Predictors of cardiovascular risk factors in Tehranian adolescents: Tehran Lipid and Glucose Study

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Abstract: Introduction: Cardiovascular disease (CVD) is one of the major health and social problems in Iran. The aim of this study is to determine the predictors of CVD risk factors in adolescents residing in district 13 of Tehran.

Methods: Dietary intake assessment was undertaken with two separate 24-hour recall interviews with adolescents aged 11–18 years, selected from among 15005 subjects who were participants of the Tehran Lipid and Glucose Study. After excluding the under- and over-reporters, 290 adolescents remained in the study. Data related to cigarette smoking was collected. Height and weight were assessed and body mass index (BMI) was calculated. Blood pressure was measured twice at intervals in a seated position. Serum cholesterol, triglycerides, and high-density lipoprotein (HDL) concentrations were measured in a blood sample after 12 hours of fasting, and low-density lipoprotein (LDL) was calculated. To determine the predictors of CVD risk factors stepwise linear regression was used.

Results: There were strong positive correlations between BMI and both systolic and diastolic blood pressure in girls: ($\beta = 1.8$, $p < 0.001$; $\beta = 0.8$, $p < 0.001$) and boys ($\beta = 0.04$, $p < 0.001$; $\beta = 0.05$, $p < 0.01$). There was an inverse association between calcium intake and systolic ($\beta = -0.16$, $p < 0.05$) and diastolic blood pressure in boys ($\beta = -0.36$, $p < 0.01$), as well as inverse association between calcium intake and systolic ($\beta = -1.2$, $p < 0.05$) and diastolic blood pressure ($\beta = -0.05$, $p < 0.05$) and serum triglycerides ($\beta = -0.1$, $p < 0.01$) in girls. Positive correlations were found between BMI and cholesterol in girls ($\beta = 0.2$, $p < 0.01$) and boys ($\beta = 0.31$, $p < 0.01$).

Conclusion: Certain dietary and life style factors predict CVD risk factors in Tehranian adolescents.

Key words: Cardiovascular disease (CVD), risk factors, adolescent, BMI, blood pressure.

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Introduction

Although significant reductions have occurred in the incidence of cardiovascular disease (CVD) since the mid-1970s, this is still the primary cause of morbidity and mortality in many countries [1, 2]. Further progress in prevention may depend on identifying the population at increased risk of CVD [1]. There is evidence from epidemiological, pathological, clinical, and genetic studies that atherosclerosis begins during childhood, and that serum lipid profile concentration in childhood is a useful parameter in predicting adult dyslipoproteinemia [3]. Fibrous plaques are often evident in adolescents [4] and it is indicated that the earliest development of atherosclerotic lesions begins in childhood [5]. For preventing CVD, it is important to determine its risk factors. In various studies both systolic blood pressure (SBP) and diastolic blood pressure (DBP) have been shown to be associated with a risk of CVD. In the 1980s, DBP was determined as the main risk factor of CVD [6]. Many researchers have shown that elevated levels of low-density lipoprotein (LDL) cholesterol, total cholesterol, triglycerides, and low levels of high-density lipoprotein (HDL) are powerful risk factors for CVD [7, 8]. In various epidemiological studies, a strong positive relationship has been reported between some dietary and non-dietary factors and risk factors of CVD. During the last few years, a large number of studies has suggested that dietary factors, age, sex, weight, body mass index (BMI), waist-to-hip ratio (WHR), education, and cigarette smoking may have an important relation to CVD risk factors [9–11]. Because of controversy regarding predictors of CVD risk factors in different populations, the aim of this study is to determine the predictors of CVD risk factors in adolescents residing in an urban distinct of Tehran.

Methods

Study population: The Tehran Lipid and Glucose Study (TLGS) is a study conducted to determine the risk factors of atherosclerosis among Tehran's urban population and to develop population-based measures to prevent the rising trend of diabetes mellitus and dyslipidemia. The design of this study encompasses two major components; phase 1 is a cross sectional prevalence study of cardiovascular disease and associated risk factors and phase 2 is a prospective follow-up study for 20 years [12]. A multistage stratified cluster random sampling technique was used to select 15 005 people aged 3 to 69 years from district 13 of Tehran.

