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ROLE OF SERUM APOLIPOPROTEIN LEVELS IN INDIAN CHILDREN AND ADOLESCENTS.

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ABSTRACT

The incidence of obesity among childhood in India is largely increasing. The serum apolipoproteins and its correlation with anthropometric and biochemical parameters were evaluated in 296 school children and adolescents (96 obese, 97 overweight, were compared with 103 normal controls, aged between 10-17 years). Anthropometric variables, lipid profile, fasting serum glucose analyzed by auto- analyzer and serum apolipoproteins by Immunoturbidimetry assay. Serum Apo-AI levels were decreased in obese and overweight children (130.94±9.24mg/dl, 132.26±10.80mg/dl Vs 153.08±17.98mg/dl) ($p<0.001$) than control children. Serum Apo-B levels were significantly elevated in obese and overweight children (88.54±11.4mg/dl, 82.6±12.64mg/dl Vs 73.55±12.03mg/dl) ($p<0.001$) than controls. Serum Apo-B levels showed positive correlation with BMI, WHR, Apo-B/Apo-AI ratio, TCHR, TC, TG, LDL-C and showed negative correlation with fasting glucose levels, and no association with HDL-C. Serum Apo-AI levels showed negative correlation with BMI, WHR, Apo-B/Apo-AI ratio, TCHR, TC, TG, LDL-C and showed positive correlation with HDL-C and fasting glucose levels. These findings suggest that childhood obesity is associated with abnormal lipid patterns. Prevention campaigns aimed at identifying obese children and reducing their weight would probably also improve the lipid profile.

KEY WORDS: **Apolipoproteins, Children,Obesity**

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INTRODUCTION

The prevalence of obesity among children has dramatically increased in India. Obesity in childhood is associated with an increased mortality due to cardiovascular disease in adulthood independent of adult weight[1] A consistent association between obesity and levels of Apo-B and A-1 were observed, which are considered to be the most important risk factor for Ischemic heart disease[2] Accumulating evidences indicate that increased Apo-B and low blood serum Apo-A1 concentrations dictate cholesterol accumulation in arterial wall cells and the early formation of atherosclerotic plaques and they are reflective of cardiovascular risk[3,4] Apoproteins bind with phospholipids to form a surface monolayer in all mature lipoprotein particles. Apolipoprotein (Apo-B) is found in all atherogenic lipoproteins, including low-density lipoprotein (LDL), very-low-density lipoprotein (containing cholesterol and triglycerides), remnant particles, intermediate-density lipoprotein and lipoprotein(a). Apo-AI and Apo-AII are the major apolipoproteins constituting the antiatherogenic high-density lipoprotein (HDL) and its subfractions[5]There are conflicting reports on the role of apolipoproteins in obese children. Some studies reported higher levels of Apo B in obese children, while others have not detected any correlation[6,7] The present study aims to evaluate the levels of serum apolipoproteins in children and adolescents of Indian population and its correlation with anthropometric and biochemical parameters. To the best of our knowledge, a similar study has not been reported with respect to serum apolipoprotein levels in Indian children and adolescents so far.

MATERIALS & METHODS

A total of 296 school children of Chennai with ages ranging from 10 to 17 years were enrolled as study participants. Informed written consent from the parents was obtained before the commencement of the study. Children with overweight, and obesity were included in the study. The study was carried out at the International Centre for Cardio -Thoracic and Vascular Diseases, a unit of the Dr.K.M.Cherian Heart Foundation, Chennai. Children with secondary causes of obesity and insulin dependent and independent diabetes mellitus and also, children undergoing treatment for any other disorder were excluded from the study. Anthropometric measurements such as height, weight, body mass index (BMI), and Waist-to-hip ratio were recorded. Weight was measured using a beam balance to the nearest 0.1 kg and height to the nearest centimeter using a tape stuck to the wall. Abdominal girth was measured at the level of umbilicus with the subject relaxed and in a standing posture. Hip girth was measured at widest point of the hips at the level of the greater trochanter with the patient standing with both feet together. Waist–to-hip ratio (WHR) was calculated from these measurements. Children with BMI>85th percentile for age and gender, were considered as overweight and children with BMI >95th percentile for age and gender considered as obese by using CDC growth charts. Blood pressure levels were also recorded for all the children using mercury sphygmomanometer. A detailed questionnaire regarding the medical history of the parents and the children were recorded. This study was approved by the Institutional Ethics Committee. Twelve hour fasting samples were collected from all the children, serum separated and the samples stored at -20^{0}c until analysis. Lipid profile which includes total cholesterol, LDL and HDL were analyzed by enzymatic methods and triglycerides by GPO-PAP method and fasting glucose levels were analyzed by GOD-POD method using an auto analyzer (Randox Daytona). Serum Apo-B and Apo-AI levels were measured using Immunoturbidimetric

