

Factors associated with the metabolic syndrome in a national sample of youths: CASPIAN Study

Roya Kelishadi ^{a,*}, Mohammad Mehdi Gouya ^b, Khosrow Adeli ^c, Gelayol Ardalan ^b, Riaz Gheiratmand ^d, Reza Majdzadeh ^e, Minou Sadat Mahmoud-Arabi ^b, Alireza Delavari ^b, Mohammad Mehdi Riazi ^b, Hamed Barekati ^b, Molouk Motaghian ^d, Keivan Shariatinejad ^a, Ramin Heshmat ^e, for the CASPIAN Study Group

^a Preventive Paediatric Cardiology Department, Isfahan Cardiovascular Research Centre (WHO Collaborating Centre in EMR), Isfahan University of Medical Sciences, P.O. Box 81465-1148, Isfahan, Iran

^b Ministry of Health, Tehran, Iran

^c Clinical Biochemistry Department, Hospital for Sick Children, University of Toronto, Toronto, ON, Canada

^d Ministry of Education, Tehran, Iran

^e Epidemiology and Biostatistics Department, Public Health School and Institute of Public Health Research, Tehran University of Medical Sciences, Tehran, Iran

Received 18 August 2006; received in revised form 31 December 2006; accepted 22 February 2007

KEYWORDS Metabolic syndrome; Children; Birth weight; Nutrition; Physical activity **Abstract** Background and aim: To date, research on the influence of environmental factors on metabolic syndrome (MS) among youths is limited. This study was conducted to investigate for the first time the association of these factors with MS in a large national, representative sample of children from a non-Western population.

Methods and results: The study population comprised of 4811 students (2248 boys and 2563 girls) aged 6–18 years, living in six different provinces in Iran. MS, defined based on criteria analogous to those of the Adult Treatment Panel III, was detected in 14.1% of participants.

A birth weight of >4000 g in boys and <2500 g in girls increased the risk of having the MS [OR, 95% CI: 1.4 (1.007, 2.05) and 1.2 (1.1, 1.4), respectively]. Poorly educated parents and a positive parental history of chronic disease were other risks factors associated with MS. Low levels of physical activity significantly increased the risk of having MS [boys: 1.3 (1.1, 1.7); girls: 1.4 (1.2, 1.6)]. The risk of MS increased in-line with the consumption of solid hydrogenated fat [boys: 1.2 (1.07, 1.3); girls, 1.3 (1.1, 1.5)] and bread made with white flour [boys: 1.6 (1.3, 2.1); girls, 1.4 (1.1, 1.7)]. In contrast, an increased frequency of consumption of fruits and vegetable, as well as dairy products decreased the risk of having MS.

* Corresponding author. Tel.: +98 311 337 7881x8; fax: +98 311 337 3435. *E-mail addresses*: kroya@aap.net, kelishadi@med.mui.ac.ir (R. Kelishadi). *Conclusion:* Considering the effect of modifiable lifestyle habits and birth weight on MS in youths, urgent public health approaches should be directed towards primordial and primary prevention of this rapidly growing problem.

© 2007 Elsevier B.V. All rights reserved.

Introduction

The metabolic syndrome (MS) comprises a major risk for chronic disease and is rapidly increasing in prevalence worldwide in-line with rising childhood obesity and sedentary life style. Therefore, it poses a serious and growing problem for clinicians and public health officials alike [1].

The prevalence of chronic diseases is rising far more rapidly in low- and middle-income countries compared to industrialized nations, and MS is now well recognized as a growing problem for low- and middle-income countries, with a suggested ethnic predisposition in Asians [2].

It is now well established that the origins of MS can be traced back to early life [3]. An underlying genetic tendency or adverse events in early life may contribute to MS and its related complications, notably in non-European populations [4].

Some lifestyle behaviours, including physical inactivity, smoking and unhealthy dietary habits, particularly high carbohydrate and fat intake, are associated with MS in adults [5,6]. In addition some studies have shown that foetal growth and birth weight may be associated with the development of MS in later life [7]. However, it is well documented that environmental changes can influence these programmed effects [8].

However, there is only limited data regarding MS among youths, and major efforts are needed to enable a better understanding of the factors associated with this complex disorder in the paediatric population. In our previous studies we found that Iranian youths are prone to chronic diseases in adulthood [9,10]. In the current study we investigated the association of birth weight, feeding during infancy, and family history of chronic disease, as well as some lifestyle habits and environmental factors, with MS in a large national, representative sample of children and adolescents in Iran. This is the first time that such a study has been carried out in Iran, and to the best of our knowledge in a non-Western population. This national project, entitled the Childhood and Adolescence Surveillance and Prevention of Adult Non-communicable Disease: CASPIAN¹ Study, was conducted to establish a school-based surveillance system for risk factors and behaviours relating to chronic diseases.

Methods

We have previously described the methods of this study in detail [11,12], and we report a brief summary here. This multi-centre study was conducted in 2003–2004 on 21,111

school students, aged 6–18 years, living in urban and rural areas in 23 (out of 28) provinces of Iran. The present paper describes the findings obtained from a sub-sample of 4811 elementary, middle and high school students (91% participation rate), randomly selected from six provinces located in diverse parts of the country and with populations of varying ethnicities. Biochemical variables were examined in this cohort, and behavioural and biological risk factors were also evaluated in all subjects studied.

The study was approved by ethics committees and other relevant national regulatory organizations. The Data and Safety Monitoring Board for the project was involved in closely supervising the quality control and quality assurance measures for the survey at a national level. We obtained written informed consent from parents and oral assent from students. The project team selected students by multistage, random cluster sampling. They stratified schools according to location (urban/rural), and the socioeconomic nature of their uptake areas, taking into consideration the proportion of the different types of schools (public/private) to avoid a socioeconomic bias.