A subsidiary population of 1470 subjects was randomly selected for dietary assessments. After excluding the under- and over-reporters (EI: BMR < 1.35 and ≥ 2.4), 290 subjects 11–18 years old, who had no previous history of diabetes, myocardial infarction, cerebrovascular disease, pancreatitis, thyroid, renal, and hepatic disorders, and were not consuming any lipid-lowering agents, diuretics, beta-blockers, corticosteroids, androgens, or fish liver oil, remained in this study.

Anthropometric measures: Weight and height were determined, using a digital electronic weighing scale (Seca 707; range 0.1–150.0 kg) and tape meter stadiometer, respectively. Waist and hip circumferences were also measured using standard protocols. Body mass index [BMI = weight (kg)/height (m^2)] and waist-to-hip ratio [WHR = waist circumference (cm)/hip circumference (cm)] were calculated [13].

Dietary assessment: Two 24-hour dietary recalls were completed by nutritionists through face-to-face interviews. The first recall was performed at subject's home and the second at the TLGS clinic within one to three days after the first visit. Mothers were asked about the type and quantity of meals and snacks when subjects were unable to recall. Standard reference tables were used to convert household portions to grams, data were entered into the Nutritionist III (3) software package, and daily energy and nutrients intake for each individual was obtained from mean energy of two 24-hour dietary recalls.

The basal metabolic rate (BMR) was calculated based on age and sex according to standard equation [15]. Under- and over-reporting of energy intake were defined as EI: BMR < 1.35 and > 2.4, respectively [16, 17]. The range of 1.35–2.39 was considered as normal reporting of dietary intake.

Cigarette smoking category: Data related to cigarette smoking was classified into four groups according to WHO guidelines. 1 – daily smoker: smokes cigarettes at least once a day (including people who smoke every day, but have to stop temporarily because of religious fasting or medical reasons). 2 – occasional smoker: smokes cigarettes but not every day. 3 – Ex-smoker: Formerly a daily or occasional smoker, but currently does not smoke at all. 4 – Never-smoked: Never smoked before or smoked very little in the past.

Serum lipid and blood sugar analysis: A blood sample was drawn between 7:00 and 9:00 AM into vacutainer tubes from all study participants after 12–14 hours overnight fasting. Blood samples were taken in the sitting position according to the standard protocol and centrifuged within 30 to 45 minutes of collection. All blood lipid analyses were done at the TLGS research laboratory on the day of blood collection. The analyses of samples were performed using Selectra 2 auto-analyzer (Vital Scientific, Spankeren, Netherlands). Total cholesterol and triglycerides were measured with TC and TGs Kits (Pars Azmon Inc, Iran). TC and TGs were assayed using enzymatic colorimetric tests with cholesterol esterase, and cholesterol oxidase and glycerol phosphate oxidase, respectively. HDL was measured after precipitation of the apolipoprotein-β containing lipoproteins with phosphotungstic acid. Serum glucose level was measured by enzymatic method (CHOD-PAP). Assay performance was monitored at every 20 test intervals using the lipid control serum, precinorm (normal range) and precipath (pathologic range) wherever applicable (Boehringer Mannheim, Germany; cat. No. 1446070 for precinorm and 171778 for precipath). Lipid standard was used to calibrate the Selectra 2-auto-analyzer in each day of laboratory analyses. LDL was calculated according to the Friedwald equation [18].

Blood pressure measurement: Participants were initially told to rest for 15 minutes. Then a qualified physician measured blood pressure two times with subjects in a seated position during physical examinations. Hypertension was defined as a systolic blood pressure more than 140 mmHg and a diastolic blood pressure more than 90 mmHg [19].

Statistical methods: Data were analyzed by SPSS (SPSS, Inc. Chicago IL; Version 9.05). Stepwise multiple linear regression was used to determine the predictors of CVD. This study was approved by the Research Ethics Committee of the Endocrine Research Center of Shaheed Beheshti University of Medical Sciences and informed written consent was obtained from each subject.

Results

Data related to BMI and WHR are shown in Table 1. BMI increased with age in both boys and girls. This increase was significant in girls ($p < 0.05$). The median (second quartile) of BMI was 17.7 in 11- to14-year-old girls and 21.2 in 15- to 18 year-old girls. There was no increase in WHR with age. There was also no difference in smoking in the two age groups. None of the girls or boys in the 11- to 14-year-old group were smokers.

