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Prevalence and Predictors of Dyslipidemia in Children and Adolescents in Yazd Greater Area, Yazd, Iran

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Abstract

Background: Dyslipidemia, a genetic and multifactorial disorder of lipoprotein metabolism, is defined by elevations in the levels of total cholesterol, low-density lipoprotein cholesterol (LDL-C), non-high-density lipoprotein cholesterol (non–HDL-C), triglyceride, or some combination thereof as well as lower levels of high-density lipoprotein (HDL) cholesterol.

Objectives: This study aimed to investigate the prevalence and predictors of dyslipidemia in children and adolescents in the Yazd Greater Area, Yazd, Iran.

Methods: This cross-sectional study was conducted as a part of the national project implemented in Yazd Greater Area, Yazd, Iran. The sampling was performed using a multi-stage cluster sampling method on three age groups of girls and boys, including 6-9, 10-14, and 15-18 years old. Out of the total 1,035 children and adolescents who initially participated in this study, only 784 participants remained until the end. Data collection was performed using lifestyle questionnaires including Kiddie-SADS-Present and Lifetime Version software.

Results: The rate of high triglyceride was estimated at 1.4% and 4.2% in 6-9 and 10-18 years old children and adolescents, respectively. Moreover, the prevalence of high cholesterol, LDL, and HDL were obtained at 3.2%, 3.2%, and 25.6%, respectively. The prevalence of dyslipidemia in the total population of children and adolescents was estimated at 64.6% and 57.3% in boys and girls, respectively (P=0.038) in terms of demographic variables. Gender and increase in body mass index (BMI) were significantly associated with dyslipidemia with OR=1.35; 95% CI: 1.01-1.81 and OR=13.781; 95% CI: 3.78- 46.43, respectively. However, after adjustment for other factors, only an increase in BMI was significantly associated with dyslipidemia (OR=16.08; 95% CI: 4.49-57.59).

Conclusion: Overweight and obese adolescents had a higher concentration of serum blood triglycerides, compared to their counterparts. Weight control, lifestyle, and diet modification are three ways to reduce lipid disorders in adolescents.

Keywords: Adolescents, Children, Dyslipidemia, Predictors, Prevalence

1. Background

Cardiovascular is the most prevalent and severe pathologies in third-world countries and as the main cause of death in Iran inflicts a huge financial burden on the health system (1). This scenario may worsen with the growing prevalence of obesity in children and adolescents, a phenomenon that is associated with lipid abnormalities. Dyslipidemia has different patterns and is one of the most important risk factors for atherosclerotic plaque formation that begin early in life. The combination of some lipid abnormalities may have higher atherogenic potential (2). Therefore, the adaptation of a healthy lifestyle at an early age is one of the best preventative strategies in this regard (3). Lipid concentration in healthy children starts at birth, increases slowly in the first two years of life, and stabilizes until adolescence. Subsequently, the total cholesterol and low-density lipoprotein cholesterol (LDL-C) concentrations decrease by 10 to 20% or more during adolescence, before rising again during late adolescence and young adulthood (4).

The prevalence of cholesterol and LDL is higher in girls and reaches to peak one year earlier in girls than in boys (5). Furthermore, the National Health and Nutrition Examination Survey (NHANES) described the relationship between dyslipidemia and high body mass index (BMI) among the youth (6). Pediatric dyslipidemias are heterogeneous disorders consisting of familial and multifactorial dyslipidemias caused by various genetic and environmental factors. Regarding the recent guidelines, the cut-off values for total, LDL, triglyceride (TG), and HDL cholesterol for definition of dyslipidemia are >200mg/dl, >130mg/dl, >130mg/dl, and <40mg/dl, respectively (7).

A study conducted on Brazilian adolescents revealed that the combination of high TG levels with low HDL-C levels was the most prevalent. The BMI level has a positive relationship with the lipid abnormalities and prevalence of combined lipid abnormalities. The BMI can be considered as an indicator for the diagnosis of dyslipidemia in adolescents (2). In this regard, another study

conducted in Denmark (North-Europe) revealed that children and adolescents with obesity had increased concentrations of circulating lipids and exhibited an increased prevalence of dyslipidemia (8).