We prepared our questionnaires in Farsi and based them on those of the World Health Organization (WHO) STEPwise approach to non-communicable diseases (Tools version 9.5) and the WHO global school-based student health survey (GSHS). The questions concerning the sociodemographic characteristics, the child's birth weight, and his/her feeding during infancy, as well as family dietary habits were included in the parents' questionnaire. Birth weights of <2500 g and >4000 g were considered as small for gestational age (SGA) and large for gestational age (LGA), respectively [13]. A set of questions regarding family history of chronic disease in parents, grandparents, uncles and aunts, was included in the parents' questionnaire. Those with a positive family history were subdivided into positive history in parents, and positive history in other relatives [14].

In Iran, students do not have a lunch period during school hours and have their main meals with their families. We therefore asked the parents about the family's dietary habits. Given that the largest proportion of Iranian meals usually comprises bread and/or rice, and consumption of solid hydrogenated fat (rich in saturated and trans-fatty acids) is common in Iranian families, we included questions about the type of bread (i.e. prepared from white or wholegrain flour) and the type of fat consumed in meals at home. In addition, students completed a validated food-frequency questionnaire (FFQ). The validity of our questionnaire's content was previously affirmed based on observations by a panel of experts, item analysis and reliability measures [9,10]. Food items were grouped into the following categories: carbohydrates (rice, bread, pasta, potato), vegetables (potato and French fries not included), fruit (fresh, dried, juice), dairy products (milk, cheese, yogurt), proteins, including both animal-derived (red meat, poultry,

¹ Caspian is the name of the World's largest lake, located in Northern Iran.

fish, egg) and plant-derived (beans, soy, nuts), fast foods (pizza, hamburgers, sausages etc.), as well as salty/high-fat snacks and sweets/candies [11].

The students' physical activity patterns were assessed using a scaled questionnaire organized into nine different metabolic equivalent (MET) levels, ranging from sleep/rest (0.9 METs) to high-intensity physical activities (>6 METs). This instrument was assessed by performing a concurrent validation against accelerometry and a physical activity diary [15]; we have previously modified and validated it using Iranian youths [16]. For each activity level, the MET-value was multiplied by the time spent on that particular activity. The MET-time from each level was added to the total 24-h MET-time, representing the level of physical activity on an average weekday. In the current study, we categorized the level of physical activity according to the tertiles computed in the population studied, and scored it from 1 to 3, representing the 1st to the 3rd tertiles.

Under the supervision of expert health-care professionals, the students and one of their parents, who was invited to the school, filled out the self-administered questionnaire at the same time. The nurses recorded age and birth date, and measured height and weight twice to ± 0.2 cm and ± 0.2 kg, respectively, with subjects being barefoot and lightly dressed; the averages were recorded. Body mass index (BMI) was computed as weight in kilograms divided by the square of height in metres. Waist circumference (WC) was measured to the nearest 0.5 of a centimetre with a non-elastic tape applied at a point midway between the lower border of the rib cage and the iliac crest at the end of normal expiration [17].

Blood pressure (BP) was measured using a mercury sphygmomanometer after 5 min rest in the sitting position. The subjects were seated with the heart, cuff and zeroindicator on the manometer positioned at the observer's eye level. All readings were taken in duplicate in the right arm. Appropriately sized cuffs were used with the cuffwidth 40% of mid-arm circumference, and cuff bladders covering 80-100% of the arm circumference and approximately two-thirds of the length of the upper arm, without overlapping. The procedure was explained to the students and the cuff inflated and deflated once, the first BP measured was not used in the analysis of this study. The readings at the first and the fifth Korotkoff phase were taken as systolic and diastolic BP (SBP and DBP), respectively. The average of the two BP measurements was recorded and included in the analysis [18].

For blood sampling, students were invited to the health centre nearest to their school, in accordance with the rules of the national Ministry of Education. The students were instructed to fast for 12 h before the screening; compliance with fasting was determined by interview on the morning of the examination. Parents accompanied their child while blood samples were taken from the antecubital vein between 08.00 and 09.30 h. After collecting blood samples, the participants were served a healthy snack, which was provided by the project team.

The blood samples were centrifuged for 10 min at 3000 rpm within 30 min of venipuncture. In each district, the biochemical analysis was performed at the central provincial laboratory, which meets the standards of the National Reference Laboratory, a WHO-collaborating centre in Tehran.

Fasting blood sugar (FBS), total cholesterol (TC), high density lipoprotein-cholesterol (HDL-C) and triglyceride (TG) were measured enzymatically using auto-analysers. HDL-C was determined after dextran sulphate/magnesium chloride precipitation of non-HDL-C [19]. Low-density lipoprotein-cholesterol (LDL-C) was calculated in serum samples with TG <400 mg/dL, according to the Friedewald equation [20]. A sub-sample of sera was frozen and transported from different districts to the central laboratory at Isfahan Cardiovascular Research Centre (a WHO-Collaborating Centre), which meets the standards of the National Reference Laboratory and is also under the quality control of the Centres for Disease Control and Prevention (CDC, USA), and the Department of Epidemiology, St. Rafael University, Leuven, Belgium. In addition, a sub-sample of frozen sera was stored at -70 °C, awaiting future biochemical analyses for new risk factors.

Since no universally accepted definition of MS exists for children, we used a definition similar to that in the study by de Ferranti et al. [21]., which is based in turn on criteria analogous to those in the Adult Treatment Panel III (ATP III) [22] and defines MS as having >3 of the following: (1) fasting TG >100 mg/dL; (2) HDL-C <50 mg/dL (except in boys aged 15-19 years, in whom the cut-off was <45 mg/dL): (3) WC >75th percentile for age and gender in the population under study, as suggested by other investigators [21,23,24]; (4) SBP/DBP >90th percentile for gender, age and height from the National Heart, Lung and Blood Institute's recommended cut-off point [18]; and (5) FBS \geq 100 mg/dL. It should be noted that de Ferranti et al. [21] used the cut-off of FBS \geq 110 mg/dL, but we decided to follow the latest recommendation of the American Diabetes Association [25].