Table 2 presents the means and standard error of the mean (SEM) of biochemical, anthropometric, and dietary data. Table 3 presents results obtained by stepwise linear regression for various variables in girls. BMI was a predictor of total cholesterol ($\beta = 0.2$, $p < 0.001$), BMI and WHR were the predictors of triglyceride levels ($\beta = 4.6$, $p < 0.01$ & $\beta = 8.2$, $p < 0.05$) and WHR was also a predictor of LDL ($\beta = 1.8$, $p < 0.05$). Vitamin C was a predictor of HDL ($\beta = 0.036$, $p < 0.05$). There was a positive correlation between BMI and systolic and diastolic blood pressure in girls ($\beta = 1.8$, $p < 0.001$ & $\beta = 0.8$, $p < 0.01$). Calcium intake had a negative correlation with serum triglyceride, and with systolic and diastolic blood pressure in girls. There was a negative correlation between linoleic acid intake and systolic and diastolic blood pressure.

Table II: The means and SEM of biochemical, anthropometric, and dietary data

Data	Boys	Girls
Biochemical Data		
Blood cholesterol (mg/dL)	162 ±2.8	167±2.1
LDL (mg/dL)	96.7±2.7	101±1.9
HDL (mg/dL)	43 ±0.8	43±0.8
Triglycerides (mg/dL)	114 ±5.7	116±4.5
Anthropometric Data		
Weight (kg)	52 ± 1.2	49 ± 0.9
BMI (kg/m^2)	19.7 ± 0.3	19.9 ± 0.3
Dietary Data		
Carbohydrate (%)	59.3 ± 6.1	56.9 ± 6.8
Protein (%)	11.1 ± 1.5	11.0 ± 1.8
Fat (%)	29.4 ± 6.4	32.0 ± 7.1
Cholesterol (%)	223 ±13.7	188 ± 9.1
Vitamin C (mg/day)	126 ± 5.6	124 ± 5.6
Vitamin B6 (mg/day)	0.7 ± 0.02	0.6 ± 0.02
Vitamin B12 (μg/day)	2.06± 0.1	2.03± 0.1
Calcium (mg/day)	688 ±21	619 ±16
Selenium (μg/day)	0.02± 0.01	0.02± 0.02
Potassium (mg/day)	2276 ±62	2186 ±53

Table I: BMI and WHR percentile in adolescents

	Boys							Girls						
Age group (years)	Percentiles of BMI (kg/m^2) n	25	50	75	Percentiles of WHR 25	50	75	Percentiles of BMI (kg/m^2) n	25	50	75	Percentiles of WHR 25	50	75
11-14	59	16.5	18.3	21.4	0.76	0.81	0.84	89	15.7	17.7	20.9	0.74	0.78	0.82
15-18	69	17.9	19.7	22.6	0.76	0.79	0.82	73	18.8	21.2*	24.4	0.71	0.74	0.8

* $p < 0.05$ vs P50 of BMI in 11-to 14-year-old girls

Table III: Regression coefficients to determine the relation between nutritional and non-nutritional factors and CVD risk factors in girls

Independent variable Dependent variable	Constant	BMI	WHR	Vit C	Calcium	Linoleic Acid	Waist circumference
Total cholesterol	124.6						
β		0.2	*				0.41
R^2		0.04					0.16
P		0.0001					0.02
Triglyceride	203.9						
β		4.6	8.2				
R^2		0.04	0.04				
P		0.001	0.019				
LDL	63.1						
β		1.8					
R^2		0.04					
P		0.012					
HDL	79.4						
β		-0.6	-1	0.036			
R^2		0.04	0.04	0.04			
P		0.02	0.037	0.019			
Systolic blood pressure	78.1						
β		1.8			-0.012	-1.2	
R^2		0.16			0.04	0.16	
P		0.0001			0.02	0.01	
Diastolic blood pressure	56.1						
β		0.8			-0.014	-0.05	
R^2		0.16			0.04	0.04	
P		0.001			0.001	0.013	
Blood sugar	75.1						
β			0.12				
R^2			0.16				
P			0.003				

* The space shows that there was no relation between the two variables

We found a positive correlation between blood sugar and WHR (β = 0.12, $p < 0.01$). Table 4 presents the results obtained by stepwise linear regression for various variables in boys. Positive correlations were found between BMI and smoking and total cholesterol (β = 0.31, $p < 0.001$ & β = 0.11, $p < 0.05$) as well as BMI and WHR and energy intake and triglycerides (β = 1.5, $p < 0.01$; β = 1.8, $p < 0.05$ & β 1.3, $p < 0.01$). There was a positive correlation between blood sugar and WHR in boys (β = 0.15, $p < 0.01$).

