

## Original Article

# Low Carbohydrate Diet Score does not Predict Metabolic Syndrome in Children and Adolescents: Tehran Lipid and Glucose Study

Ghazaleh Eslamian MSc<sup>1</sup>, Parvin Mirmiran PhD<sup>2,3</sup>, Golaleh Asghari MSc<sup>2</sup>, Firoozeh Hosseini-Esfahani MSc<sup>2</sup>, Emad Youzbashian BSc<sup>2</sup>, Fereidoun Azizi MD<sup>4</sup>

## Abstract

**Background:** The aim of the study was to evaluate the ability of a low carbohydrate diet score (LCD) to predict the occurrence of the metabolic syndrome (MetS) and its components in a group of Tehrani children and adolescents after 3.6 years of follow-up.

**Methods:** Diet scores were calculated using a validated semi-quantitative food frequency questionnaire for participants aged 6–19 years, selected from the Tehran Lipid and Glucose Study cohort. The LCD was calculated based on intake of carbohydrate, monounsaturated fatty acids, refined grains and vegetable protein intake, expressed as a percentage of energy as well as fiber, n3/n6 polyunsaturated fatty acids and glycemic load. The higher the score, the more closely the participant's diet followed the pattern of LCD. The incidence of MetS and its components was calculated three years later.

**Results:** The mean age of the participants was  $13.8 \pm 3.6$  years and 45.4% were boys. The incidence rates of MetS, high blood pressure, high triglycerides, low HDL-C, abdominal obesity, and high blood glucose were 7.5%, 11%, 15%, 6.9%, 18.3%, and 12.3%, respectively. Compared to those in the lowest quartile of LCD score, after adjusting for age, sex, physical activity, and energy intake, participants in the highest quartile of LCD score had odds ratios of 0.74 (95% CI: 0.24–2.28), 1.16 (95% CI: 0.47–2.81), 0.55 (95% CI: 0.21–1.44), 0.49 (95% CI: 0.11–2.08), 0.91 (95% CI: 0.42–1.98), and 1.28 (95% CI: 0.51–3.20) with the incidence of MetS, high blood pressure, high triglycerides, low HDL-C, abdominal obesity, and high blood glucose.

**Conclusion:** No association was found between LCD and the incidence of MetS or its components in children and adolescents in Tehran after 3.6 years of follow up.

**Keywords:** Adolescents, children, low carbohydrate diet, metabolic syndrome

**Cite this article as:** Eslamian G, Mirmiran P, Asghari G, Hosseini-Esfahani F, Youzbashian E, Azizi F. Low Carbohydrate Diet Score does not Predict Metabolic Syndrome in Children and Adolescents: Tehran Lipid and Glucose Study. *Arch Iran Med.* 2014; **17(6)**: 417 – 422.

## Introduction

The prevalence of childhood overweight and obesity has increased at an alarming rate worldwide.<sup>1</sup> Since overweight or obese children are much more likely to become overweight or obese adults,<sup>2,3</sup> increased childhood overweight and obesity is clearly a major contributor to adulthood obesity<sup>4</sup> as well as the global burden of diseases.<sup>5</sup> Childhood obesity is linked to underachievement and lower self-esteem in school<sup>6</sup> and is strongly associated with risk factors for cardiovascular diseases, diabetes, orthopedic problems, mental disorders and also the metabolic syndrome (MetS).<sup>7,8</sup> According to the third report of the National Cholesterol Education Program Adult Treatment Panel III (ATP

III), the MetS is now recognized as a secondary target for risk-reduction therapy<sup>9</sup> and according to the International Diabetes Federation (IDF), the global prevalence of MetS is increasing in children.<sup>10</sup> A recent study in Tehran showed that the MetS is highly prevalent in Iranian adolescents, particularly among overweight adolescents.<sup>11</sup>

It is evident that obesity develops as the result of an inactive lifestyle and a positive energy balance.<sup>12</sup> However, the evidence remains inconclusive in children. Some studies have indicated a positive association between adiposity and dietary fat<sup>13–16</sup> while others have not.<sup>17–20</sup> There are only few studies which have specifically showed macronutrient intake in relation to Body Mass Index (BMI) and Waist circumference (WC) in children.<sup>21,22</sup> Although a relationship has been observed between fat intake and the insulin sensitivity index (SI) in adolescents,<sup>23</sup> neither dietary fat nor carbohydrate was associated with SI in a prepubertal subset of their cohort.<sup>24</sup> Limited data exist in children on dietary determinants of features of the MetS in children. A study showed that the dietary macronutrient composition is a predictor of Insulin resistance (IR) and systolic blood pressure (BP), but not resistin, adiponectin, or leptin concentrations.<sup>25</sup>

Considering the elevated prevalence of MetS in Iranian adolescents and the importance of distribution of macronutrients in dietary intakes, the purpose of the current study was to investigate

**Authors' affiliations:** <sup>1</sup>Students' Research Committee, Faculty of Nutrition Sciences and Food Technology, Shahid Beheshti University of Medical Sciences, Tehran, Iran. <sup>2</sup>Nutrition and Endocrine Research Center, Obesity Research Center, Research Institute for Endocrine Sciences, Shahid Beheshti University of Medical Sciences, Tehran, Iran. <sup>3</sup>Department of Clinical Nutrition and Dietetics, Faculty of Nutrition Sciences and Food Technology, National Nutrition and Food Technology Research Institute, Shahid Beheshti University of Medical Sciences, Tehran, Iran. <sup>4</sup>Endocrine Research Center, Research Institute for Endocrine Sciences, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