Statistical methods

The data-entry staff entered data for all forms and guestionnaires twice and checked for completeness and inconsistencies. The data-checking process was conducted at the district and then at the national level. After editing, the data were analysed using the SPSS software package, version 13.0 (SPSS Inc., Chicago, USA). The categorical and continuous variables were compared between boys and girl using the Chi-square and t-tests, respectively; the Mann-Whitney U-test was used for comparison of TG that had a non-normal distribution. The mean $(\pm SD)$ values for biological and biochemical variables (other than TG) were compared between different age groups by ANOVA and Tukey post-hoc tests; for comparison of TG the Kruskal-Wallis test was used. After adjustment for age and gender similar tests were used for comparison of variables studied according to the birth weight category.

After age-adjustment, a logistic regression model was employed to evaluate the gender-specific associations of MS with possible associated factors, i.e. birth weight, level of physical activity, parents' education, parents' occupation, type of milk and weaning food consumed in infancy, type of fat and bread consumed, passive smoking, and family history of obesity/hypertension/cancers/premature cardiovascular disease. One model of logistic regression analysis was also used to assess the age-adjusted association of the frequency of consumption of different food groups (based on FFQ) with the risk of having MS. The significance level was set at p < 0.05.

Results

The participants in our study comprised 2248 boys and 2563 girls, with a mean age of 12.07 (± 3.2) years. There was no significant difference between boys and girls in terms of mean ages or birth weight categories.

Most of the students' fathers worked in the private sector (34.9%) or were government employees (31.5%), and most of their mothers (88.9%) were housewives. Most (88.2%) of the students' parents were literate; the mean (\pm SD) duration of education for fathers and mothers was 10.7 (\pm 4.4) and 8.4 (\pm 4.1) years, respectively.

Most children (72.1%) were breast-fed during infancy, and their weaning food was home-made (71.7%). The most frequent type of fat consumed for food preparation in the students' home was hydrogenated solid fat (78.2%). Most students (59.2%) consumed breads prepared with white wheat flour. Birth weights of <2500 g and >4000 g were reported in 14.3% and 10.1% of participants, respectively.

Overall, dairy products, foods containing animal and plant proteins, snacks (salty/high-fat/sweet), as well as vegetables and fruit (together), had a similar consumption frequency of almost twice daily. Carbohydrates (mostly bread and rice) and fast foods were consumed three times a day and twice a week, respectively.

In all age groups, boys were more physically active than girls. The mean (\pm SD) time spent watching television daily was 4.1 (\pm 0.5) h, and was significantly higher in girls than in boys [4.5 (\pm 0.5) vs. 4.03 (\pm 0.4) h, p < 0.01]. The mean (\pm SD) time spent performing vigorous physical activity daily (activities >6 METs of intensity) was 0.6 (\pm 0.02) h, which was significantly higher in boys than in girls [0.6 (\pm 0.1) vs. 0.4 (\pm 0.02) h, p < 0.01]. In boys, the 1st tertile of physical activity included participants with less than 35.1 MET-h/day of physical activity, and those with more than 49.2 MET-h/day of physical activity were included in the 3rd tertile; subjects between these limits were considered in the 2nd tertile of physical activity. In girls, these limits were 31.1 and 42.2 MET-h/day, respectively.

Boys had higher mean levels of Wt, Ht, BMI, WC, SBP and DBP than girls; other variables were not significantly different in terms of gender. Other than HDL-C, all variables studied increased significantly with increasing age (Table 1).

Table 2 presents the age- and gender-adjusted biological and biochemical characteristics of the participants, according to their birth weight category. The mean SBP, DBP and WC of subjects with normal birth weight was lower than the other two groups; the mean TC, LDL-C and BMI for subjects with a birth weight of \geq 4000 g was higher than the other two groups.

As presented in Table 3, MS was detected in 14.1% of participants. with no significant difference detected between boys and girls. However, in different age groups its prevalence varied significantly between the two genders. The most frequent components of MS were low HDL-C, followed by high TG and high WC, respectively.

Age-adjusted logistic regression analysis revealed that a birth weight >4000 g in boys, and <2500 g in girls increased

the risk of having MS [OR, 95% CI: 1.4 (1.007, 2.05) and 1.2 (1.1, 1.4), respectively]. Poor parental education and a positive history of chronic disease in parents were other risk factors for MS in boys and girls. Overall, 32% of students reported having a smoker in their household; this history did not significantly increase the odds of having MS. In both genders, low levels of physical activity significantly increased the risk of having MS [boys: 1.3 (1.1, 1.7); girls, 1.4 (1.2, 1.6); Table 4].

In both genders the risk of MS rose with the consumption of solid hydrogenated fat [boys: 1.2 (1.07, 1.3); girls, 1.3 (1.1, 1.5)] and white-flour bread [boys: 1.6 (1.3, 2.1); girls, 1.4 (1.1, 1.7)]. While the frequency of intake of sweets/ candies increased the risk of MS in both genders, the frequency of eating fast foods and carbohydrates increased this risk in boys or girls, respectively. In both genders, the frequency of consumption of fruit and vegetables, as well as dairy products, decreased the risk of having MS (Table 5).

Discussion

In this the first national study of its kind in a non-Western population, we sought to identify the association between early-life influences and some lifestyle behaviours with MS in children and adolescents. We found a considerably high prevalence of MS—14.1%. Birth weight, family history of chronic disease, level of education of parents, and dietary and physical activity habits had diverse effects on the risk of developing MS.

Birth weight reflects the pattern of intrauterine growth, and being born either LGA or SGA might have long-term impacts on chronic disease in adulthood [26-28]. In our study, in boys, being LGA, and in girls, being SGA, increased the risk of having MS. In some ethnic groups, e.g. in Pima Indians, those children born either SGA or LGA are found to be at risk for the development of type 2 diabetes mellitus [29]. While some cross-sectional [8] and longitudinal [30] studies have shown that a lower birth weight increased the risk for having MS in adulthood, a longitudinal study showed that LGA newborns were at higher risk of developing MS in childhood [31]. A recent study revealed a U-shaped relationship between birth weight and several components of MS, but post-natal weight gain was the dominant factor associated with the high-risk cluster [32]. Future research is needed to determine the mechanisms by which environmental changes lead to the programmed effects of foetal growth. In addition, the gender differences that we found in terms of the association between birth weight and the risk of developing MS in childhood should be examined in longitudinal studies.

