of 10.1% and 2.5% respectively. In another study reported from Chennai, India by Tharkar *et al.*, 13.5% of the subjects were reported to be overweight and 7.5% were confirmed obese among the 2 376 participants with age group from 8-13 years[36]. In addition, another study conducted by Mishra *et al.* stated high prevalence of insulin resistance in post-pubertal urban Asian Indian children with excess body fat, abdominal adiposity and excess truncal subcutaneous fat[37]. In the present study when we analyzed the history of their parents, we observed 5/45 (11.1%) of the adolescents' mothers were reported to be obese and 3/19 (15.8%) of the adolescents' fathers were reported to be obese. Thus it is clear that with the advancement of age, the mean level of BMI as well as the number of subjects with BMI values more than the risk level has increased.

In spite of mean BMI value which was well below the risk level, mean values of TC, HDL-C and TC/HDL have reached cut-off values of 200 mg/dL, 110 mg/dL and 4 respectively, which indicated all biochemical parameters approach to risk levels as given in ATP III for adults[38]. The mean HDL-C level has also reached the risk level of <50 mg/dL. Therefore, it was clear that even in the presence of normal anthropometric as indicated by BMI values, the biochemical parameters (lipid profile) have reached risk levels. This proved and alarmed the significance of screening of all asymptomatic subjects for the presence of abnormal lipid profiles.

Elevated serum TC contributed to coronary atherosclerosis throughout life and also serum cholesterol levels measured in young adulthood correlate with CHD rates later in life and over a

lifetime[39].

In Muscatine, Iowa study, for example, reported that 75% of children who were 5-18 years old at baseline had TC levels greater than the 90th percentile of elevated TC (200 mg/dL) at 20-25 years of age[40]. The Bogalusa Heart Study reported that 70% of children with elevated TC in childhood were persisted with elevated levels in adulthood[41].

In a study of 611 children who had TC measured at age 12 years and subsequently re-measured at age 21-24 years, 49% of those in the top quintile of age 12 years distribution remained there, while 70% of those in the top two quintiles were similarly placed at follow up. This phenomenon is called as tracking which is seen in plasma TC, but the relationship is variable and less constant than that of height or weight. In the Bogalusa Heart Study, higher serum TC levels were noted among 67 black boys of 14 years old than in 116 white boys in the same age group[42].

Obese children ranging from 2-5 years old have 4 times likelihood of becoming obese adults compared with normal weight children[43]. About 80% of children who were overweight at 10-15 years old became obese adults at 25 years old. About 25% of obese adults were overweight during childhood[44]. Obesity in childhood has been associated with increased arterial stiffness, carotid intima media thickness and increased risk of CHD in adult life[45].

In a study conducted in India by Madhavan *et al.,* Asian Indian adolescents aged 14-18 years consisting of 680 boys and 521 girls were reported to have lower levels of serum TC, LDL-C and HDL-C and higher levels of TG compared to the same aged population in the USA[46]. They also hypothesized that it could be due to dietary pattern and physical activity in this age group in India.

The serum TC concentration in the present study had showed a significant increase with increasing age. Though it was thought that the serum TC concentration in the age group of 18 years probably reflected level that may be found in adults 34, the mean TC value for our study being (190.00±35.60) mg/dL (*n*=402), which indicated more than a 15% elevation with the advancing age in young adolescents.

Elevated serum TG are associated with increased risk for CHD and with other lipid and non lipid risk factors[47]. A TG level of >150 mg/dL is considered as risk level in the ATP III report. TG, however, rises more markedly in puberty and this is more so in young adolescents. Some species of TG rich lipoproteins, notably, cholesterol-enriched remnant lipoproteins, promote atherosclerosis and predispose to CHD[48].