**Corresponding author and reprints:** Parvin Mirmiran PhD, Nutrition and Endocrine Research Center, Obesity Research Center, Research Institute for Endocrine Sciences, Shahid Beheshti University of Medical Sciences, Tehran, Iran. P.O. Box: 19395-4763, Tehran, Iran. Tel: +98 (21) 223 57 484, Fax: +98-21-224 16 264, 224 02 463, E-mail: mirmiran@endocrine.ac.ir

the association between MetS and its individual components and the dietary proportion of carbohydrates, protein and fat as well as fatty acid and protein subtypes and glycemic load (GL) in the frame of a low carbohydrate diet (LCD) score in Tehrani children and adolescents.

## Materials and Methods

### Study population

The subjects in this study were selected from the third phase (2006–2008) of the Tehran Lipid and Glucose Study (TLGS)<sup>26</sup> and were followed up to the fourth phase (2009–2011). Out of the 12523 initial participants, 3462 were randomly selected for dietary assessment, categorized by age and sex. For the current study, 621 individuals aged  $\geq 6$  yr and  $< 20$  yr, were included. Subjects with incomplete physical activity, anthropometric, and biochemical data ( $n = 29$ ) and those over- or underreported ( $n = 6$ ) were excluded. Over- or under-reporting was defined as the reported energy intake divided by the predicted energy intake, and reports that did not qualify for  $\pm 3SD$  range were excluded. Furthermore, subjects who had MetS ( $n = 69$ ), high blood pressure ( $n = 53$ ), high triglycerides ( $n = 168$ ), low HDL-C ( $n = 242$ ), high blood glucose ( $n = 12$ ), or abdominal obesity ( $n = 145$ ) were excluded for individual analysis of incidence of MetS and its components. Some individuals fell into more than one exclusion category. After an average follow-up of 3.6 years, 401, 437, 347, 290, 479, and 352 subjects remained for the analysis of MetS, blood pressure, triglycerides, HDL-C, blood glucose, and waist circumference, respectively.

The design of this study was approved by the institutional ethics committee of the Research Institute for Endocrine Sciences, affiliated with the Shahid Beheshti University of Medical Sciences, and informed written consent was obtained from the participants' parents.

### Clinical and laboratory measurements

To measure blood pressure, the participants remained seated for 15 minutes; then, a qualified physician, using a standard mercury sphygmomanometer with the cuff placed on the right arm, measured blood pressure twice and the mean values were used. Blood samples, at baseline and during follow up, were drawn between 7:00 and 9:00 a.m. from all study participants after 12–14 hr overnight fasting. All the blood analyses were done at the TLGS research laboratory on the day of blood collection. Fasting plasma glucose (FPG) was measured by the enzymatic colorimetric method using glucose oxidase. Serum HDL-C was measured after precipitation of the apolipoprotein B-containing lipoproteins with phosphotungstic acid and serum triglycerides (TGs) were assayed using an enzymatic colorimetric method with glycerol phosphate oxidase. These analyses were performed using commercial kits (Pars Azmoon Inc., Tehran, Iran) and a Selectra 2 auto analyzer (Vital Scientific, Spankeren, The Netherlands).

Inter- and intra-assay coefficients of variations at baseline were both 2.2% for FPG, 2 and 0.5% for HDL-C and 1.6 and 0.6% for TGs, respectively.

### Anthropometric measurements

Weight was measured, while participants were minimally clothed without shoes, using digital scales (Seca 707, Seca Corp., Hanover, MD; range 0.1–150 kg) and recorded to the nearest 100 g. Standing height was measured without shoes, using a tape to

the nearest 0.1 cm, while the shoulders were in a normal position. BMI was calculated as weight (Kg) divided by square of height ( $m^2$ ) (28).

### Dietary intake assessment

A validated semi-quantitative food frequency questionnaire (FFQ),<sup>27</sup> which contained 168 food items, was used by trained dietitians with at least 5 years of experience in the TLGS survey<sup>28</sup> in face-to-face interviews to evaluate the usual dietary intakes of participants. The participants were asked to report their consumption frequency during the previous year on a daily, weekly, or monthly basis, and data were then converted to the mean daily intakes assuming that one month equals 30.5 days.

Portion sizes of consumed foods, which were reported in household measures, were specified according to the US Department of Agriculture (USDA) standard portion sizes (e.g., apple, 1 medium; bread, 1 slice; dairy, 1 cup) and were then converted to grams. When unable to use the USDA portion sizes, household measures (e.g., beans, 1 tablespoon; chicken meat, 1 leg or wing; rice, 1 large or small plate) were used alternatively.<sup>29</sup> The estimates of nutrient intake are derived from the dietary sources alone. Since the Iranian food composition table (FCT) is incomplete and provides limited data on the nutrient content of raw foods and beverages,<sup>30</sup> analyses of energy and nutrients of foods and beverages were carried out using the USDA FCT.<sup>31</sup> However, for some food items such as *Kashk* which are not listed in the USDA FCT, Iranian FCT was used alternatively.<sup>30</sup> Moreover, for analyzing the energy and nutrient contents of mixed food items (e.g. pizza), usual restaurant recipes were used.