Evidence is growing that the factors operating early in life influence cardiovascular risk factors later in life. Consistent with a recent meta-analysis [33], the findings from the CASPIAN study population confirmed the protective role of breast feeding on high BP [34]. In addition, we found an inverse association between breast feeding and being overweight [11]. However, in the current study we did not find such a protective role against MS. As mentioned by Lawlor et al., the association between breast feeding and some components of MS, but not with their cluster in MS, may be due to an interaction with age [35].

Table 1	Characteristics (mean \pm SD) of the participants by gender and age group: CASPIAN Study					
	6–9.9 years	10–13.9 years	14–18 years	Total		
Boys						
Ν	757	842	649	2248		
Age	8.24 (1.34)	12.49 (1.15)	16.10 (1.02)	12.10 (3.33)		
BMI	16.41 (3.00)	18.49 (3.72)	20.41 (3.41)	18.34 (3.75) [#]		
WC	58.56 (7.29)	67.62 (9.75)	72.63 (8.98)	66.00 (10.44) [#]		
SBP	96.11 (12.58)	102.77 (12.71)	111.80 (12.85)	103.12 (14.13) [#]		
DBP	59.46 (10.29)	62.84 (10.27)	71.96 (9.95)	64.32 (11.37) [#]		
LDL-C	88.95 (30.05)	87.31 (29.88)	77.20 (29.06)	84.94 (30.11) [#]		
HDL-C	43.76 (12.50)	45.46 (11.97)	43.72 (11.96)	44.38 (12.17) [#]		
тс	150.72 (32.12)	153.93 (38.10)	139.71 (31.53)	148.75 (34.82) [#]		
TG	91.07 (43.75)	98.94 (61.53)	95.53 (46.18)	95.31 (51.83)		
FBS	82.20 (11.20)	82.14 (12.08)	80.18 (12.28)	81.60 (11.88) [#]		
Girls						
Ν	859	1045	659	2563		
Age	8.26 (1.36)	12.55 (1.11)	16.15 (1.06)	12.04 (3.26) [#]		
BMI	16.16 (2.80)	19.43 (3.68)	21.18 (3.71)	18.78 (3.96) [#]		
WC	56.98 (7.18)	66.64 (8.75)	70.08 (8.48)	64.28 (9.79) [#]		
SBP	92.57 (11.41)	99.57 (12.34)	102.77 (12.92)	98.03 (12.86) [#]		
DBP	57.49 (10.38)	62.49 (10.14)	64.17 (9.97)	61.23 (10.54) [#]		
LDL-C	88.41 (33.05)	86.57 (28.32)	80.75 (28.34)	85.70 (30.13) [#]		
HDL-C	44.11 (12.04)	43.40 (12.31)	45.70 (14.28)	44.23 (12.79) [#]		
тс	150.13 (35.59)	150.49 (30.93)	144.81 (32.99)	148.91 (33.16) [#]		
TG	91.41 (43.79)	103.68 (51.29)	94.69 (45.97)	97.25 (47.82) [#]		
FBS	80.28 (10.02)	81.28 (9.47)	79.80 (9.16)	80.55 (9.60)#		
Total						
Ν	1616	1887	1308	4811		
Age	8.25 (1.35)	12.53 (1.13)	16.12 (1.04)	12.07 (3.2) [#]		
BMI	16.27 (2.90)	19.01 (3.73)**	20.80 (3.58)**	18.5 (3.8)** ^{,#}		
WC	57.72 (7.27)**	67.08 (9.22)*	71.34 (8.82)**	65.08 (10.1)** ^{,#}		
SBP	94.23 (12.10)**	101.03 (12.61)**	107.24 (13.65)**	100.4 (13.7)** ^{,#}		
DBP	58.42 (10.38)**	62.65 (10.20)	68.03 (10.69)**	62.6 (11.05)** ^{,#}		
LDL-C	88.66 (31.67)	86.90 (29.01)	78.99 (28.75)*	85.3 (30.1) [#]		
HDL-C	43.95 (12.26)	44.32 (12.20)**	44.71 (13.21)**	44.3 (12.5)		
TC	150.41 (34.00)	152.03 (34.35)*	142.28 (32.36)**	148.8 (33.9) [#]		
TG	91.25 (43.76)	101.56 (56.12)	95.11 (46.06)	96.3 (49.7) [#]		
FBS	81.18 (10.63)**	81.67 (10.74)	79.99 (10.81)	81.04 (10.7)***,#		

BMI, body mass index (kg/m²); WC, waist circumference (cm); SBP, systolic blood pressure (mmHg); DBP, diastolic blood pressure (mmHg); TC, total cholesterol (mg/dl); LDL-C, low-density cholesterol (mg/dl); HDL-C, high -density cholesterol (mg/dl); TG, triglyceride (mg/dl); FBS, fasting blood sugar (mg/dl).

*Significant at p < 0.05 between genders, **significant at p < 0.01 between genders, [#]significant at p < 0.01 between age groups.

Childhood socioeconomic status can affect the development of chronic diseases in adulthood; for instance significant associations are found between early socioeconomic disadvantage and high BP later in life [36]. As an indicator of socioeconomic status, education level is reported to be negatively correlated with the relative risk of MS among adults [37,38]. In our study, a lower level of education in parents increased the odds of having MS in children. This poorer education in parents seems to be associated with the adoption of harmful habits, such as unhealthy diet and physical inactivity among family members.

Different studies among adults have shown that among the risk factors, a positive family history for chronic diseases is related to MS [37,39,40]. In the current study, a positive family history of obesity and/or hypertension in parents increased the risk of MS in both genders, and that of premature cardiovascular disease increased the risk in boys. A positive history of diabetes in parents and or other relatives increased the odds of having MS in the youths studied. Our findings suggest that genetic and/or non-genetic familial influences play a role in the development of MS in the paediatric population.