method (Spinreact, Spain.) Apo-B/Apo-AI ratio, LDL/Apo-B ratio, TCHR (Total cholesterol to HDL ratio) calculated by following formula. Apo-B/Apo-AI ratio = Apo-B (mg/dl) / Apo-AI (mg/dl). LDL/Apo-B ratio = LDL-Cholesterol (mg/dl) / Apo-B (mg/dl). TCHR = Total Cholesterol (mg/dl) / HDL-Cholesterol (mg/dl).

RESULTS

The biochemical and anthropometric characteristics of study subjects are summarized in Table1. Out of 296 subjects (103 control, 96 obese, 97 overweight children and adolescents), 156 were boys and 140 were girls with age ranging between 10-17 years. Out of 156 boys (55 were controls, 47 were overweight, 54 were obese). Out of 140 girls (48 were control, 50 were overweight, 42 were obese). A total of 78 children and adolescents were excluded, who refused to participate in the study protocol and either had incomplete data (or) had previously diagnosed with various disorders.

Table 1
Comparison between controls and overweight, obese children.

	Control (103)	Overweight (97)	Obese (96)
Age	14.45±1.36	13.93±1.47	14.07±1.56
BMI(Kg/m^2)	18.04±2.14	24.09±1.42**	28.35±2.56**
WHR	0.85±0.09	0.99±0.13**	1.02±0.13**
Systolic B.P(mmHg)	117.57±5.51	120.52±7.13†	124.48±8.81**
Diastolic B.P(mmHg)	75.44±6.68	77.94±9.01 ^{NS}	76.56±9.04 ^{NS}
ApoAI (mg/dl)	153.08±17.98	132.26±10.80**	130.94±9.24**
ApoB (mg/dl)	73.55±12.03	82.6±12.64**	88.54±11.4**
ApoB/apoA Ratio	0.49±0.11	0.63±0.12**	0.68±0.11**
LDL/ApoB Ratio	1.21±0.23	1.11±0.21†	1.06±0.19**
TCHR	3.6±0.48	3.93±0.68**	4.3±0.66**
TC (mg/dl)	140.93±18.22	151.93±21.76**	164.19±22.05**
TG (mg/dl)	75.72±26.85	90±32.31†	103.26±36.18**
LDL-C (mg/dl)	87.93±12.27	90.70±12.28 ^{NS}	92.57±12.34 ^{NS}
HDL-C (mg/dl)	39.46±4.83	38.99±4.03 ^{NS}	38.36±3.46 ^{NS}
Fasting glucose(mg/dl)	87.83±6.55	81.98±6.16**	80.97±6.5**
Non Veg(%)	64	74.2	86.4

Results are expressed in Mean ± SD.
*****P<0.001; *P<0.005; ††P<0.01; †P<0.05; NS-non - significant.***
BMI- Body Mass Index, WHR-Waist-to-hip ratio, TC- Total Cholesterol, TG- Triglycerides, TCHR- Total Cholesterol to HDL Ratio.

The anthropometric measurements were found to be significantly higher in overweight and obese children compared to controls. Serum Apo-AI levels were significantly decreased in obese (130.94±9.24mg/dl) and overweight children (132.26±10.80mg/dl) ($p<0.001$) when compared with controls (153.08±17.98). Serum Apo-B levels were significantly elevated in obese (88.54±11.4mg/dl) and overweight children (82.6±12.64mg/dl) ($p<0.001$) than controls (73.55±12.03mg/dl). On further comparison between boys and girls, we found no marginal differences of serum Apo-AI and serum Apo-B levels between them in all the groups. The relationship between biochemical and anthropometric parameters for all the groups to that of serum Apo-AI and Apo-B are shown in Table2 and Table3 respectively.