Since the Iranian Food Table of GI is incomplete,<sup>32</sup> analyses of GI content of foods and beverages were carried out using the international tables of GI and GL values: 2008.<sup>33</sup> However, the Iranian Food Table of GI was used for some foods (like traditional Iranian breads) that are not listed in the international tables of GI and GL values: 2008. Food items for which a GI had not been reported were attributed the GI of the nearest comparable food item (e.g., tangerines were assigned the GI of oranges) or were calculated using recipes. Lack of information about the GI of vegetables and legumes was resolved by calculating a mean GI for usually consumed vegetables and legumes in our study. The GI is based on the postprandial blood glucose response compared with white bread. Average dietary GI and GL were derived from the FFQ as follows:

Average dietary GI = [(carbohydrate content of each food item)  $\times$  (number of servings/d)  $\times$  (GI)] / total daily carbohydrate intake

Dietary GL = (carbohydrate content of each food item)  $\times$  (number of servings/d)  $\times$  (GI)

### Calculation of the low-carbohydrate-diet score

We divided the study participants into 11 strata for each component; i.e. carbohydrate, mono unsaturated fatty acids (MUFA), refined grains and vegetable protein intake, expressed as a percentage of energy as well as fiber (g/1000 Kcal), n3/n6 poly unsaturated fatty acids (PUFA) and GL (Table 1). For MUFA, n3/n6 PUFA, vegetable protein and fiber, adolescents in the highest stratum received 10 points for that macronutrient; adolescents in the next stratum received 9 points, and so on down to adolescents in the lowest stratum who received 0 points. For carbohydrates, refined grains and GL the order of the strata was reversed; those with the lowest carbohydrate intake received 10 points and those

**Table 1.** Criteria for determining low carbohydrate diet score.

Score	CHO (% energy)	Fiber (g/1000 kcal)	MUFA (% energy)	n3/n6 PUFA ratio	Refined grains CHO (% energy)	Vegetable protein (% energy)	Glycemic load
0	≥65.34	≤8.14	≤7.97	≤0.06	≥34.30	≤3.92	≥114.44
1	62.62–65.33	8.15–9.50	7.98–8.89	0.07–0.07	29.56–34.29	3.93–4.51	92.66–114.43
2	60.76–62.61	9.51–10.67	8.99–9.56	0.08–0.07	26.48–29.55	4.52–4.94	79.98–92.65
3	59.22–60.75	10.68–11.77	9.57–10.21	0.08–0.08	23.77–26.47	4.95–5.22	71.16–79.88
4	57.57–59.21	11.78–12.85	10.22–10.94	0.09–0.08	21.59–23.76	5.23–5.51	65.69–71.15
5	56.38–57.65	12.86–13.88	10.95–11.53	0.09–0.09	19.52–21.58	5.52–5.76	57.78–65.68
6	54.82–56.37	13.89–15.19	11.54–12.04	0.10–0.09	17.39–19.51	5.77–6.08	51.75–57.77
7	53.26–54.81	15.20–16.87	12.05–12.65	0.10–0.10	15.33–17.38	6.09–6.42	45.93–51.74
8	50.81–53.25	16.88–18.81	12.66–13.41	0.11–0.11	13.12–15.32	6.43–7.02	38.31–45.92
9	46.65–50.80	18.82–21.68	13.42–14.91	0.12–0.13	10.23–13.11	7.03–7.94	31.00–38.30
10	≤46.64	≥21.69	≥14.92	≥0.14	≤10.22	≥7.95	≤30.99

CHO = carbohydrate; MUFA = monounsaturated fatty acid; PUFA = polyunsaturated fatty acid

with the highest carbohydrate intake received 0 points. We used the percentage of energy consumed instead of absolute intake to reduce bias due to underreporting of food consumption and to represent dietary composition. The points for each of the items were then summed to create the overall diet score, which ranged from 0 (the lowest fat and protein intake and the highest carbohydrate intake) to 70 (the highest protein and fat intake and the lowest carbohydrate intake). Therefore, the higher the score, the more closely the participant's diet followed the pattern of a low-carbohydrate diet, which was named as "low carbohydrate-diet score."

#### Definition of the components of the metabolic syndrome

Because no universally accepted definition exists for MetS in children, the definition proposed by Cook *et al* was used.<sup>34</sup> It defines MetS as three or more of the following: Fasting TGs ≥110 mg/dL; HDL cholesterol <40 mg/dL; WC ≥90<sup>th</sup> percentile for age and sex, according to national reference curves<sup>35</sup>; systolic blood pressure (SBP) and/or diastolic blood pressure (DBP) ≥90<sup>th</sup> percentile for sex, age and height, from the National Heart, Lung, and Blood Institute's recommended cut-off points<sup>36</sup>, and fasting blood glucose ≥100 mg/dL, according to the recent recommendations of the American Diabetes Association.<sup>37</sup>

After about 3 years of follow up, the following criteria were used for defining MetS in adults, according to the joint interim statement (JIS)<sup>38</sup> which requires the presence of any three of five risk factors of the following: (i) Abdominal obesity as WC ≥91 cm for women and ≥89 cm for men according population- and country-specific cut-off points for Iranians<sup>39</sup>; (ii) FPG ≥100 mg/dL or medical treatment; (iii) Fasting TGs ≥150 mg/dL or medical treatment; (iv) Fasting HDL-C <50 mg/dL for women and <40 mg/dL for men or medical treatment and (v) Raised blood pressure was defined as systolic blood pressure (SBP) ≥130 mmHg, diastolic blood pressure (DBP) ≥85 mmHg or antihypertensive medical treatment.

