Original Article

Childhood cardiovascular risk factors, a predictor of late adolescent overweight

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Abstract

Background: We conducted a prospective study to elucidate the effects of increased cardiovascular risk factors on future weight gain and also the relation between body mass index (BMI) and other cardiovascular risk factors in children and adolescents.

Materials and Methods: This study was conducted on 1525 nonobese children and adolescents with an age range of 3-16 years old, participating in the 1st phase and follow-up phases of Tehran Lipid and Glucose Study. The subjects were evaluated 4 times with a 3-year time interval regarding lipid profile status and BMI, and other cardiovascular disease (CVD) risk factors. All the cases had a BMI <85% and had been appraised in at least two evaluation points.

Results: Cardiovascular risk factors, high-density lipoprotein (HDL) ($P = 0.019$), low-density lipoprotein ($P = 0.016$), triglyceride (TG) ($P < 0.001$), and blood pressure (BP) ($P = 0.001$); had significant effects on weight gain. There was also no difference between boys and girls and no age trend for increasing weight in both groups. The associations between BMI with cardiovascular risk factors were assessed cross-sectionally. For both sexes, BMI was significantly correlated to systolic and diastolic BP and TG ($P = 0.05$). For girls, BMI was significantly related to HDL ($P = 0.05$) regardless to age, but in boys, the relation of BMI with HDL only increased with age ($P = 0.05$).

Conclusion: Increased CVD risk factors are predictors of future overweight in childhood and adolescent and increased weight is linked significantly with dyslipidemia and hypertension in this age group.

Key Words: Cardiovascular risk factors, children, dyslipidemia, obesity

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INTRODUCTION

Childhood and adolescent obesity is an important factor and is strongly associated with other cardiovascular disease (CVD) risk factors.[1-22] The incidence of hyperlipidemia, hypertension, and insulin resistance is more in obese children.[4,5,23-28] There are a few reports regarding childhood hypertriglyceridemia[29] and hypercholesterolemia,[30-32] and other cardiovascular risk factors as a predictor of adolescent obesity and in the literature.

To elucidate this issue and also the relation between body mass index (BMI) and other cardiovascular risk factors, we conducted a community-based prospective study on children and adolescents age 3-16 years and followed them for increasing weight and other CVD risk factors.

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MATERIALS AND METHODS

Subjects

The Tehran Lipid and Glucose Study (TLGS) is a long-term (at least 20 years) large scale community-based prospective study, for prevention of noncommunicable disease by implementation of a healthy lifestyle modification and reduction of coronary artery disease (CAD) risk factors. A total of 15,005, residents of district 13 of Tehran, aged 3 years and over were selected by multistage cluster random sampling method. Age distribution and socioeconomic status of the population in the district no. 13 are delegate of the overall population of Tehran.[33]

This study was conducted on 1525 nonobese children and adolescents (723 boys and 802 girls) with an age range of 3–16 years old (mean 10.65 ± 3.75), participating in the 1st phase and follow-up of TLGS. The subjects were evaluated 4 times with a 3-year time interval regarding lipid profile status and BMI and other CVD risk factors. All the cases had a BMI <85% and had been appraised in at least two evaluation points. The data was gathered for age, weight, height, blood pressure (BP), lipid profile (total cholesterol, low-density lipoprotein [LDL], high-density lipoprotein-cholesterol [HDL-C], triglyceride [TG], and non-HDL-C), and glucose concentrations. To evaluate the relation between BMI and cardiovascular risk factors, hypercholesterolemia was used as a predefined risk factor and subjects were categorized into hypercholesterolemic and nonhypercholesterolemic groups.

Baseline characteristics of subjects are shown in Table 1.

According to National Heart, Lung, and Blood Institute (NHLBI) panel report,[34] subjects with age and sex-specific elevations in LDL-C concentration >75th percentile at all 4 evaluation points were classified as hypercholesterolemic. Subjects with LDL-C persistently less than the 75th percentile were considered nonhypercholesterolemic. Serum TG, non-HDL-C <75%, and serum HDL-C >20% were considered normal. Fasting blood sugar (FBS) >100 mg/dl was reported as abnormal.