A complex interaction of genetic, environmental, and behavioural factors is suggested as the underlying cause of MS. However, the data relating to the influence of diet and physical activity on this global health problem are inconclusive. Consistent with some previous studies [41,42], we found that low levels of physical activity significantly

	All Weights	Birth weight(g)	Birth weight(g)			
		<2500	2500-4000	>4000		
n (%)	4811 (100)	767 (15.9)	3431 (71.4)	613 (12.7)	<0.0001	
SBP	100.4 (13.7)	100.4 (13.7)	99.5 (13.7)	102.07 (13.6)	0.007	
DBP	62.6 (11.05)	63.8 (11.05)	62.0 (11.1)	63.7 (11.4)	0.01	
тс	148.8 (33.9)	147.9 (34.4)	148.8 (32.4)	154.04 (34.8)	0.003	
LDL-C	85.3 (30.1)	84.7 (30.7)	84.8 (28.6)	89.3 (29.7)	0.01	
HDL-C	44.3 (12.5)	44.2 (12.5)	44.5 (12.3)	44.4 (12.1)	0.8	
TG	96.3 (49.7)	96.02 (49.2)	97.4 (47.8)	98.5 (48.6)	0.5*	
FBS	81.04 (10.7)	81.07 (10.8)	81.5 (10.5)	81.3 (10.5)	0.5	
BMI	18.5 (3.8)	18.6 (3.8)	18.1 (3.6)	19.2 (4.09)	<0.0001	
WC	65.08 (10.1)	65.1 (10.1)	63.9 (9.6)	66.6 (10.7)	<0.0001	

 Table 2
 Age and gender-adjusted mean (SD) of biological and biochemical variables by birth weight: CASPIAN Study

SBP, systolic blood pressure (mmHg); DBP, diastolic blood pressure (mmHg); TC, total cholesterol (mg/dL); LDL-C, low-density cholesterol (mg/dL); HDL-C, high -density cholesterol (mg/dL); TG, triglycerides (mg/dL); FBS, fasting blood sugar (mg/dL); BMI, body mass index (kg/m²); WC, waist circumference (cm).

increased the risk of having MS in both genders [43]. In addition, the present study showed a similar frequency of consumption of dairy products, fruit, vegetables, and salty/high-fat/sweet snacks, which indicates a low intake of healthy foods, particularly fruit and vegetables, and considerably higher intake of unhealthy snacks among children and adolescents. Dietary habits correlated with MS in our study: while the frequency of intake of sweets/candies increased the risk of MS in both genders, the frequency of eating fast foods and carbohydrates increased this risk in boys or girls, respectively. In both genders, the frequency of consumption of fruit and vegetables, as well as dairy products, decreased the risk of having MS. Our findings are in line with the results of a study among young adult Americans that showed that low fruit and vegetable consumption and high sweetened beverage consumption were independently associated with the prevalence of MS in some ethnic groups [44].

Usually, the largest portion of Iranian meals consists of bread and/or rice. As indicated in the current study, the consumption of whole grain products was low in most families and the popular habit of eating white-flour bread increased the risk of having MS. Moreover, we found that most families consumed this solid hydrogenated fat, 60% of which constitutes saturated and trans fatty acids [45]. In this study, the prevalence of low HDL-C and hypertriglyceridaemia were higher than that reported from Western countries. The prevalence of this type of dyslipidaemia is relatively high in Iran and its neighbouring countries [46-48], suggesting an ethnic predisposition to MS. In addition, a genetic/environmental interaction might explain the difference with Western countries, i.e. diets high in trans fatty acids may lower HDL-C, increase TG levels and interfere with fatty acid metabolism. We have previously documented the role of solid fats on dyslipidaemia in youths from our community [10], and in the current study the use of this

Table 3	Prevalence of the metabolic s	yndrome and its com	ponents according to t	the gender and age	group: CASPIAN Study
					J I J

	Age groups (years)	High TG (%)	Low HDL-C (%)	High WC (%)	High BP (%)	High FBS (%)	Metabolic syndrome (%)
Boys	6–9.9 (<i>n</i> = 757)	33	72	21	5	1	14.01#
	10-13.9 (n = 842)	38	68	26	6	5	14.07 [#]
	14–18 (<i>n</i> = 649)	34	74	22	8	4	15.01 [#]
	Total ($n = 2248$)	35*	71	23*	7**	5	14.1
Girls	6–9.9 (<i>n</i> = 859)	35	72	20	7	1	12.4 [#]
	10–13.9 (<i>n</i> = 1045)	46	73	26	4	4	16.01 [#]
	14–18 (<i>n</i> = 659)	35	71	21	3	3	11.7 [#]
	Total ($n = 2563$)	40**	72	23**	5**	3	14.2
Total	6–9.9 (<i>n</i> = 1616)	34	72	20	9*	1*	13.5
	10–13.9 (<i>n</i> = 1887)	43**	71*	26	5	4	15.1** ^{,#}
	14–18 (<i>n</i> = 1308)	35	72	21	8**	3	13.2
	Total ($n = 4811$)	38** ^{,†}	72	23**	7** ^{,#}	4 [†]	14.1

TG, triglyceride (mg/dL); HDL-C, high-density-cholesterol (mg/dL); WC, waist circumference (cm); BP, blood pressure (mmHg); FBS, fasting blood sugar (mg/dL).

*p < 0.05 between age groups, **p < 0.01 between age groups, $^{\dagger}p < 0.05$ between genders, $^{\#}p < 0.01$ between genders.