Obesity, overweight, and normal BMI were defined based on the standardized percentile curves of BMI suggested for Iranian children and adolescents as ≥95<sup>th</sup>, between ≥85<sup>th</sup> to <95<sup>th</sup>, and <85<sup>th</sup> percentiles of BMI for age and sex, respectively.<sup>40</sup>

#### Statistical analysis

All statistical analyses were performed using the IBM SPSS version 19 (IBM Corporation, New York, NY, USA, 2010). A 2-sided *P* value <0.05 was considered significant. Descriptive statistics of the baseline anthropometric and cardiometabolic characteristics of the participants were described using means and standard de-

viation (SD), after testing for normal distribution for quantitative variables and percentages for qualitative variables. Student's *t* test and  $\chi^2$  test were used for comparison of continuous and categorical variables between genders, respectively. Normality of all variables was checked by Kolmogorov-Smirnov test. The participants were categorized according to quartiles of carbohydrate score (≤29, 30 – 35, 46 – 41, and ≥42). To test linear trend across quartiles of LCD, the median of the respective quartile was assigned as the exposure and the intake of food items or food groups as the continuous dependent variable. Logistic binary regression was used to assess the association of LCD score and incidence of MetS and its components. Two models were constructed: Model 1 was adjusted for age and gender, and model 2 was additionally adjusted for physical activity and energy intake. Age and physical activity score were entered in all models as continuous variables.

## Results

The study population was composed of 45.4% boys and 54.6% girls with mean ages of 13.4 ± 3.6 and 14.3 ± 3.7 years, respectively. In this population, over an average follow-up of three years, there were 7.5%, 11%, 15%, 12.3%, 18.3%, and 6.9% documented cases of MetS, high blood pressure, high triglycerides, high FBS, abdominal obesity, and low HDL-C, respectively. Participants with higher adherence of LCD were more likely to be girls, and have lower WC, FPG, SBP, and DBP (*P* < 0.05, Table 2).

Baseline dietary intakes of the participants across quartiles of the low carbohydrate diet score are shown in Table 3. The daily intakes of total protein, animal protein, total fat, SFA, MUFA, PUFA, n3-n6 ratio and fiber/1000 kcal significantly increased across quartiles, while those of the daily intakes of energy, carbohydrate, refined grains, simple sugars, and fruits significantly decreased across quartiles.

Using logistic regression analysis after controlling for age, sex, physical activity, and energy intake, low carbohydrate diet score showed no significant association with risk of MetS and its components (Table 4). Specifically, participants with the highest adherence to LCD (score) showed an odds ratio of 0.74 (95% CI: 0.24–2.28) in comparison to those with the lowest adherence for MetS incidence (*P* for trend = 0.793). Regarding the incidence of high triglycerides, low HDL-C, and abdominal obesity, the comparison between extreme categories of adherence (quartile 4 versus quartile 2) showed similar point estimates of 0.55 (95% CI: 0.21–1.44), 0.49 (95% CI: 0.11–2.08), and 0.91 (95% CI: 0.42–1.98), respectively.

**Table 2.** Baseline anthropometric and cardio-metabolic characteristics of participants by age and sex.

	Quartile 1	Quartile 2	Quartile 3	Quartile 4	P for trend*
Age (yr)	14.3 ± 3.4	13.7 ± 3.5	13.5 ± 3.8	13.7 ± 3.9	<0.114
Sex (% male)	52	47	43	37	0.006
BMI (Kg/m <sup>2</sup> )	21.7 ± 4.5	20.3 ± 4.5	20.8 ± 4.5	20.8 ± 4.5	0.146
WC (cm)	74.7 ± 12.7	70.6 ± 12.7	70.5 ± 13.3	70.4 ± 12.18	0.004
TC (mg/dL)	155.0 ± 29.5	156.4 ± 29.0	154.5 ± 29.6	156.2 ± 31.4	0.900
TG (mg/dL)	108.6 ± 58.0	97.1 ± 49.6	99.2 ± 68.6	94.9 ± 57.9	0.073
HDL-C (mg/dL)	43.1 ± 8.9	45.2 ± 11.6	44.7 ± 10.6	45.8 ± 11.3	0.056
LDL-C (mg/dL)	89.5 ± 24.2	92.0 ± 25.6	89.4 ± 23.5	91.1 ± 28.0	0.822
FBG (mg/dL)	86.1 ± 6.9	85.8 ± 6.1	85.0 ± 6.7	84.2 ± 6.3	0.007
SBP (mmHg)	100.3 ± 12.3	97.4 ± 12.5	99.9 ± 12.4	99.3 ± 11.4	<0.001
DBP (mmHg)	66.2 ± 9.5	64.5 ± 11.4	65.1 ± 9.5	65.6 ± 9.2	0.039
Overweight (%) <sup>a</sup>	16.3	16.3	19.4	19.7	0.421
Obesity (%) <sup>b</sup>	15.6	9.2	12.1	10.9	0.611
Abdominal obesity (%) <sup>c</sup>	31.0	17.6	25.2	21.8	0.337