Table 1: Baseline characteristics of subjects

Variables	Boys	Girls
Age	10.51±3.76 (723)	10.77±3.73 (802)
Weight	34.46±15.28 (703)	35.7±14.59 (786)
Height	139.37±22.61 (703)	139.12±20.1 (786)
BMI*	16.71±2.68 (703)	17.18±3.24 (786)
SBP (mm Hg)*	103.02±11.09 (683)	101.56±11.11 (776)
DBP (mm Hg)	69.57±9.11 (682)	69.7±9.89 (776)
Glucose*	87.48±8.64 (663)	86.35±8.35 (770)
LDL cholesterol	101.03±29.31 (647)	107.62±27.75 (764)
TG*	93.34±44.61 (661)	105.16±50.09 (770)
HDL cholesterol	45.74±11 (650)	44.71±11.04 (765)

Mean±SD, *n* in brackets. *Significant difference between boys and girls, $P<0.05$. SBP: Systolic blood pressure, DBP: Diastolic blood pressure, BMI: Body mass index, LDL: Low-density lipoprotein, HDL: High-density lipoprotein, SD: Standard deviation, TG: Triglyceride

The informed written consent from the parents of guardians of all children and adolescents participating in the study was obtained.

Anthropometric assessment

Trained medical doctors and personnel collected the information and samples according to the standard methods. Height and weight were measured to ± 0.1 cm and ± 0.1 kg, respectively. BMI was calculated by dividing weight in kilograms to the square of height in meters. Waist circumference was assessed by measuring the waist girth at the level of the umbilicus. Obesity and overweight in children and adolescents were defined according to international cut-off points for BMI.[35]

On the basis of the circumference of the participant's arm, a pediatric, regular adult of a large cuff was used on the right arm at the heart level. BP was measured in 2 replicates with at least a 30-s interval while they were in a relaxed sitting position. The systolic BP was recorded at the 1st Korotkoff phase (appearance of the 1st sound) and diastolic BP was measured at the 5th Korotkoff phase (disappearance of the sound). According to NHLBI panel report, age, sex, and height matched systolic and diastolic BP <90% were taken into accounted as normal.[36].

Laboratory analysis

A blood sample was drawn between 7:00 and 9:00 am. After 12–14 h overnight fast. Samples were centrifuged within 30-45 min of collection and sent to TLGS Research Laboratory (RL) on the day of blood collection.

Total cholesterol and TG were measured by enzymatic colorimetric method (Iran Pars Azmun) on Selectra II auto analyzer. The coefficient of variations was calculated 2.2 and 1.6%, respectively. HDL was measured after precipitation of non-HDL lipoproteins with an enzymatic method of CHOD-PAP. HDL-C concentration was deduced from total cholesterol for non-HDL-C calculation. LDL-C was calculated with Friedwall formula in samples with TG >400 mg/dl. Blood glucose concentrations were measured by a glucose analyzer with standard chemical procedures in TLGS RL.

Baseline characteristics, lipid profile, and other CVD risk factors of the subjects were compared, using one-way analysis of variance [Tables 1 and 2]. To assess

Table 2: Baseline characteristics of hypercholesterolemic and nonhypercholesterolemic subjects