Elevation of plasma lipid concentrations for a long period of time results in cholesterol deposition in the arteries. Normally these disorders are asymptomatic in childhood and are rarely associated with cardiovascular disease in the first two decades of life. Nevertheless, they are associated with a high incidence of premature atherosclerotic cardiovascular diseases in adulthood (4). Recent estimates from the NHANES indicated that 7.8% and 7.4% of children aged 8-17 years and adolescents aged 12-19 years had elevated levels of total cholesterol (≥200 mg/dL) and LDL-C (≥130 mg/dL), respectively (6). It should be noted that the development of inappropriate habits, such as sedentary lifestyle, unhealthy dietary habits, electronic games results in obesity and dyslipidemia, especially in childhood and adolescence. It is worth mentioning that, the rate of dyslipidemia and obesity has increased significantly in the past decade among children (9).

Identifying dyslipidemia in childhood or adolescence allows individuals to prevent the progression of these conditions into atherosclerotic diseases. The observance of screening protocols can result in the diagnosis of dyslipidemia type and correlated risk factors and provides the opportunity to intervene before the development of clinically significant atherosclerosis (9). The prevalence of overweight and obesity is inevitable in the Iranian community where there is interest in high-calorie foods, while physical activity is mostly neglected. This situation increases the risk of developing heart disease (10). The modification of one's lifestyle and diet is the best treatment suggested for adolescents with dyslipidemia risk factors (11). Some organizations recommend selective screening of children with high-risk factors, such as a family history of dyslipidemia. A recent report from the NHLBI Panel on Integrated Guidelines for Cardiovascular Health and Risk Reduction in Children and Adolescents recommended universal screening of children and adolescence aged 9-11 years and 17-21 years, as well as targeted screening of high-risk younger children and adolescents (12). However, there is not enough evidence to support the effectiveness of routine screening on health outcomes and the safety of lipid-lowering interventions during childhood.

2. Objectives

This study aimed to evaluate the prevalence of dyslipidemia and correlating risk factors in Iranian (Yazd) children to describe the importance of this condition and schedule effective programs to modify their lifestyle.

3. Methods

3.1. Study Design

This study was a part of an analytical cross-sectional national project study implemented in all provinces of Iran entitled Iranian Children and Adolescents' Psychiatric Disorders Study (IRCAP). Preliminary work was undertaken in 2013 to conduct this study. Moreover, this study was financially supported by the National Institute for Medical Research Development (NIMAD).

3.2. Sampling

The study population was collected through the random and multi-stage cluster sampling method. In total, 167 clusters were randomly selected based on postal code in Yazd Greater Area. Each cluster included 3 girls and 3 boys in three age groups including 6-9, 10-14, and 15-18 years old. Initially, 1,174 individuals participated in the study; however, only1, 035 people remained following the application of inclusion and exclusion criteria. Afterward, 251 participants refused to give blood samples and the attrition rate reached 24%. Eventually, 784 children and adolescents remained in the study. Sample size determination was measured based on the following formula:

$$n \geq \frac{\left(z_{1-\frac{\alpha}{2}}+z_{1-\beta}\right)^2 \left(\delta_1{}^2+\frac{\delta_2{}^2}{r}\right)}{(\mu_1-\mu_2)^2}$$

$\alpha = 0.05$

Power = 80%

3.3. Inclusion and Exclusion Criteria

The inclusion criteria included Iranian children and adolescents aged 6-8 years old who lived in Yazd, Iran, for at least one year. However, those with serious physical illness were excluded from the study.

3.4. Procedure

The trained psychologists referred to the participants' homes. Informed consent was obtained from the parents of the participants after they were informed about the study's purpose and procedure. Initially, the research group collected demographic information and inquired about the history of heart disease in first-degree relatives of the participants. Furthermore, they measured anthropometric dimensions of the participants including height, weight, and waist circumference (WC). Subsequently, participants were sent to Afshar Hospital in Yazd, Iran, for specialized tests.

First, an experienced nurse took the participants' blood pressure (BP) in a sitting position from their right hand (using Automatic Blood Pressure Monitor, Model M3 Comfort, Omron Co. Osaka, Japan). The BP

was measured three times: 15 to 20 min after the participant's arrival, after the completion of the first blood sampling, and 20 min after the second blood sampling. The final BP was determined by taking the average of the three BP measurements. Afterward, venous blood was taken from each participant to measure fasting blood sugar (FBS), TG, cholesterol, LDL, and HDL after 8 to 12 hours of fasting. Blood samples were then centrifuged for serum separation. A biochemical auto-analyzer (model BT 3000, Italy) and PARS Azmoon Kits (Pars Azmoon Kit, Pars Azmoon Inc., Tehran, Iran) were used to assess FBS, TG, HDL, and LDL cholesterol. All measurements were performed in standard positions using calibrated tools.