BMI = body mass index, WC = waist circumference, TC = total cholesterol, TG = triglycerides, HDL-C = high density lipoprotein-cholesterol, LDL-C = low density lipoprotein-cholesterol, FBG = fasting blood glucose, SBP = systolic blood pressure, DBP = diastolic blood pressure  
 \*Linear regression; <sup>a</sup>Overweight was defined as 95<sup>th</sup> < BMI > 85<sup>th</sup> percentile according to national cut-off (40); <sup>b</sup>Obesity was defined as BMI ≥ 95<sup>th</sup> percentile according to national cut-off (40); <sup>c</sup>Abdominal obesity was defined as WC > 90<sup>th</sup> percentile according to national cut-off (35).

**Table 3.** Baseline dietary intakes of the participants across quartiles of the low carbohydrate diet score.

	Quartile 1	Quartile 2	Quartile 3	Quartile 4	P for trend*
Range	≤29	30-35	36-41	≥42	
Energy (Kcal)	3017 ± 1295	2548 ± 1196	2533 ± 1050	2305 ± 1090	<0.001
Carbohydrate (%)	62.3 ± 5.4	57.9 ± 5.9	54.7 ± 6.3	50.8 ± 6.4	<0.001
Total protein (%)	12.4 ± 2.1	12.9 ± 1.9	13.46 ± 2.6	13.9 ± 3.4	0.001
Vegetable protein (%)	5.8 ± 1.4	5.6 ± 1.5	5.8 ± 1.5	5.8 ± 1.6	0.467
Animal protein (%)	6.3 ± 2.4	6.8 ± 2.4	7.2 ± 3.1	7.6 ± 3.9	<0.001
Total fat (%)	27.3 ± 4.8	31.6 ± 5.7	34.4 ± 6.4	38.1 ± 6.1	<0.001
SFA (%)	9.5 ± 2.5	11.0 ± 2.7	11.8 ± 4.8	12.9 ± 3.0	<0.001
MUFA (%)	9.2 ± 1.8	10.8 ± 2.2	12.1 ± 2.6	13.4 ± 2.6	<0.001
PUFA (%)	5.4 ± 1.5	6.4 ± 2.0	7.3 ± 2.4	8.0 ± 2.3	<0.001
n3 to n6 ratio	0.08 ± 0.03	0.09 ± 0.03	0.10 ± 0.07	0.10 ± 0.05	<0.001
Fiber (g)	41.0 ± 30.0	36.3 ± 23.1	37.9 ± 22.3	34.7 ± 18.9	0.039
Fiber (g/1000Kcal)	13.1 ± 5.8	14.2 ± 5.6	14.9 ± 6.2	15.3 ± 4.8	<0.001
Whole grains (g)	75.4 ± 94.4	79.6 ± 129.1	97.2 ± 122.8	75.4 ± 67.1	0.611
Refined grains (g)	618.0 ± 365.6	381.7 ± 173.5	332.0 ± 144.6	264.9 ± 150.3	<0.001
Simple sugars (g)	93.1 ± 126.3	71.1 ± 82.5	62.4 ± 95.6	45.9 ± 59.1	<0.001
Starchy vegetables (g)	34.2 ± 33.2	32.2 ± 36.6	34.8 ± 33.2	28.2 ± 38.8	0.242
Vegetables (g)	277.2 ± 196.0	233.5 ± 166.5	263.3 ± 166.2	241.7 ± 182.6	0.178
Fruits (g)	531.8 ± 433.9	407.3 ± 321.8	370.0 ± 293.2	323.4 ± 277.2	<0.001
Legumes (g)	15.9 ± 28.4	12.6 ± 13.5	17.1 ± 20.9	20.5 ± 29.7	0.063
Red meat (g)	30.8 ± 27.0	33.2 ± 31.7	34.3 ± 25.6	36.7 ± 50.4	0.136
Nuts (g)	9.2 ± 12.2	10.7 ± 18.4	10.2 ± 13.1	12.2 ± 26.4	0.182
Fish (g)	12.7 ± 19.7	9.9 ± 9.5	20.8 ± 114 ± 6	23.6 ± 126.6	0.190
Poultry (g)	24.3 ± 23.1	23.5 ± 28.5	32.3 ± 50.9	33.2 ± 98.3	0.109

\* Linear regression. SFA = saturated fatty acid, MUFA = monounsaturated fatty acid, PUFA = polyunsaturated fatty acid.

**Table 4.** Odds ratio (95% confidence interval) for metabolic syndrome (MetS) and its components incident by quartiles (Qs) of low carbohydrate score diet.