Table 2
Pearson's correlation analysis between Serum Apo-AI and anthropometric and biochemical variables of the study subjects

	Overall(296)		Boys(156)		Girls(140)	
	r value	P value	r value	P value	r value	P value
BMI(kg/m^2)	-0.59	0.001	-0.60	0.001	-0.59	0.001
WHR	-0.37	0.001	-0.35	0.001	-0.41	0.001
Systolic B.P(mmHg)	-0.32	0.001	-0.36	0.001	-0.30	0.001
Diastolic B.P(mmHg)	-0.24	0.001	-0.27	0.001	-0.27	0.001
Apo B(mg/dl)	-0.38	0.001	-0.36	0.001	-0.39	0.001
ApoB/ApoAI Ratio	-0.76	0.001	-0.75	0.001	-0.77	0.001
LDL/ApoB Ratio	0.19	0.001	0.12	0.10	0.22	0.005
TCHR	-0.28	0.001	-0.32	0.001	-0.27	0.001
TC (mg/dl)	-0.26	0.001	-0.39	0.001	-0.19	0.015
TG (mg/dl)	-0.06	0.237	-0.06	0.43	-0.08	0.30
LDL-C (mg/dl)	-0.17	0.001	-0.26	0.001	-0.11	0.14
HDL-C(mg/dl)	0.062	0.252	-0.05	0.47	0.18	0.026
FastingGlucose(mg/dl)	0.38	0.001	0.35	0.001	0.38	0.001

BMI- Body Mass Index, WHR-Waist-to-hip ratio, TC- Total Cholesterol, TG- Triglycerides, TCHR- Total Cholesterol to HDL Ratio.

Table 3
Pearson's correlation analysis between Serum Apo-B and anthropometric And biochemical variables of the study subjects

	Overall(296)		Boys(156)		Girls(140)	
	r value	P value	r value	P value	r value	P value
BMI(kg/m^2)	0.40	0.001	0.43	0.001	0.37	0.001
WHR	0.21	0.001	0.22	0.001	0.23	0.003
Systolic B.P(mmHg)	0.26	0.001	0.30	0.001	0.23	0.003
Diastolic B.P(mmHg)	0.19	0.73	-0.01	0.98	-0.01	0.91
Apo AI(mg/dl)	-0.38	0.001	-0.36	0.001	-0.39	0.001

ApoB/ApoAI Ratio	0.87	0.001	0.87	0.001	0.86	0.001
LDL/ApoB Ratio	-0.62	0.001	-0.59	0.001	-0.64	0.001
TCHR	0.35	0.001	0.44	0.001	0.29	0.001
TC (mg/dl)	0.32	0.001	0.40	0.001	0.28	0.001
TG (mg/dl)	0.28	0.001	0.32	0.001	0.25	0.001
LDL-C (mg/dl)	0.28	0.001	0.35	0.001	0.24	0.002
HDL-C(mg/dl)	-0.12	0.030	-0.13	0.07	-0.09	0.23
Fasting Glucose(mg/dl)	-0.16	0.003	-0.17	0.026	-0.13	0.101

BMI- Body Mass Index, WHR-Waist-to-hip ratio, TC- Total Cholesterol, TG- Triglycerides, TCHR- Total Cholesterol to HDL Ratio.

Family history of obesity, diabetes, hypertension and heart disease of all children enrolled for the study are summarized in Table4. Socio-economic status and physical training programme of all children enrolled for the study were found to be almost similar.

Table 4
Comparison of family history between obese, overweight, and controls.