Variables	Boys		Girls	
	Normal LDL	High LDL	Normal LDL	High LDL
Age	11.01±3.61 (505)	10.41±3.55 (142)	11.05±3.61 (552)	10.792±3.66 (212)
Weight	35.99±14.88 (491)	34.48±15.99 (140)	35.89±14.25 (540)	35.68±14.60 (210)
Height[a,b]	142.37±21.73 (491)	138.04±21.19 (140)	140.82±19.32 (540)	138.88±19.41 (210)
BMI[d]	16.83±2.59 (491)	17±3.05 (140)	17.21±3.19 (540)	17.52±3.28 (210)
SBP (mmHg)[d]	102.742±10.9 (481)	104.15±10.583 (140)	101.3152±11.243 (533)	102.714±10.231 (210)
DBP (mmHg)[b]	69.123±9.027 (481)	70.629±9.136 (140)	69.317±9.951 (533)	70.876±9.255 (210)
Glucose[d]	87.06±8.52 (505)	88.60±8.15 (142)	86.24±8.24 (552)	86.65±8.39 (212)
TG*[,a,b,c,d]	88.86±40.74 (505)	105.41±45.57 (142)	102.11±48.96 (552)	111.40±46.58 (212)
HDL cholesterol	45.78±11.13 (505)	45.56±10.31 (142)	44.93±11.14 (552)	44.21±10.73 (212)

Mean±SD, *n* in brackets. [a]Significant difference between normal LDL and high LDL boys; $P<0.05$, [b]Significant difference by LDL status; $P<0.05$, [c]Significant difference between normal LDL and high LDL girls; $P<0.05$, [d]Significant difference between boys and girls; $P<0.05$. TG $P<0.05$. HDL not significant at baseline in different groups and sexes. SBP: Systolic blood pressure, DBP: Diastolic blood pressure, BMI: Body mass index, LDL: Low-density lipoprotein, HDL: High-density lipoprotein, SD: Standard deviation, TG: Triglyceride

the changes in weight in subjects with abnormal lipid profiles and cardiovascular risk factors (FBS and BP) repeated-measures analysis of variance was used with BMI as the dependent variable and age, sex [Figure 1].

Spearman's correlation was used to determine the associations among BMI, BP, glucose, and lipid concentrations for hypercholesterolemic and nonhypercholesterolemic subjects [Tables 3 and 4]. Statistical significance was defined as a $P \leq 0.05$ and data were analyzed by the statistical package for the social sciences (SPSS) 19 (SPSS Inc., Chicago, IL, USA).

RESULTS

There was a significant difference in BMI, systolic BP, glucose, and TG at baseline between boys and girls [Table 1]. There were 354 (25%) hypercholesteromic and 1057 (75%) nonhypercholestromic children identified. Hypertriglyceridemia and low HDL were observed in 362 (25.3%) and 321 (22.7%) of cases, respectively. 365 (25.8%) of cases had increased serum non-HDL-C level. Abnormal BP and blood glucose were detected in 320 (21.95%) and 91 (6.4%) of subjects orderly. Baseline characteristics of the cases are shown in Table 2. BMI was significantly higher in girls (17.18 ± vs. 16.71 ± 2.68, $P < 0.05$). There was a notable difference in systolic BP between boys and girls ($P < 0.05$) and in diastolic BP by LDL status ($P < 0.05$). Glucose was significantly more in boys ($P < 0.05$). TG concentrations were higher in girls and by LDL status in both sexes ($P < 0.05$) [Table 2].

To assess the longitudinal changes in relative weight, separate repeated-measures analysis of variance were completed, with BMI as the dependent variable and HDL, LDL, non-HDL, TG, FBS, and BP as independent variables. All analyses were adjusted for age and sex. Significant effects were found for the following factors: HDL ($P = 0.019$), LDL ($P = 0.016$), TG ($P < 0.001$), and BP ($P = 0.001$); nonsignificant factors were non-HDL and FBS ($P = 0.258$ and 0.446, respectively). To take into account the individual effects of independent variables on BMI, independent variables were concurrently considered in repeated-measures analysis of variance. The relation between BMI and age, sex, and LDL, TG, HDL, BP, and FBS did not change after the adjustment for baseline independent variables concentrations. There was also no difference between boys and girls and no age trend for increasing weight in both groups [Figure 1].

The associations among BMI, BP, glucose, and lipid concentrations were assessed cross-sectionally with the use of Spearman's correlations at the 4 phases of the study for the hypercholesterolemic and nonhypercholesterolemic girls and boys [Tables 3 and 4, respectively].