	Q1	Q2	Q3	Q4	P for trend*
MetS (n = 401)					
Model 1	1.00	0.60 (0.20-1.77)	0.99 (0.37-2.70)	0.72 (0.24-2.16)	0.753
Model 2	1.00	0.61 (0.20-1.84)	1.01 (0.37-2.78)	0.74 (0.24-2.28)	0.793
High blood pressure (n = 437)					
Model 1	1.00	0.61 (0.23-1.58)	1.25 (0.55-2.87)	1.19 (0.50-2.82)	0.428
Model 2	1.00	0.58 (0.22-1.53)	1.21 (0.52-2.81)	1.16 (0.47-2.81)	0.456
High triglycerides (n = 347)					
Model 1	1.00	1.21 (0.55-2.64)	0.79 (0.33-1.86)	0.59 (0.23-1.53)	0.231
Model 2	1.00	1.11 (0.50-2.46)	0.73 (0.31-1.73)	0.55 (0.21-1.44)	0.191
Low HDL-C (n = 290)					
Model 1	1.00	0.35 (0.08-1.45)	0.84 (0.27-2.56)	0.40 (0.09-1.63)	0.320
Model 2	1.00	0.44 (0.10-1.84)	1.02 (0.32-3.22)	0.49 (0.11-2.08)	0.574
High blood glucose (n = 479)					
Model 1	1.00	2.06 (0.90-4.69)	1.50 (0.63-3.54)	1.40 (0.54-3.42)	0.543
Model 2	1.00	1.93 (0.84-4.45)	1.40 (0.58-3.34)	1.28 (0.51-3.20)	0.678
Abdominal obesity (n = 352)					
Model 1	1.00	0.72 (0.34-1.52)	0.63 (0.29-1.40)	0.88 (0.41-1.87)	0.691
Model 2	1.00	0.75 (0.35-1.60)	0.65 (0.29-1.45)	0.91 (0.42-1.98)	0.752

\* Linear regression; Model 1 was adjusted for age and gender; Model 2 was additionally adjusted for physical activity and energy intake.

## Discussion

In this population-based cohort study, the performance of LCD in relation to incidence of MetS and its components in children and adolescents was evaluated, and no significant association was found.

Several studies conducted in adults have found that diet composition may play a pivotal role in the development of obesity and its risk factors.<sup>41,42</sup> However, data from previous studies regarding the role of dietary composition in relation to the development of childhood obesity and its risk factors remains inconclusive.

Similar to our findings, Elliott et al.,<sup>43</sup> investigated the possible relationship between BMI and WC and energy intake and percentage energy intake from macronutrients in Australian children and adolescents; no evidence of an association between percentage macronutrient intake and BMI or WC was found. Numerous studies investigating the relationship between BMI, WC and/or skin fold measurements and energy intake have suggested that the macronutrient composition of the diet (protein, carbohydrate, fat) may contribute considerably to obesity in childhood as it does in adults. As shown by Aeberli et al., in children aged 6 to 14 years, dietary macronutrient composition was a predictor of insulin resistance and SBP.<sup>44</sup> Casazza et al., reported that energy intake from fat was positively and energy from carbohydrate and protein was inversely associated with fasting insulin.<sup>45</sup> Gillis et al., showed that more dietary energy and fat are associated with juvenile adiposity; the total consumed energy is more important than dietary fat or type of dietary fat.<sup>46</sup> Atkin and Davies showed that body fat percentage was not significantly correlated with dietary intake of total energy or percentage of energy from fat, carbohydrate, or protein.<sup>47</sup> Gazzaniga et al., examined the relationship between diet composition and body fatness in children aged 9–11 years. The percentage of body fat correlated positively with intake of total, saturated, monounsaturated, and polyunsaturated fatty acids, and negatively with carbohydrate intake and total energy intake, adjusted for body weight.<sup>48</sup> Also, Hassapidou et al., found that overweight and obese adolescents consumed fewer carbohydrates than lean participants.<sup>49</sup>

Some mechanisms have been proposed to shed light on the association of a low carbohydrate diet and cardio-metabolic factors. It has been reported that high intake of carbohydrates and foods with a high GI, particularly fructose, and relatively low intake of cholesterol and saturated fat leads to rapid stimulation of lipogenesis and accumulation of triglycerides, adipocyte hypertrophy, obesity-associated macrophage accumulation in adipose tissue, increased fructose end products like glyceraldehyde and dihydroxyacetone phosphate, and glycation end products.<sup>50</sup> In the current study, the range of LCD and its components was narrow, which indicated that scores in the top and bottom quartiles were not far from each other and could not clearly distinguish differences in dietary patterns, and could attenuate the association of diet and outcome.

The current study is among the first follow-up studies to be performed in countries undergoing nutrition transition, and its prospective design makes it easy to interpret the association of low carbohydrate diet with cardio-metabolic factors in children and adolescents. To our knowledge, the present study, based on a valid and detailed FFQ, is the first population-based cohort to examine the relationship between MetS and LCD in a non-Western population. Some limitations of our analysis deserve comment; measurement bias was unavoidable, as an FFQ was used to assess dietary

intake, which might have led to underestimation of the associations. However, we used a validated FFQ and excluded the participants who were misreporting (under or over reporting) their energy intake. Other limitations were a relatively small sample size and short follow up duration.

## Conclusion

This study reports new findings in the field of macronutrient intake in Iran and demonstrates that there is no relationship between MetS and LCD after 3.6 years of follow-up. Evidently, more robust longitudinal studies are needed to elucidate the relationship linking MetS and obesity and carbohydrate intake.