The mean TG value of our subjects [(100.00±40.50) mg/dL (*n*=402)] was well below the cut-off level as given in the ATP III report and it was significantly greater than the value reported in 18-26 year old students conducted earlier[35]. About (50/402) 12.4% subjects in our study had TG levels above the risk level of 150 mg/dL, while about (16/402) 4.0% subjects had levels greater than 200 mg/dL, which was very much greater than the number of subjects as indicated by risk level of BMI. A study reported at Chennai showed TG levels of >118 mg/dL of 2376 school children at the age of 8-13 years[36]. Another study conducted by Misra *et al.* stated the prevalence of TG levels of 117.8 mg/dL among 16% of their study subjects from New Delhi[37].

The role of LDL in atherogenesis is confirmed by a wide variety of observational and experimental evidence amassed over several decades from animal, pathological, clinical, genetic and different types of population studies and also by genetic disorders in which serum LDL-C is markedly increased in the absence of other CHD risk factors *e.g*. homozygous and heterozygous form of familial hypercholesterolemia[48].

LDL-C lowering earlier in life slows atherosclerotic plaque development and the foundation of the unstable plaque. The importance of elevated LDL-C to cause CHD is shown by the fact that advanced coronary atherosclerosis and premature CHD occur even in the absence of other risk factors[49]. The LDL-C level <100 mg/dL throughout life is associated with a very low risk for CHD and regarded as optimal. However, atherogenesis occurs even when LDL-C levels are near optimal 100-129 mg/dL. At level that are borderline high (130-150 mg/dL), atherogenesis proceeds at a significant rate.

In the study of school children (*n*=611) in Sri Lanka, elevated serum LDL-C levels (>110 mg/dL, 2.84 mmol/L) were noted in 134 subjects (21.9%) and LDL-C were seen in 15.7% of the population of 14-18 years children. The percentage of subjects with high LDL-C levels was the highest (29.8%) in the age group of 17-18 years[50]. Only the mean LDL level has reached the risk level (110 mg/dL) for this young population, which indicated increased risk of future CVD (while HDL and TC/HDL levels were within the normal level). However present study encountered 250 subjects (50%) in the age group of 18-21 years who had LDL-C levels >110 mg/dL, while more than 130 mg/dL was observed in 135/402 subjects that was 32.3% of the subjects, which is considered to be very highly atherogenic.

A low HDL-C level is strongly and inversely associated with risk for CHD[51]. Higher risk for CHD at lower HDL levels is multifactorial causation[51]. Although this relationship shows no inflection points, any reduction in HDL-C from population means is accompanied by increased risk for CHD[51]. Clinical trials provide suggestive evidence that raising HDL cholesterol levels will reduce risk for CHD[52]. However, it remains uncertain whether raising HDL-C levels alone and independent of other changes in lipid and/or nonlipid risk factors will reduce risk of CHD.

The mean HDL-C in our study was (51.51±4.90) mg/dL (*n*=402), which was very closer to the cut-off value as recommended in ATP III report. The mean HDL value reported among subjects in the age group of 14-18[34] was almost similar to the findings reported by Madhavan *et al.* where they reported the HDL-C levels in Indian adolescents ranging from 46.5 mg/dL to 47.7 mg/dL[46]. Study of Tharkar *et al*. also reported HDL-C levels were ≤38 mg/dL in school-going children aged 8-13 years[36]. Similarly, Misra *et al.* reported a prevalence of 10% of the study subjects whose HDL-C levels were <37 mg/dL[37]. When HDL-C (<35 mg/dL) levels were noted in 27.3% of subjects in the age group of 14-18[34], our study reported 38.1% (153/402) subjects who have risk levels of

HDL (<50 mg/dL). Study conducted by Dhruv *et al*. among young adolescent girls from Gujrat, India reported that they have lower levels of HDL-C [(41.0±2.9) mg/dL] compared to our study, though we have used a little higher value as the cut-off value which is recommended by ATP III report[35].