For both sexes, BMI was significantly correlated to systolic and diastolic BP and TG ($P = 0.05$). For girls, BMI was significantly related to HDL ($P = 0.05$), but in boys, the relation of BMI with HDL increased with age ($P = 0.05$). There was no noticeable difference between hypercholesterolemic and nonhypercholesterolemic subjects in either sex. BMI was significantly related to FBS only in hypercholesterolemic girls at 1st and 4th phases and in boys at 1st phase of the study.

DISCUSSION

In this longitudinal study, we observed that increased CVD risk factors are predictors of overweight risk in adolescents. This is discordant with literature reporting the precedence of obesity to theses CVD risk factors.[4,5,9,10,23-28] Our findings are consistent with others reporting age-related increase in weight in children and adolescents with high cholesterol, TG, BP, and low HDL serum concentrations[29,30]

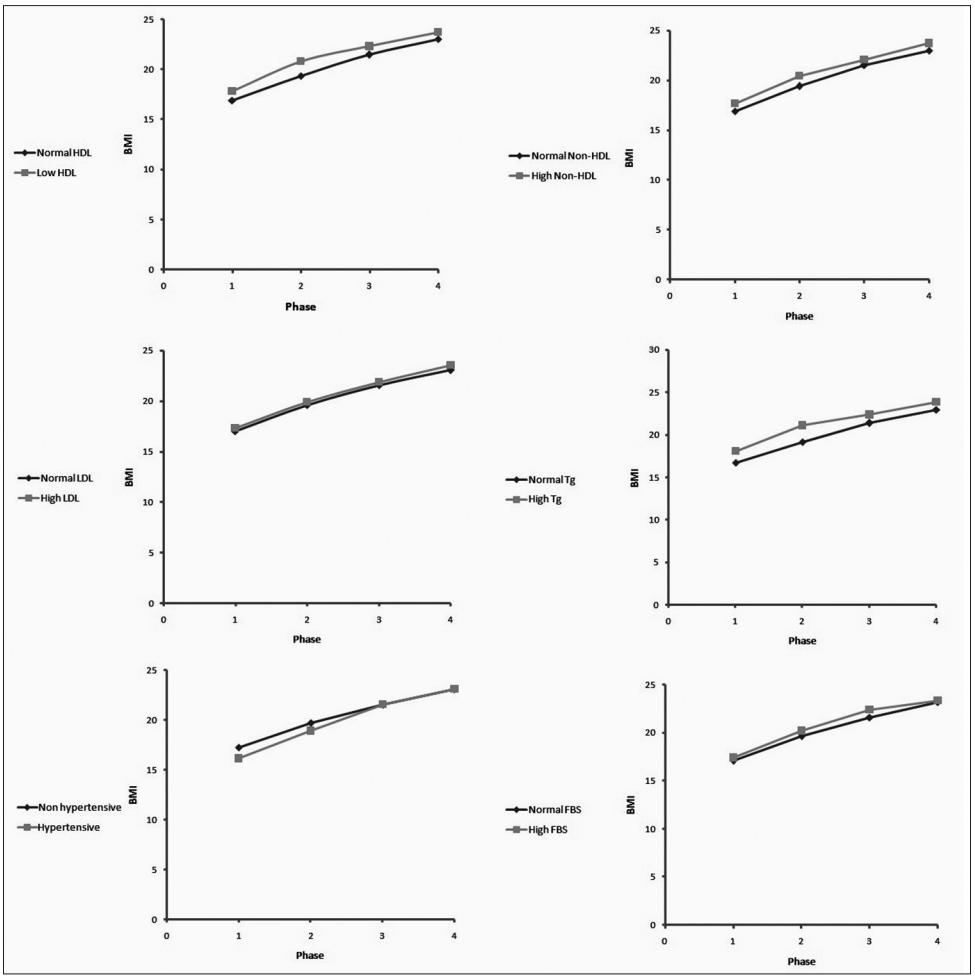

Figure 1: Serum lipids, fasting blood sugar and blood pressure in relation to weight status (body mass index, kg/m^2) in each phase of the study. There was no difference between the two sexes

and in contrast to Byrnes's study[37] observing no relationship between weight change and plasma levels of HDL-C and TG in a 12 months period. We could not also identify any difference between boys and girls in developing overweight at follow-up. This is in keeping with Savva's study[29] and in contrast with Tershakovec's survey reporting increased relative weight in girls.[30] In the present study, we were unable to find any age trend for increasing weight in either sex. This finding is opposed with others explaining a greater increment in BMI from 5 to 12 years in girls[30] and between 6 and 10 years in both sexes.[31]