## Sources of support

This study was supported by a grant from the Research Institute for Endocrine Sciences, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

## Acknowledgment

*The present study was supported by grant no. 098 from the combined support of the National Research Council of the Islamic Republic of Iran and the Research Institute for Endocrinology and Metabolism, Shahid Beheshti University of Medical Sciences. We would like to acknowledge Ms. N. Shiva for critical editing of English grammar and syntax of the manuscript. None of the authors had any personal or financial conflicts of interest.*

## References

1. Deckelbaum RJ, Williams CL. Childhood obesity: the health issue. *Obes Res.* 2001; **9** (suppl 4): 239S – 243S.
2. Boreham C, Robson PJ, Gallagher AM, Cran GW, Savage JM, Murray LJ. Tracking of physical activity, fitness, body composition and diet from adolescence to young adulthood: The Young Hearts Project, Northern Ireland. *Int J Behav Nutr Phys Act.* 2004; **1**: 14.
3. Kvaavik E, Tell GS, Klepp KI. Predictors and tracking of body mass index from adolescence into adulthood: follow-up of 18 to 20 years in the Oslo Youth Study. *Arch Pediatr Adolesc Med.* 2003; **157**: 1212 – 1218.
4. Krassas GE, Tzotzas T. Do obese children become obese adults: childhood predictors of adult disease. *Pediatr Endocrinol Rev.* 2004; **1**(suppl 3): 455 – 459.
5. Kelly T, Yang W, Chen CS, Reynolds K, He J. Global burden of obesity in 2005 and projections to 2030. *Int J Obes (Lond).* 2008; **32**: 1431 – 1437.
6. Eisenberg ME, Neumark-Sztainer D, Story M. Associations of weight-based teasing and emotional well-being among adolescents. *Arch Pediatr Adolesc Med.* 2003; **157**: 733 – 738.
7. Williams J, Wake M, Hesketh K, Maher E, Waters E. Health-related quality of life of overweight and obese children. *JAMA.* 2005; **293**: 70 – 76.
8. Reilly JJ. Descriptive epidemiology and health consequences of childhood obesity. *Best Pract Res Clin Endocrinol Metab.* 2005; **19**: 327 – 341.
9. Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report. *Circulation.* 2002; **106**: 3143 – 421.
10. Zimmet P, Alberti KG, Kaufman F, Tajima N, Silink M, Arslanian S, et al. The metabolic syndrome in children and adolescents - an IDF consensus report. *Pediatr Diabetes.* 2007; **8**: 299 – 306.
11. Esmailzadeh A, Mirmiran P, Azadbakht L, Etemadi A, Azizi F. High prevalence of the metabolic syndrome in Iranian adolescents. *Obesity (Silver Spring).* 2006; **14**: 377 – 382.
12. Kemper HC, Stasse-Wolthuis M, Bosman W. The prevention and treat-