Table 4	Age-adjusted Odds rat	ios (95% Cls) for havi	ng the metabolic syndrome b	based on the variables assessed:	CASPIAN Study
---------	-----------------------	------------------------	-----------------------------	----------------------------------	----------------------

	Boys		Girls	
	Odds ratio (95% CI)	p	Odds ratio (95% CI)	р
Birth weight (g)				
2500-4000				
<2500	1.1 (0.9,1.2)	0.06	1.2 (1.1,1.4)	0.03
>4000	1.4 (1.007,2.05)	0.04	1.1 (0.6,1.4)	0.07
Type of fat consumed				
Liquid oil				
Hydrogenated solid fat	1.2 (1.07, 1.3)	0.002	1.3 (1.1,1.5)	0.03
Others	1.04 (0.8,1.6)	0.08	1.07 (0.9,1.5)	0.06
Type of bread consumed				
Whole-grain				
White floor	1.6 (1.3,2.1)	<0.001	1.4 (1.1,1.7)	0.01
Physical activity level				
Tertile 3				
Tertile 2	1.02 (0.7,1.3)	0.1	1.08 (0.6,1.1)	0.06
Tertile 1	1.3 (1.1,1.7)	0.02	1.4 (1.2,1.6)	0.01
Father's education				
12 years				
Illiterate	1.4 (1.2,1.8)	0.01	1.3 (1.1,1.7)	0.01
\leq 5 years	1.2 (1.1,1.8)	0.03	1.3 (1.1,1.6)	0.02
8 years	0.7 (0.4, 1.5)	0.2	0.8 (0.4, 1.5)	0.4
\geq 16 years	0.6 (0.4,1.09)	0.08	0.7 (0.5,1.1)	0.06
Mother's education				
12 years				
Illiterate	1.3 (1.2,1.9)	0.01	1.4 (1.3,1.8)	0.001
\leq 5 years	1.2 (1.1,1.8)	0.03	1.3 (1.1,1.7)	0.02
8 years	0.7 (0.4, 1.5)	0.2	0.6 (0.4, 1.5)	0.3
\geq 16 years	0.6 (0.4,1.09)	0.08	0.7 (0.5,1.1)	0.07
FH of obesity				
No one				
Father or mother	1.6 (1.2,2.2)	<0.001	1.7 (1.3,2.3)	<0.001
Others	1.5 (1.1,2.04)	0.003	1.04 (0.7,1.3)	0.06
FH of premature CVD				
No one				
Father or mother	1.2 (1.1,1.4)	0.02	1.2 (0.8,1.6)	0.08
Others	1.04 (0.7,1.1)	0.09	1.09 (0.7,1.5)	0.1
FH of diabetes				
No one				
Father or mother	1.8 (1.2,2.5)	0.001	1.4 (1.2,2.1)	0.03
Others	1.5 (1.2,2.05)	0.003	1.1 (1.04,1.5)	0.04
FH of hypertension				
No one				
Father or mother	1.3 (1.1,1.6)	0.01	1.5 (1.1,2.2)	0.02
Others	1.2 (0.9,1.5)	0.06	1.2 (0.9,1.5)	0.1

FH, family history; premature CVD, cardiovascular disease before 55 years of age.

Variables included in the model: birth weight, physical activity level, parents' education, parents' occupation, type of milk and weaning food consumed in infancy, the type of fat and bread consumed, passive smoking, family history of obesity/hypertension/cancers/diabetes/premature cardiovascular diseases.

type of fat raised the probability of having MS. Fortunately, in addition to increasing awareness about healthy nutrition, many efforts are currently being made at a national level to improve the quality of fat produced in Iran.

As the Middle East has the highest dietary energy surplus of all the developing countries, and considering the epidemiological transition, a rapid rise in chronic diseases is a potential emerging public health issue [49]. Data concerning the youth living in the Middle East are very limited in this regard, but overall it is assumed that that the picture of health and nutritional status in this region has changed drastically during the last decades. Iran has undergone a rapidly occurring nutritional transition. This is suggested to be secondary to the rapid change in fertility and mortality patterns and to urbanization, which have led to a considerable imbalance in food consumption, with low nutrient density characterizing diets

	Boys		Girls		
	OR (95% CI)	р	OR (95% CI)	р	
Dairy products	0.7 (0.6,0.8)	0.03	0.8 (0.6,0.9)	0.04	
Animal protein	1.008 (0.9,1.04)	0.6	1.003 (0.9,1.03)	0.8	
Plant protein	0.9 (0.9,1.01)	0.1	0.9 (0.9,1.007)	0.1	
Fast foods	1.2 (1.04,1.5)	0.01	1.01 (0.9,1.08)	0.6	
Salty/fat snacks	0.9 (0.9,1.02)	0.6	1.02 (1.000,1.05)	0.06	
Sweets/candies	1.4 (1.1,1.6)	0.01	1.2 (1.05,1.3)	0.04	
Vegetables ^a	0.8 (0.7,0.9)	0.04	0.8 (0.6, 0.9)	0.03	
Fruits(fresh, dried, juice)	0.8 (0.7,1.04)	0.06	0.9 (0.7,1.04)	0.08	
Fruits and vegetables	0.8 (0.7, 0.9)	0.04	0.7 (0.6,0.9)	0.03	
Carbohydrates	1.1 (0.976,1.2)	0.06	1.2 (1.07,1.3)	0.04	

Table 5 Age-adjusted odds ratios (95% CIs) for having the metabolic syndrome based on the foods consumed: CASPIAN Study

The frequencies of consumption of foods consumed (based on a food frequency questionnaire) were included in the model. Potato and French fries not included.

and over-consumption evident among more than a third of households [50].

Although passive smoking is found to be associated with MS in adolescents [51], we did not find such an association. We suggest that this is because our findings relating to passive smoking were questionnaire-based and were not assessed biochemically.

Study limitations

One of the limitations of this study is the recall bias for the process of recalling and recording food intake and physical activity habits, which requires attention and involves perception. However, the magnitude of these factors is estimated to be low. Considering the large number of subjects studied, only a quantitative FFQ was used in the present survey and such data cannot provide the precise nutrient and energy intake of the subjects studied. Given that we could not assess the pubertal stage in such a large population, the influences of puberty on MS and its components cannot be determined. The findings from the analysis of factors associated with MS should therefore be interpreted with caution given the cross-sectional nature of the associations.

Conclusion

Considering the effect of modifiable lifestyle habits on MS in the paediatric population, encouraging healthy dietary habits such as increasing fibre intake, reducing the consumption of junk foods and saturated fat, as well as increasing physical activity starting in childhood, may have important effects on public health, especially in low- and middleincome countries faced with an epidemic of chronic diseases in the near future. Those children with a positive family history of chronic disease need special attention in this regard. Given the possible link between birth weight and MS, as well as the possible impact of environmental factors on foetal maturation and metabolism, urgent public health approaches should be directed towards primordial and primary prevention of chronic diseases.