Studies focusing on the expression of other cardiovascular risk factors, especially in hyperlipidemic children are limited. As opposed to our study most surveys stress on evaluating cardiovascular risk factors in children without predefined risk factors, like hypercholesterolemia.[1-4,7,8,10,11,38] Our data complying with others[30,39] illustrated a significant correlation between BMI and other cardiovascular risk factors. In the present study, BMI was significantly correlated to systolic and diastolic BP and TG in both sexes. This is in line with other studies reporting three-fold higher risk of hypertension in overweight and obese children and adolescents especially for those who had BMI ≥ 95th percentile for age and sex.[40,41]

The existing literature indicates that dyslipidemia occurs among overweight and obese children and adolescents, particularly those with a central fat distribution[42,43] and especially with a positive family history of premature CAD.[44] The typical pattern is one of the elevated concentrations of serum LDL-C and TGs and decreased concentration of HDL-C.[13,41,45]

This is in agreement with our findings that BMI was significantly related to TG and inversely to HDL concentrations but in contrast not to hypercholesterolemia. Tershakovec's study[30] suggested that as was shown by the association between BMI and lipid concentrations, obesity further intensifies dyslipidemia especially in girls.

Table 3: Spearman's correlation coefficients (*r*) between BMI and other cardiovascular risk factors for boys by age group

Variables	Boys	
	Hypercholesterolemic	Nonhypercholesterolemic
Phase one		
SBP	0.238* (138)α	0.181* (478)
DBP	0.068 (138)	−0.016 (478)
Glucose	0.238* (140)	0.278* (491)
HDL cholesterol	−0.145 (140)	−0.154* (491)
LDL cholesterol	0.042 (140)	−0.074 (491)
TG	0.248*(140)	0.232* (491)
Phase two		
SBP	0.472* (102)	0.444* (340)
DBP	0.320* (102)	0.302* (340)
Glucose	−0.056 (100)	0.058 (332)
HDL cholesterol	−0.374* (100)	−0.290* (331)
LDL cholesterol	0.001 (99)	0.042 (330)
TG	0.382* (100)	0.334* (332)
Phase three		
SBP	0.465* (101)	0.516* (367)
DBP	0.353* (101)	0.23* (367)
Glucose	−0.129 (102)	0.005 (368)
HDL cholesterol	−0.346* (102)	−0.235* (367)
LDL cholesterol	0.08 (98)	0.229* (356)
TG	0.338* (102)	0.334* (368)
Phase four		
SBP	0.513* (104)	0.543* (371)
DBP	0.277* (104)	0.287* (371)
Glucose	0.113 (104)	0.088 (368)
HDL cholesterol	−0.429*(104)	−0.302* (368)
LDL cholesterol	0.24* (103)	0.342* (367)
TG	0.418* (104)	0.44* (368)

[a]*n* values in brackets. **P*<0.05. SBP: Systolic blood pressure, DBP: Diastolic blood pressure, BMI: Body mass index, LDL: Low-density lipoprotein, HDL: High-density lipoprotein, TG: Triglyceride

Table 4: Spearman's correlation coefficients (*r*) between BMI and other cardiovascular risk factors for girls by age group