Serum lipid percentile (13) and standard cut-off points, was used to classify dyslipidemia according to the Nelson Textbook of Pediatrics and IRCAP classifications (14) as follows:

1. IRCAP classification:

-High: TG, cholesterol, and LDL at or greater than 95th percentile

-Borderline: TG, cholesterol, and LDL at or greater than 75th percentile and less than 95th percentile

- High: HDL at or less than 5th percentile

-Borderline: HDL at or less than 25th percentile and greater than 5th percentile

2. Nelson classification:

- High Triglyceride:
- 6-9 year's old >75mg/dL
- 10-18 year's old > 90 mg/dL
- High Cholesterol >170 mg/dL
- High LDL>110 mg/dL
- Low HDL<45 mg/dL

BMI was calculated by dividing the weight by the square of height. A standard wall-height gauge was used to measure the height of the participants while they had stood in a standing position without shoes. Their weight was also measured using a calibrated scale while wearing light clothing. The measurement of WC was done after normal exhalation, using a non-stretchable tape meter placed at the middle space between the lowest rib and the iliac crest with the individual had the light clothing. Clinical symptoms of heart disease (palpitations, shortness of breath, and chest pain) were also recorded in children and adolescents.

In this study, 50th, 90th, 95^{th,} and 99th blood pressure percentiles were determined for seven height percentiles (5th, 10th, 25th, 50th, 75th, 90th, and 95th) in both genders, according to the Fourth Report on the Diagnosis, Evaluation, and Treatment of high BP in children and adolescents. These calculations were performed using STATA (version 11) and Excel 2010 software. The definition and classification of hypertension (HTN) in 6-15 years old children was conducted based on the 4th Report on Diagnosis, Evaluation, and Treatment of NHBEP (National High Blood Pressure Program working group in children and adolescences). Therefore, the normal condition, PreHTN, and HTN were defined as BP at or less than 90th percentile, BP at or greater than 90th percentile and less than 95th percentile plus 5 mmHg, and BP at or greater than 95th percentile plus 5 mmHg, respectively.

3.5. Kiddie-SADS-Present and Lifetime Version (K-SADS-PL)

This questionnaire is a structured interview that was designed in three sections for children and adolescents. The first, the second, the third parts of the questionnaire involved items related to demographic characteristics, screening questions to determine the criteria for psychiatric disorders, and an overall assessment to determine the level of the child's performance, respectively (13). The validity and reliability of this questionnaire have been approved for the evaluation and diagnosis of psychiatric disorders in Iranian children and adolescents (15). The reliability and inter-rater reliability of the Persian version of this questionnaire was determined at 0.81 and 0.69 using the test-retest method. Moreover, the Cronbach's alpha coefficient was used to assess the reliability of the questionnaire that was determined at 0.87 in this study. The K-SADS-PL questionnaire is often scored based on a 4-point Likert scale from 0 to 3; here 0= not enough information, 1= no symptoms, 2= there are symptoms, and 3= the threshold criterion (16).

3.6. Lifestyle Questionnaire (LSQ)

This questionnaire has 10 subscales including physical health, exercise and health, weight control and nutrition, illness prevention, psychological health, spiritual health, social health, drug and alcohol avoidance, accident prevention, and environmental health. Only subscales of physical health, as well as weight control and nutrition, were adopted in this research. The validity and reliability of LSQ were assessed by Lalie et al. The Cronbach's alpha ranged from 0.79 to 0.89 for different subscales. Moreover, reliability coefficients by the retest method were in the range of 0.84-0.94. The questionnaire was scored based on a 4-point Likert scale ranging from 0 (=never) to 3 (=always). The higher scores indicated a better and healthier lifestyle (17).

3.7. Ethics

All information was collected and kept confidential. Informed consent was obtained from either the participants or their parents (in the case of children younger than 15 years). Children and adolescents with psychiatric disorders were treated for free by a psychiatrist who participated in the project. The study was approved by the Ethics

Committee of NIMAD (IR.NIMAD.REC.1395.001) and Shahid Sadoughi University of Medical Sciences in Yazd, Iran (IR.SSU.REC.1396.49).