The higher values (>4) of TC/HDL was also thought to indicate increased risk of developing CVD. The mean value of TC/HDL in our study population was (3.71±0.64) (*n*=402) which was very close to the risk level. Further we also observed 80 subjects (20.0%) had greater values than the risk levels. The mean value of HDL-C in the study carried out by Dhruv *et al.* was (41.0±2.9) mg/dL among 1 301 subjects[35]. Therefore, it was very clear that when compared to the anthropometric and biochemical parameters of the younger subjects reported earlier in India, both parameters, specially the biochemical parameters, varied towards the risk level with the advancement of age. So it was very important to see how these parameters vary in the subjects with and without parents with non-modifiable risk factors. In this study we envisaged to study the effects of the presence of these risk factors in the parents, which will be on the changes in lipid profiles of young adults.

A study of adolescent boys in the age group of 14-18 years in Sri Lanka was to determine the prevalence of risk factors for CVD in later life. It was noted that 33.3% of them had a family history of CVD, HTN, diabetes mellitus, or more than one of the above disease states[50]. They have not considered the frequency of incidence of the presence of risk factors in parents separately. We found that 140 (34.8%) mothers and 154 (38.3%) fathers had any one of the risk factors studied when the presence of risk factors were considered separately. This also indicated that the incidence of paternal risk factors has increased during the past decade.

Although some people who actually have a large muscle mass were classified as overweight, most persons with BMIs of 25-29.9 kg/m^2 have excess body fat. Overweight and obesity are classified as BMI 30 kg/m^2 and 25-29.9 kg/m^2 respectively, which are not only predisposed to CHD, stroke and numerous other conditions, but also associate with greater all-cause mortality. People who are overweight or obese have a high burden of other CHD risk factors including dyslipidemia (high LDL-C, low HDL-C, high VLDL and TG), type 2 diabetes and HTN[48]. Obese individuals who do not yet have these risk factors are at increased risk for developing them.

Our data showed that maternal obesity was associated with significantly higher levels of TC (P<0.009), LDL-C (P<0.008), TC/HDL (P<0.027) when compared to the same levels in the subjects without obese mothers. However, no differences were observed in BMI and in HDL-C levels between two groups of subjects. Though there were greater values of TC/HDL when both parents were considered separately for the presence of obesity, only the levels in subjects who had a obese mother were significant (P<0.027). This confirmed the previous observation that having an obese mother was associated with earlier age at obesity onset across all race/ethnic groups, particularly non-Hispanic blacks in the study of U.S. adolescent followed into adulthood[53]. Early-onset obesity has important health consequences because of its association with more severe adult obesity and future development of CVD.

The fact that the significant elevation observed in TC, LDL-C, TC/HDL levels in subjects of our study when mother was obese and only LDL-C has elevated significantly when the father was obese, confirmed that obesity with mother was a stronger determinant of CVD in the offspring than the obesity in the father as suggested in a previous study[54,55].

When the number of subjects with risk levels was considered, higher frequencies were observed in BMI, TC, LDL-C, TG in subjects with maternal history of obesity than the subjects without obese mothers. The parameters of TC (48.9%) and LDL-C (77.8%) had the highest number of subjects with risk levels. Even in the subjects without obese mothers, risk levels of LDL were seen in 215 subjects (60.2%), which indicated an increase in frequency of elevated LDL.

When the paternal obesity was considered only the LDL levels [(132.00±34.00) mg/dL (*n*=29) and (118.00±31.70) mg/dL (*n*=373)] were significantly higher in the subjects with obese fathers. Our data indicated that maternal obesity was a stronger predictor of CVD events in the offspring when compared with the paternal obesity.

Diabetes is a major, independent risk factor for CHD and other forms of CVD and since growing evidence suggests that many people with diabetes which carry a risk for CHD are similar to that of people with established CHD. It is considered that diabetes should be treated as a separate category of higher risk[48].