Discussion

The results of this study showed that there were correlations between a few nutritional and non- nutritional factors and there was a positive significant correlation between anthropometric indices and CVD risk factors. Other researchers have shown that anthropometric indices are independently associated with the prevalence of hypertension [20]. Obesity could have a close association with hypertension. Hypertension occurred when vascular resistance decreased due to an increased cardiac output. It seems that this type of hypertension is multifactorial, as are the other types [21]. Some researchers have theorized leptin to be the cause of this hypertension. The Trp64Arg mutation in the beta-3-adrenergic receptor gene may be attributed to blood pressure in obese people. This mutation was seen in obesity and diabetes, which had similar effects on weight, BMI, abdominal fat, and blood pressure (22).

In the present study, BMI was a good predictor of total cholesterol. Cigarette smoking was a predictor of high levels of total cholesterol and LDL in boys in this study. It has also been mentioned in the literature that cigarette smokers had higher levels of serum lipid profiles than the nonsmokers. Hughes *et al* found that smokers had lower mean serum HDL and higher mean serum fasting triglyceride levels, which increases the risk of atherosclerosis. This effect of smoking on the serum lipid profile might be due to increased activity of lipase as well as insulin resistance [23].

Calcium was inversely correlated with systolic and diastolic blood pressure in this study. Jorde *et al* and Cap-

Table IV: Regression coefficients to determine the relation between nutritional and non-nutritional factors and CVD risk factors in boys

	Independent variable							
Dependent variable	Constant	BMI	WHR	Age	Smoking	energy	Calcium	Waist circumference
Total cholesterol	126.1		*					
β		0.31			0.11			0.47
R^2		0.16			0.16			0.22
P		0.0001			0.012			0.013
Triglycerides	201.4							
β		5.1	8.4			1.3		1.3
R^2		0.04	0.04			0.16		0.07
P		0.001	0.039			0.001		0.003
LDL	49.1							
β		2.1	0.9		0.4			
R^2		0.04	0.04		0.04			
P		0.16	0.01		0.001			
HDL	71.3							
β				0.3		0.41		
R^2				0.16		0.04		
P				0.0001		0.016		
Systolic blood pressure	78.2							
β		0.25					-0.16	
R^2		0.16					0.04	
		0.05					0.014	
Diastolic blood pressure	77.1							
β		0.05					-0.361	
R^2		0.04					0.04	
P		0.001					0.001	
Blood sugar								
β	72.8		0.15					
R^2			0.04					
P			0.008					

* The space shows that there was no relation between the two variables

puccio *et al* reported an inverse relationship between calcium intake and blood pressure [24, 25]. Osborn *et al* found that calcium had an important role in blood pressure regulation and that adequate intake of calcium might reduce the risk of hypertension [26]. Some mechanisms responsible for this effect of calcium may be the natriuretic effect, regulation of the sympathetic nervous system, and prevention of vessel constriction [27]. In this study, linoleic acid was inversely associated with blood pressure. Goldberg showed a reduction in systolic and diastolic blood pressure after increasing the ratio of polyunsaturated fatty acids to saturated fatty acids (PUFA/SFA) [28].

There was a inverse relationship between calcium intake and triglycerides in the present study. It is assumed that calcium could bind to fatty acids and inhibit the absorption of fats [29]. In this study we found an association between WHR and blood sugar, which might contribute to insulin resistance, according to the literature. A lack of homocysteine and salt intake measures were two limitations of this study. However, accurate blood pressure assessment along with quality control were the positive points of this research.

It is essential to find ways to begin prevention of atherosclerosis in childhood and adolescence. The significant associations found between certain dietary and non-dietary factors and CVD in this study should be noted, as they could be beneficial for prevention of CVD.

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