	Control %	Overweight %	Obese %
Obesity	20.3	56.7	55.2
Diabetes	11.6	36	30.2
Hypertension	15.5	32	37.5
Heartdisease	4.0	9.2	7.3

DISCUSSION

Numerous studies have shown the vital role of apolipoproteins and its relation with obesity in children[6, 8].Unfortunately, data for children and adolescents particularly in Indian population are scarce. The purpose of this study was to elucidate the relationship between serum apolipoprotein levels and anthropometric, clinical and biochemical parameters in Indian children and adolescents. Data reported in the present study show significantly elevated Apo-B levels and significantly decreased Apo-AI levels in both obese and overweight children and adolescents on comparison with the controls. The available information suggests cardiovascular abnormalities starts in obese children during childhood and adolescence and apolipoproteins serve as a marker for coronary heart disease. The present study reaffirms the previous results [6, 8, 9, 10]. It has been consistently observed that anthropometric parameters such as BMI and WHR were significantly elevated in both obese, overweight children and adolescents than controls. This is natural as per the diagnostic criteria. The results of our study also show close positive association between Apo-B and anthropometric parameters and negative association between Apo-AI and anthropometric parameters. The available information suggests that BMI is the main determinant for the variations of apolipoprotein levels and our results are in agreement with the study of Bellu *et al*.,[8]In contrast, another study found no relation between obesity and apoproteins[7] In our study, we found elevated systolic and diastolic blood pressure in both

obese and overweight children and adolescents than controls. Hypertension in obese children may occur due to increased intravascular volume, increased sympathetic nervous system activity, sodium retention and hyperinsulinemia[11, 12]. We observed negative correlation between serum Apo-AI levels and systolic and diastolic blood pressure. This indicates pathophysiological role of apolipoproteins in obesity related hypertension and our data agree with those reported by others[13, 14].

Higher serum Apo-B/Apo-AI ratio, TCHR, and lower LDL/Apo-B ratio were observed in both obese and overweight children and adolescents on comparison with the controls. Several studies suggest that higher levels of Apo-B/Apo-AI ratio, TCHR and decreased LDL/Apo-B ratio are associated with the risk of future cardiovascular disease even after modification of the usual risk factors and there is an increasing evidence that Apo-B/Apo-AI ratio may be more sensitive than LDL-C and HDL-C in predicting CHD risk[8,15,16]. Serum TC, TG, and LDL-C levels were found to be elevated in obese and overweight children on comparison with controls, and no marginal differences of HDL-C levels were found between obese, overweight and controls. Despite, we observed good correlation between serum Apo-B and TC, TG, and LDL-C. Serum Apo-AI levels negatively correlated with TC, TG, and LDL-C. Our observations raise the possibility that childhood obesity is associated with dyslipidemia and the investigated data confirm the previous reports[8, 17].One of the most striking points in our data is fasting glucose levels were found to be decreased in both obese and overweight children and adolescents and this implies a negative correlation between serum Apo-B and fasting glucose and positive correlation with serum Apo-AI levels. The reason for this could be that obesity causes insulin resistance. In obesity, probably insulin decreases blood glucose concentrations by reducing hepatic gluconeogenesis and glycogenolysis and by enhancing glucose uptake into striated muscles and adipocytes[18]. On further comparison of apolipoprotein levels between boys and girls, interestingly, we noticed less specific sex differences for both Apo-AI and Apo-B concentrations. Our data are also in agreement with earlier study reported[19]. However, some studies have not supported these findings in children[20]. Among overweight and obese children and adolescents the parental history of obesity, hypertension, diabetes, heart diseases was 56%, 35%, 33%, 8.5% respectively and this confirms the strong genetic influence on childhood obesity, diabetes, CVD [21]. The main limitation of our study was the lack of puberty assessment and measurement in detail of the dietary habits of children and adolescents. In conclusion serum Apo-B levels showed positive correlation with BMI, WHR, Apo-B/Apo-AI ratio, TCHR, TC, TG, and LDL-C and showed negative correlation with fasting glucose levels, and no association with HDL-C. Serum Apo-AI levels showed negative correlation with BMI, WHR, Apo-B/Apo-AI ratio, TCHR, TC, TG, LDL-C and showed positive correlation with HDL-C and fasting glucose levels. These findings suggest that childhood obesity is associated with lipid patterns, considered to be atherogenic. Periodic monitoring of children at school for overweight would help reduce the risk of these children being prone to major cardiovascular anomalies in adulthood. Regular camps should be conducted at schools to counsel the identified obese and overweight children for physical exercises and balanced diet. However, further prospective studies on larger sample size are needed to elucidate the role of apolipoproteins in childhood obesity and its complications.

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