In the study reported earlier among the subjects with a family history of diabetes (*n*=110), 16% of the subjects had BMI values greater than risk level and 21% had high serum TC level greater than the risk level[42].

Except for TC/HDL, the body weight, BMI, TC, TG and TC/HDL levels of the subject with a history of maternal and paternal diabetes were significantly greater than that of the subjects without such history in our study. However an inverse relationship has been established between birth weight and paternal non-insulin dependent diabetes mellitus[56]. In addition, paternal diabetes in our study was associated with significantly increased level of LDL.

This frequency data revealed the most unexpected observation. Though the mean levels of TC and LDL were significantly greater in the subjects with a history of maternal diabetes, the number of subjects with risk levels were less in that group. This was because of the TC and LDL levels in greater proportion of the subjects with a history of diabetes (*i.e.* 7/9 exceeds 290 level for TC and 10/16 exceeds 200 level for LDL), which resulted greater mean values for TC and LDL. This highlighted the necessity of screening subjects individually.

The number of subjects with risk level of BMI, TC, LDL and TG was very much greater in the group with a history of paternal diabetes when compared to the number of subjects without paternal diabetes.

Thus our data reveal that history of diabetes in both parents would result in a lipid profile that will reaching risk levels when they grew up to the adulthood which is more strong with respect to the paternal

diabetes.

Family history of premature CHD has been found as an independent risk factor for CVD due to increased susceptibility to atherosclerosis and thrombosis[30]. Elucidation of this relationship in children and adolescent is very important because of its beneficial effects of determining primary preventive therapies[57].

We encountered only few subjects with parents having MI. It is also important to note that all parents of the subjects were <65 years and no death of parents was reported among these subjects.

Body weight and BMI were not significantly different in subjects when both of their parents are having history of MI. Though not significant, TC/HDL levels were greater in subjects with parents having MI. Significantly greater values were observed for TC, TG, LDL levels together with a significant reduction of HDL in the subjects with a history of maternal MI. In the previous study carried out in Sri Lanka, it has been found that of the 48 subjects with a family history of CVD, 14.6% had BMI values above the desirable range, while 10.4% had high concentration of serum TC (>185 mg/dL, 4.78 mmol/L)[50].

The effects of parental MI on the frequency of subjects with or without a history of parental MI in our subjects were not analyzed due to the fewer number of cases.

In the previous study carried out in Sri Lanka, it was revealed that among the 98 subjects with a family history of HTN, 7.1% had high BMI, 12.2 % had high serum TC and 25.5% had high apolipoprotein B levels[50].

We observed an significant elevation in TC and LDL-C in the presence of parental HTN in our subjects which was in agreement with the finding that parental HTN was an independent risk factor of future CVD events[58].

However, in contrast to the previous study, we did not observed any difference in BMI between these two groups. Yet we observed higher frequencies for BMI, TG, HDL, TC/HDL in subjects with a history of maternal HTN. The frequency of subjects who had abnormal values with and without paternal HTN indicated that except for TG frequency, all the other parameters were higher in subjects with paternal HTN.

An important finding in our study is that the observation of mean BMI among subjects with a family history of CHD, HTN or diabetes is significantly higher when compared with those that do not have a family history of the above diseases.

Furthermore, the change towards risk level is much greater when mother is having those risk factors than when father is having risk factors. From the data available we may conclude that:

1. Advancing age may result changes that could be atherogenic in the future.

2. Such atherogenic changes have already initiated when they are about 21 years of age.

3. The incidence of atherogenic changes is far greater when mothers are having any of the risk factors such as obesity, diabetes, HTN and MI than when fathers are having similar risk factors.

Thus, it is of paramount importance to screen individual adolescents when any parent is having any one of the above mentioned risk factors.

Conflict of interest statement

I declare that I have no conflict of interest.

Acknowledgements

This work was supported by Confederation of Epidemiological Associations registered under Govt of Kerala (Grant No. 30-955/2012 CEA).

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