3.8. Statistical analysis

All data were analyzed using SPSS (version 16) and STATA software (version 11). The Frequency and Crosstab were used to measure the prevalence of dyslipidemia. Logistic regression analysis was used to define potential predictors of dyslipidemia in children and adolescents. A p-value less than 0.05 was considered statistically significant.

4. Results

The study population included 784 children and adolescents. It should be noted that a number of missing data were removed from the study. Table 1 compares dyslipidemia in Yazd and with the reference numbers from the Nelson textbook of pediatrics. In an overview, the rate of dyslipidemia category was higher in Nelson's textbook of pediatrics than in Yazd, Iran, in terms of triglycerides, cholesterol, and LDL. Therefore, based on the Nelson category, children and adolescents are at more risk of developing dyslipidemia caused by an abnormal level of triglycerides, cholesterol, and LDL. However, the evaluation of the rate of HDL indicated that children and adolescents are at less risk of developing dyslipidemia caused by an abnormal level of HDL.

Table 2 gives some information about the prevalence of dyslipidemia in children and adolescents in terms of demographic variables. The highest prevalence of dyslipidemia was observed in adolescents in the age range of 15-18 (62.3%) and among children and adolescents living in urban areas (60.9%). Furthermore, in terms of BMI

Table 1. Comparison between the prevalence of dyslipidemia according to Nelson textbook of pediatric and IRCAP criteria

Category		NELSON (Ref.)						IRCAP			
		Acceptable		Borderline		High		Borderline		High	
		N	%	N	%	N	%	N	%	N	%
TG	6-9	160	15.5	74	7.1	71	6.9	63	6.1	14	1.4
	10-18	277	26.8	122	11.8	79	7.6	96	9.3	43	4.2
Cholesterol		531	51.3	178	17.2	74	7.1	157	15.2	33	3.2
LDL		552	53.3	159	15.4	71	6.9	152	14.7	33	3.2
HDL		254	24.5	150	14.5	378	36.5	172	16.6	265	25.6
Total		93	9	215	20.8	476	46	411	39.7	357	34.5

Table 2. Crude odds ratios (95% Confidence Interval) of dyslipidemia in the total population of children and adolescents in terms of demographic variables

Demographic variables		CI (95%)	P-value	N	%	Confidence interval
Age	6-9	1		181	59.2	53.41-64.70
	10-14	0.87(0.60-1.26)	0.478	171	61.3	55.30-67.30
	15-18	0.95(0.65-1.39)	0.821	124	62.3	55.18-69.06
Gender	Boys	1		237	64.6	57.19-64.15
	Girls	1.35(1.01-1.81)	0.038	239	57.3	
Place of residence	Urban	1		463	60.9	57.34-64.40
	Rural	0.758(0.33-1.71)	0.506	13	54.2	32.82-74.44
BMI	Underweight	1		4	28.6	8.38-58.10
	Normal	3.085(0.95-9.69)	0.060	290	55.2	50.87-59.54
	Overweight	4.375(1.26-15.09)	0.019	56	12.3	52.69-73.63
	Obesity	13.781(3.78-46.43)	0.0001	106	84.1	76.55-90.02
Blood pressure	Normal	1		348	60.6	56.49-64.64
	Prehypertension	0.978(0.66-1.43)	0.910	22	59.5	42.09-75.24
	Hypertension	0.932(0.44-1.95)	0.851	85	61.2	52.52-69.29
Waist to hip ratio	Normal	1		270	59.3	44.41-52.89
	Abdominal Obesity	1.084(0.80-1.46)	0.596	182	61.3	55.48-66.85
Diabetes	No	1		474	61.1	57.55-64.52
	Yes	0.319(0.05-1.75)	0.188	2	33.3	4.32-77.72
Physical activity	Below the usual limit	1		111	62.4	54.80-69.49
	Usual	0.944(0.65-1.36)	0.757	233	61	55.90-65.91
	good	0.876(0.58-1.31)	0.519	132	59.2	52.43-65.70
Nutrition	Below the usual limit	1		127	64.8	57.66-71.46
	Usual	1.194(0.773-1.849)	0.424	255	59	54.22-63.70
	Good	0.935(0.643-1.360)	0.725	94	60.6	52.48-68.38
Mother's education level	Under diploma	1		93	62.8	54.51-70.63
	Diploma	0.914(0.60-1.37)	0.668	170	60.7	54.72-66.47
	Upper diploma	0.787(0.51-1.19)	0.260	141	57.1	50.65-63.34
Father's education level	Under diploma	1		101	59.4	51.62-66.86
	Diploma	1.084(0.72-1.61)	0.692	168	62	55.92-67.79
	Upper diploma	1.208(0.84-1.72)	0.298	135	57.4	50.85-63.85
Family history of heart disease	No	1		370	61.1	57.04-64.95
	Yes	1.065(0.75-1.46)	0.718	106	59.6	51.95-66.82
Suffering from psychiatric disorders (parents)	No	1		281	58.8	54.22-63.23
	Yes	1.232(0.91-1.65)	0.167	195	63.7	58.06-69.11