Variables	Girls	
	Hypercholesterolemic	Nonhypercholesterolemic
Phase one		
SBP	0.277* (209)α	0.280* (529)
DBP	0.164* (209)	0.242* (529)
Glucose	0.111 (210)	0.211* (540)
HDL cholesterol	−0.333* (210)	−0.112* (540)
LDL cholesterol	0.007 (210)	−0.012 (540)
TG	0.370* (210)	0.205* (540)
Phase two		
SBP	0.35* (157)	0.367* (394)
DBP	0.253* (157)	0.317* (394)
Glucose	−0.047 (149)	0.047 (390)
HDL cholesterol	−0.294* (148)	−0.127* (391)
LDL cholesterol	0.096 (148)	0.091 (389)
TG	0.211* (149)	0.1* (390)
Phase three		
SBP	0.226* (160)	0.234* (425)
DBP	0.254* (160)	0.233* (425)
Glucose	0.022 (163)	0.054 (433)
HDL cholesterol	−0.142 (163)	−0.183* (432)
LDL cholesterol	0.229* (155)	0.175* (414)
TG	0.218* (163)	0.221* (433)
Phase four		
SBP	0.428* (160)	0.259* (425)
DBP	0.268* (160)	0.18* (425)
Glucose	−0.002 (160)	0.12* (424)
HDL cholesterol	0.265* (160)	−0.282* (424)
LDL cholesterol	−0.327* (160)	−0.223* (424)
TG	0.159* (160)	0.247* (423)

[a]*n* values in brackets. **P*<0.05. SBP: Systolic blood pressure, DBP: Diastolic blood pressure, BMI: Body mass index, LDL: Low-density lipoprotein, HDL: High-density lipoprotein, TG: Triglyceride

In contrast, we could not demonstrate a noticeable difference between hypercholesterolemic and nonhypercholesterolemic subjects in either sex. It implies that increasing weight does not exacerbate dyslipidemia in our cases surprisingly. Contrasting to other studies which indicate age-related cardiovascular risk factors in children,[1,10,30,46] we failed to find this age-related association except for HDL in boys.

Impaired glucose tolerance, which predicts the development of diabetes, is a common complication of childhood and adolescent obesity.[47,48] In a study of >6000 students in the sixth grade with average age 11.8 years,[49,50] impaired fasting glucose (fasting blood glucose ≥ 100 mg/dL) was present in 15.5% of overweight children, 20.2% of obese children, and 22.5% of severely obese children. In other population of obese children and adolescents, the prevalence of impaired glucose tolerance ranges from 7% to 13.5%, and the prevalence of type 2 diabetes was <1%.[51,52] Type 2 diabetes mellitus (T2DM) is another comorbidity of obesity in children and adolescents.[53-55] In the Sinha's study, 4% of adolescents with BMI ≥ 95th percentile for age and sex had asymptomatic T2DM.[56] In accord with these studies, we were able to represent that BMI was significantly related to FBS in some occasions during our survey, but in contrast there was no case of T2DM detected.

A recent review article has reported the highest prevalence of childhood overweight in Eastern Europe and the Middle East.[57] In a study on 4500 randomly selected children aged 2-18 years in Iran, serum lipid levels were significantly higher than standard values in both sexes and all age groups. The increase in serum lipid levels was most marked in teenagers.[58]

Despite the familial propensity for obesity[59] and consistency of our findings with some other studies, we were not able to explain the rational for the predication of future adiposity by cardiovascular risk factors. Perhaps it might be a genetic susceptibility for weight gain in whom with CAD risk factors, so more studies are warranted to elucidate this issue. As a practical point hyperlipidemia

and overweight in children should be managed to prevent future cardiovascular events. Although data from adult studies demonstrate a low risk of adverse side effects with statins,[60-62] similar long-term data regarding outcome are not available in children,[63] so changing dietary practices, e.g., improper intake of high amounts of saturated fat,[64] therapeutic lifestyle changes, and maintenance of regular physical activity through parental initiative and social support interventions are the most important strategies in managing future risk of these adverse events.

CONCLUSION

Contradictory to the general opinion that obesity is associated with increased CVD risk factors in childhood and adolescents, we identified the reverse association, that is, increased CVD risk factors are predictors of future overweight. On the other hand, increased weight is linked significantly with dyslipidemia and hypertension in these age groups.

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