Acknowledgments

This national study was funded in part by the grant TSA03/ 11 WHO/EMR and was supported by the Iranian Ministry of Health and Ministry of Education. The authors would like to extend their sincere thanks to all members of the large team working on this project, as well as to the participants of this study.

References

- [1] Kohen-Avramoglu R, Theriault A, Adeli K. Emergence of the metabolic syndrome in childhood: an epidemiological overview and mechanistic link to dyslipidemia. Clin Biochem 2003;36(6):413-20.
- [2] Yusuf S, Reddy S, Ounpuu S, Anand S. Global burden of cardiovascular diseases. Part II. Variations in cardiovascular disease by specific ethnic groups and geographic regions and prevention strategies. Circulation 2001;104:2855-64.
- [3] Rosenberg B, Moran A, Sinaiko AR. Insulin resistance (metabolic) syndrome in children. Panminerva Med 2005;47:229-44.
- [4] Onat A, Ceyhan K, Basar O, Erer B, Toprak S, Sansoy V. Metabolic syndrome: major impact on coronary risk in a population with low cholesterol levels-a prospective and cross-sectional evaluation. Atherosclerosis 2002;165(2):285-92.
- [5] Wirfalt E, Hedblad B, Gullberg B, Mattisson I, Andren C, Rosander U, et al. Food patterns and components of the metabolic syndrome in men and women: A cross sectional study within the Malmö Diet and Cancer Cohort. Am J Epidemiol 2001:154:1150-9.
- [6] Liu S, Manson JE. Dietary carbohydrates, physical inactivity, obesity, and the "metabolic syndrome" as predictors of coronary heart disease. Curr Opin Lipidol 2001;12:395-404.
- [7] Mericq V. Prematurity and insulin sensitivity. Horm Res 2006; 65(Suppl. 3):131-6.
- [8] te Velde SJ, Twisk JW, van Mechelen W, Kemper HC. A birthweight questionnaire indicated that life style modifies the birth weight and metabolic syndrome relationship at age 36. J Clin Epidemiol 2005;58(11):1172-9.
- [9] Kelishadi R, Pour MH, Sarraf-Zadegan N, Sadry GH, Ansari R, Alikhassy H, et al. Obesity and associated modifiable risk factors in Iranian adolescents: IHHP-HHPC. Int Pediatr 2003;45: 435-42.

- [10] Kelishadi R, Pour MH, Zadegan NS, Kahbazi M, Sadry G, Amani A, et al. Fat intake and serum lipid profile in Iranian adolescents: IHHP-HHPC. Prev Med 2004;39:760–6.
- [11] Kelishadi R, Ardalan G, Gheiratmand R, Gouya MM, Razaghi EM, Delavari AR, et al. Association of physical activity and dietary behaviors in relation to the body mass index in a national sample of Iranian children and adolescents: CASPIAN Study. Bull World Health Organ 2007;85:19–26.
- [12] Kelishadi R, Gheiratmand R, Ardalan G, Adeli K, Mehdi Gouya M, Mohammad Razaghi E, et al., for the CASPIAN Study Group. Association of anthropometric indices with cardiovascular disease risk factors among children and adolescents: CASPIAN Study. Int J Cardiol 2007;117:340-8.
- [13] Cochran WD, Lee KG. Assessment of the newborn. In: Cloherty JP, Eichenwald EC, Stark AR, editors. Manual of neonatal care. 5th ed. Philadelphia: Lippincott Williams & Wilkins; 2004. p. 35–56.
- [14] Kelishadi R, Ardalan G, Gheiratmand R, Ramezani A. Is family history of premature cardiovascular diseases appropriate for detection of dyslipidemic children in population-based preventive medicine programs? CASPIAN Study. Pediatr Cardiol 2006;27:729–36.
- [15] Aadahl M, Jorgensen T. Validation of a new self-report instrument for measuring physical activity. Med Sci Sport Exerc 2003;35(7):1196–202.
- [16] Kelishadi R, Rabiee K, Khosravi A. Assessment of physical activity in adolescents of Isfahan. J Shahrekord Uni Med Sci 2004;3(2):55–65 (in Farsi).
- [17] WHO. Physical status: the use and interpretation of anthropometry. Report of a WHO Expert Committee. In: TRS No. 854. Geneva: World Health Organization; 1995.
- [18] National High Blood Pressure Education Program Working Group on High Blood Pressure in Children and Adolescents. The Fourth Report on the Diagnosis, Evaluation, and Treatment of High Blood Pressure in Children and Adolescents. Pediatrics 2004;114:555–76.
- [19] Mc Namara JR, Schaefer EJ. Automated enzymatic standardized lipid analyses for plasma and lipid lipoprotein fractions. Clin Chim Acta 1987;166:1–8.
- [20] Friedewald WT, Levy RI, Fredrickson DS. Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. Clin Chem 1972;18:499–502.
- [21] de Ferranti SD, Gauvreau K, Ludwig DS, Neufeld EJ, Newburger JW, Rifai N. Prevalence of the metabolic syndrome in American adolescents: findings from the Third National Health and Nutrition Examination Survey. Circulation 2004; 110:2494–7.
- [22] National Institutes of Health, Third Report of The National Cholesterol Education Program Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). Bethesda, MD: National Institutes of Health, NIH Publication; 2001. 01–3670.
- [23] Katzmarzyk PT, Srinivasan SR, Chen W, Malina RM, Bouchard C, Berenson GS. Body mass index, waist circumference, and clustering of cardiovascular disease risk factors in a biracial sample of children and adolescents. Pediatrics 2004;114:e198–205.
- [24] Moreno LA, Pineda I, Rodriguez G, Fleta J, Sarria A, Bueno M. Waist circumference for the screening of the metabolic syndrome in children. Acta Paediatr 2002;91:1307–12.
- [25] Genuth S, Alberti KG, Bennett P, Buse J, Defronzo R, Kahn R, et al. Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. Follow-up report on the diagnosis of diabetes mellitus. Diabetes Care 2003;26: 3160-7.
- [26] Barker DJP. The intrauterine origins of cardiovascular disease. Acta Pediatr 1993;391:93-9.