Table 3. Adjusted odds ratios (95% Confidence Interval) of dyslipidemia in the total population of children and adolescents in terms of demographic variables

Demographic Variables		OR_{adj} (95% CI)	P-value
Gender	Boys	1.00	
	Girls	0.75(0.551-1.03)	0.076
BMI	Underweight	1.00	
	Normal	3.55(1.084-11.63)	0.036
	Overweight	4.99(1.42-17.47)	0.012
	Obesity	16.08(4.49-57.59)	0.0001
Nutrition	Below the usual limit	1.00	
	Usual	0.77(0.534-1.13)	0.188
	Good	0.77(0.482-1.25)	0.300
Diabetes	No	1.00	
	Yes	0.277(0.047-1.64)	0.158
Suffering from psychiatric disorder (parents)	No	1.00	
	Yes	1.28(0.92-1.77)	0.136

categories, the highest prevalence of dyslipidemia was observed in the obesity category (84.1%). In terms of hypertension classifications, the highest prevalence of dyslipidemia was observed in hypertension classification (61.2%). In addition, the highest prevalence of dyslipidemia in the category of the waist to hip ratio was due to abdominal obesity (61.3%). Furthermore, children and adolescents who suffer from psychiatric disorders (63.7%) had the highest prevalence of dyslipidemia. Table 4 presents the predictors of dyslipidemia based on demographic variables. Overall, it is revealed that gender and BMI have a significant relationship with dyslipidemia. Furthermore, based on the result, females, overweight children and adolescents, and those with obesity are 1.4 times, 4.4 times, and 13.8 times more at risk of developing dyslipidemia compared to males and other children and adolescents. Other demographic variables did not have a significant relationship with dyslipidemia.

In the second model, after adjusting for determining factors, only BMI predicted dyslipidemia. It is revealed that normal, overweight, and obese children and adolescents (in terms of BMI) are 3.5 times, 5 times, and 16.1 times more at risk of developing dyslipidemia (Table 3).

Table 4 shows different percentiles of dyslipidemia in children and adolescents, in terms of gender and age group in Yazd Greater Area. Overall, the highest triglyceride cut-off point in the 95th percentile was 209 in males at the age range of 15-18 years. This number was 222 in males in the 10-14 years old age group for the cholesterol. Furthermore, the cut-off point of LDL in the 95th percentile (high LDL) was increased with the increase of age range and was the highest in females in the age range of 15-18 years old. The cut-off point for HDL in the 95th percentile (low HDL) decreased with the increase of age range and was the lowest in males in the age range of 15-18 years.

Table 4. 5th, 50th, 75th, 90th and 95th percentiles for lipids in children and adolescents in YGA in 2016

Total Triglyceride							Total Cholesterol					Low-Density Lipoprotein cholesterol					High-Density Lipoprotein cholesterol				
Percentiles		**5TH**	**Mean**	**75TH**	**90TH**	**95TH**	**5TH**	**Mean**	**75TH**	**90TH**	**95TH**	**5TH**	**Mean**	**75TH**	**90TH**	**95TH**	**5TH**	**10TH**	**25TH**	**MEAN**	**95TH**
6-9	Boy	41	67	96	115	139	92	156	178	192	204	60	95	112	127	134	24	27	33	59	65
	Girl	0.001	74	95	127	145	0.001	159	181	197	212	0.001	102	114	126	138	0.001	25	34	60	78
10-14	Boy	34	82	107	140	177	103	158	180	205	222	65	97	115	136	144	26	28	33	59	65
	Girl	47	84	115	148	162	119	156	176	201	210	59	95	110	130	138	27	29	34	56	68
15-18	Boy	46	85	120	166	209	110	153	175	194	212	70	96	115	128	142	25	27	33	49	55
	Girl	41	85	114	148	183	88	156	169	201	216	55	96	116	135	149	25	28	33	49	57

5. Discussion

A growing body of evidence showed a strong relationship between childhood dyslipidemia and future atherosclerosis (3). Therefore, the early detection of dyslipidemia would result in improved general health and quality of life. Currently, the NHLBI (National Heart, Lung, and Blood Institute) and AAP (American Academy of Pediatrics) guidelines recommend serum lipid screening for children and adolescents between the age of 9 and 11 and again when they are between 17 to 21 years old. However, the exact impact of these protocols on the health systems is not clear yet (12). In this study, the prevalence of dyslipidemia and its contributing factors were investigated in the Yazd greater area, Yazd, Iran.

Based on the results, 46.5% of children and adolescents between 6-18 years had dyslipidemia. The rate of dyslipidemia was relatively the same in both genders. Another survey conducted on Iranian children and adolescents reported a prevalence of 45.7% for dyslipidemia, especially in terms of low HDL-C and hypertriglyceridemia (18). Approximately, one in five (i.e. 20%) of boys and girls among US

children in the age range of 8-17 years had an abnormal lipid profile during 2011-2012 (19). Korsten-Reck et al. reported a 45.8% rate of dyslipidemia in 546 German children (20). These studies indicated a high prevalence of dyslipidemia early in life, especially in developing countries.

Low HDL (25.6%) was the most prevalent lipid disorder in this study. A study conducted by Ford et al. reported a higher level of cholesterol and LDL-C among boys, compared to girls (21). Another national study in Iran revealed that the level of serum HDL-C in Iranian children and adolescents was (5th percentile) lower than that in their European and American counterparts (22). The measurement of HDL concentration is part of the lipid profile assessment and predicts persistent dyslipidemia. Previous studies showed that low HDL was associated with a higher risk of cardiovascular diseases (23). This difference in the prevalence and type of dyslipidemia is probably due to genetic variation, different ethnicities, nutritional habits, and physical activity. According to recent reports of NHANES (National Health and Nutrition Examination Survey), the prevalence of dyslipidemia continues to decrease in the USA (19). Nevertheless, there is an increasing trend in the prevalence of dyslipidemia in developing countries, such as Iran, as a result of urbanization and lifestyle changes which highlights the importance of dyslipidemia prevention and screening programs.

The results of the present study indicated that the frequency of dyslipidemia correlates with the female gender and higher BMI. However, after adjustment for other variables, only BMI was strongly associated with serum lipid concentrations. In this study, 84% of obese girls had dyslipidemia. The study conducted by Kim et al. indicated that dyslipidemia had a positive association with BMI in males and females (24). Another study performed by Hashemipour showed that 69.9% of 2064 obese Iranian children had dyslipidemia, while half of this group were suffering from hypertriglyceridemia (25). In addition, it was found that lipid disorders were more frequent among the participants with poor nutritional status (64%) and psychologic disorders (63%) in this study. These results may be attributed to several factors. Psychological disorders result in poor dietary habits, a decrease in physical activity and quality of life, and hopeless conditions. Therefore, one of the most important preventive measures is to pay more attention to children and adolescents' mental health.

Limitation

Regarding the limitation of the present study, one can refer to the fact that blood pressure was taken from children and adolescents three times on one occasion. A comprehensive blood sampling was taken from other cities of Yazd province of Iran could provide a more accurate comparison.

6. Conclusion

Based on the obtained results, the prevalence of hypercholesterolemia is high among children and adolescents, which is to some extent the result of industrialization, obesity, consumption of fatty foods, and decreased physical activity. Therefore, dyslipidemia screening and preventive programs in early life should be a priority in the Iranian health system to attenuate the burden of CVDs.

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Footnotes

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Ethical Approval: The study protocol was approved by the Ethics Committee of NIMAD (IR.NIMAD.REC.1395.001) and Shahid Sadoughi University of Medical Sciences in Yazd, Iran (IR.SSU.REC.1396.49).
Informed Consent: Informed consent was obtained from the parents of the participants after they were informed about the study's purpose and procedure.
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