- [27] Cohen MS. Fetal and childhood onset of adult cardiovascular diseases. Pediatr Clin North Am 2004;51:1697–719.
- [28] Miles HL, Hofman PL, Cutfield WS. Fetal origins of adult disease: a paediatric perspective. Rev Endocr Metab Disord 2005;6(4):261-8.
- [29] McCance D, Pettitt D, Hanson R, Jacobsson L, Knowler W, Bennett P. Birth weight and non-insulin dependent diabetes: thrifty genotype, thrifty phenotype, or surviving baby genotype? BMJ 1994;308:942–5.
- [30] Ramadhani MK, Grobbee DE, Bots ML, Castro Cabezas M, Vos LE, Oren A, et al. Lower birth weight predicts metabolic syndrome in young adults: the Atherosclerosis Risk in Young Adults (ARYA)-study. Atherosclerosis 2006;184(1):21-7.
- [31] Boney CM, Verma A, Tucker R, Vohr BR. Metabolic syndrome in childhood: association with birth weight, maternal obesity, and gestational diabetes mellitus. Pediatrics 2005;115(3): e290-6.
- [32] Huang RC, Burke V, Newnham JP, Stanley FJ, Kendall GE, Landau LI, et al. Perinatal and childhood origins of cardiovascular disease. Int J Obes (Lond) 2007;31:236–44.
- [33] Martin RM, Gunnell D, Smith GD. Breastfeeding in infancy and blood pressure in later life: systematic review and metaanalysis. Am J Epidemiol 2005;161:15–26.
- [34] Kelishadi R, Gheiratmand R, Ardalan G, Majdzadeh R, Delavari A, Heshmat R, et al., CASPIAN Study Group. Blood pressure and its influencing factors in a national representative sample of Iranian children and adolescents: CASPIAN Study. Eur J Cardiovasc Prev Rehabil 2006;13:956–63.
- [35] Lawlor DA, Riddoch CJ, Page AS, Andersen LB, Wedderkopp N, Harro M, et al. Infant feeding and components of the metabolic syndrome: findings from the European Youth Heart Study. Arch Dis Child 2005;90(6):582-8.
- [36] Kivimaki M, Lawlor DA, Smith GD, Keltikangas-Jarvinen L, Elovainio M, Vahtera J, et al. Early socioeconomic position and blood pressure in childhood and adulthood. The Cardiovascular Risk in Young Finns Study. Hypertension 2006;47: 39-44.
- [37] Lee WY, Jung CH, Park JS, Rhee EJ, Kim SW. Effects of smoking, alcohol, exercise, education, and family history on the metabolic syndrome as defined by the ATP III. Diabetes Res Clin Pract 2005;67(1):70–7.
- [38] Wamala SP, Lynch J, Horsten M, Mittleman MA, Schenck-Gustafsson K, Orth-Gomer K. Education and the metabolic syndrome in women. Diabetes Care 2000;23(9):1444–5.
- [39] Panagiotakos DB, Pitsavos C, Chrysohoou C, Skoumas J, Tousoulis D, Toutouza M, et al. Young adults with family history of coronary heart disease have increased arterial vulnerability to metabolic risk factors: the Cardiovascular Risk in Young Finns Study. Arterioscler Thromb Vasc Biol 2006;26(6): 1376–82.
- [40] Wada K, Tamakoshi K, Yatsuya H, Otsuka R, Murata C, Zhang H, et al. Association between parental histories of hypertension, diabetes and dyslipidemia and the clustering of these disorders in offspring. Prev Med 2006;42(5):358–63.
- [41] Brage S, Wedderkopp N, Ekelund U, Franks PW, Wareham NJ, Andersen LB, et al. Features of the metabolic syndrome are associated with objectively measured physical activity and fitness in Danish children. Diabetes Care 2004; 27:2141–8.
- [42] Froberg K, Andersen LB. Mini review: physical activity and fitness and its relations to cardiovascular disease risk factors in children. Int J Obes (Lond) 2005;29(Suppl. 2):S34-9.
- [43] Kelishadi R, Razaghi EM, Gouya MM, Ardalan G, Gheiratmand R, Delavari A, et al. Association of physical activity and the metabolic syndrome in children and adolescents: CASPIAN Study. Horm Res 2006;67(1):46-52.
- [44] Yoo S, Nicklas T, Baranowski T, Zakeri IF, Yang SJ, Srinivasan SR, et al. Comparison of dietary intakes associated with metabolic

syndrome risk factors in young adults: the Bogalusa Heart Study. Am J Clin Nutr 2004;80:841–8.

- [45] Bahrami G, Mirzaeei SH. The evaluation of fatty acids profile in available hydrogenated oils and margarines in Iran. Iranian Heart J 2003;4:59–67.
- [46] Azizi F, Salehi P, Etemadi A, Zahedi-Asl S. Prevalence of metabolic syndrome in an urban population: Tehran Lipid and Glucose Study. Diabetes Res Clin Pract 2003;61:29–37.
- [47] Al-Lawati JA, Mohammed AJ, Al-Hinai HQ, Jousilahti P. Prevalence of the metabolic syndrome among Omani adults. Diabetes Care 2003;26(6):1781–5.
- [48] Ozsahin AK, Gokcel A, Sezgin N, Akbaba M, Guvener N, Ozisik L, et al. Prevalence of the metabolic syndrome in a Turkish adult population. Diabetes Nutr Metab 2004;17(4):230–4.
- [49] Galal O. Nutrition-related health patterns in the Middle East. Asia Pac J Clin Nutr 2003;12(3):337–43.
- [50] Ghassemi H, Harrison G, Mohammad K. An accelerated nutrition transition in Iran. Public Health Nutr 2002;5(1A):149–55.
- [51] Weitzman M, Cook S, Auinger P, Florin TA, Daniels S, Nguyen M, et al. Tobacco smoke exposure is associated with the metabolic syndrome in adolescents. Circulation 2005; 112(6):862–9.