- ment of overweight and obesity. Summary of the advisory report by the Health Council of The Netherlands. *Neth J Med.* 2004; **62**: 10 – 17.
13. Tucker LA, Seljaas GT, Hager RL. Body fat percentage of children varies according to their diet composition. *J Am Diet Assoc.* 1997; **97**: 981 – 986.
  14. Maffei C, Pinelli L, Schutz Y. Fat intake and adiposity in 8 to 11-year-old obese children. *Int J Obes Relat Metab Disord.* 1996; **20**: 170 – 174.
  15. Maillard G, Charles MA, Lafay L, Thibault N, Vray M, Borys JM, et al. Macronutrient energy intake and adiposity in non-obese prepubertal children aged 5–11 yr (the Fleurbaix Laventie Ville Sante Study). *Int J Obes Relat Metab Disord.* 2000; **24**: 1608 – 1617.
  16. McGloin AF, Livingstone MB, Greene LC, Webb SE, Gibson JM, Jebb SA, et al. Energy and fat intake in obese and lean children at varying risk of obesity. *Int J Obes Relat Metab Disord.* 2002; **26**: 200 – 207.
  17. Davies PS. Diet composition and body mass index in pre-school children. *Eur J Clin Nutr.* 1997; **51**: 443 – 448.
  18. Ricketts CD. Fat preferences, dietary fat intake and body composition in children. *Eur J Clin Nutr.* 1997; **51**: 778 – 781.
  19. Atkin LM, Davies PS. Diet composition and body composition in pre-school children. *Am J Clin Nutr.* 2000; **72**: 15 – 21.
  20. Elliott SA, Truby H, Lee A, Harper C, Abbott RA, Davies PS. Associations of body mass index and waist circumference with: energy intake and percentage energy from macronutrients, in a cohort of Australian children. *Nutr J.* 2011; **10**: 58.
  21. Ortega RM, Requejo AM, Andres P, Lopez-Sobaler AM, Redondo R, Gonzalez-Fernandez M. Relationship between diet composition and body mass index in a group of Spanish adolescents. *Br J Nutr.* 1995; **74**: 765 – 773.
  22. Trichopoulou A, Gnardellis C, Benetou V, Lagiou P, Bamia C, Trichopoulos D. Lipid, protein and carbohydrate intake in relation to body mass index. *Eur J Clin Nutr.* 2002; **56**: 37 – 43.
  23. Sunehag AL, Toffolo G, Treuth MS, Butte NF, Cobelli C, Bier DM, et al. Effects of dietary macronutrient content on glucose metabolism in children. *J Clin Endocrinol Metab.* 2002; **87**: 5168 – 5178.
  24. Sunehag AL, Toffolo G, Campioni M, Bier DM, Haymond MW. Effects of dietary macronutrient intake on insulin sensitivity and secretion and glucose and lipid metabolism in healthy, obese adolescents. *J Clin Endocrinol Metab.* 2005; **90**: 4496 – 4502.
  25. Aeberli I, Spinass GA, Lehmann R, l'Allemand D, Molinari L, Zimmermann MB. Diet determines features of the metabolic syndrome in 6- to 14-year-old children. *Int J Vitam Nutr Res.* 2009; **79**: 14 – 23.
  26. Azizi F, Ghanbarian A, Momenan AA, Hadaegh F, Mirmiran P, Hedayati M, et al. Prevention of non-communicable disease in a population in nutrition transition: Tehran Lipid and Glucose Study phase II. *Trials.* 2009; **10**: 5.
  27. Mirmiran P, Esfahani FH, Mehrabi Y, Hedayati M, Azizi F. Reliability and relative validity of an FFQ for nutrients in the Tehran lipid and glucose study. *Public Health Nutr.* 2010; **13**: 654 – 662.
  28. Azizi F, Madjid M, Rahmani M, Emami H, Mirmiran P, Hadjipour R. Tehran Lipid and Glucose Study (TLGS): rationale and design. *IJEM.* 2000; **2**: 77 – 86.
  29. Ghaffarpour M, Houshiar-Rad A, Kianfar H. *The Manual for Household Measures, Cooking Yields Factors and Edible Portion of Food.* Keshaverzi press; 1999.
  30. Azar M, Sarkisian E. *Food Composition Table of Iran.* Tehran: National Nutrition and Food Research Institute. Shahid Beheshti University Press; 1980.
  31. U.S. Department of Agriculture and U.S. Department of Health and Human Services. *Dietary Guidelines for Americans, 2010.* 7th ed. Washington, DC: U.S. Government Printing Office; 2010.
  32. Taleban f, Eamayili M. *Glycemic index of Iranian foods.* Institute of Nutrition and Food Research, Shahid Beheshti University; 1999.
  33. Atkinson FS, Foster-Powell K, Brand-Miller JC. International tables of glycemic index and glycemic load values: 2008. *Diabetes Care.* 2008; **31**: 2281 – 2283.
  34. Cook S, Weitzman M, Auinger P, Nguyen M, Dietz WH. Prevalence of a metabolic syndrome phenotype in adolescents: findings from the third National Health and Nutrition Examination Survey, 1988–1994. *Arch Pediatr Adolesc Med.* 2003; **157**: 821 – 827.
  35. Kelishadi R, Gouya MM, Ardalan G, Hosseini M, Motaghian M, Delavari A, et al. First reference curves of waist and hip circumferences in an Asian population of youths: CASPIAN study. *J Trop Pediatr.* 2007; **53**: 158 – 164.
  36. 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 – 576.
  37. Genuth S, Alberti KG, Bennett P, Buse J, Defronzo R, Kahn R, et al. Follow-up report on the diagnosis of diabetes mellitus. *Diabetes Care.* 2003; **26**: 3160 – 3167.
  38. Alberti KG, Eckel RH, Grundy SM, Zimmet PZ, Cleeman JI, Donato KA, et al. Harmonizing the metabolic syndrome: a joint interim statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity. *Circulation.* 2009; **120**: 1640 – 1645.
  39. Delavari A, Forouzanfar MH, Alikhani S, Sharifian A, Kelishadi R. First nationwide study of the prevalence of the metabolic syndrome and optimal cutoff points of waist circumference in the Middle East: the national survey of risk factors for noncommunicable diseases of Iran. *Diabetes Care.* 2009; **32**: 1092 – 1097.
  40. Kelishadi R, Ardalan G, Gheiratmand R, Adeli K, Delavari A, Majdzadeh R. Paediatric metabolic syndrome and associated anthropometric indices: the CASPIAN Study. *Acta Paediatr.* 2006; **95**: 1625 – 1634.
  41. Nelson LH, Tucker LA. Diet composition related to body fat in a multivariate study of 203 men. *J Am Diet Assoc.* 1996; **96**: 771 – 777.
  42. Tucker L, Kano MJ. Dietary fat and body fat: a multivariate study of 205 adult females. *Am J Clin Nutr.* 1992; **56**: 616 – 622.
  43. Elliott SA, Truby H, Lee A, Harper C, Abbott RA, Davies PS. Associations of body mass index and waist circumference with: energy intake and percentage energy from macronutrients, in a cohort of Australian children. *Nutr J.* 2011; **10**: 1 – 7.
  44. Aeberli I, Spinass GA, Lehmann R, Molinari L, Zimmermann M. Diet determines features of the metabolic syndrome in 6-to 14-year-old children. *Int J Vitam Nutr Res.* 2009; **79**: 14 – 23.
  45. Casazza K, DULIN KEITA A, Gower BA, Fernández JR. Relationships between reported macronutrient intake and insulin dynamics in a multi-ethnic cohort of early pubertal children. *Int J Pediatr Obes.* 2009; **4**: 249 – 256.
  46. Gillis L, Kennedy L, Gillis A, Bar-Or O. Relationship between juvenile obesity, dietary energy and fat intake and physical activity. *Int J Obes Relat Metab Disord.* 2002; **26**: 458.
  47. Atkin LM, Davies PS. Diet composition and body composition in pre-school children. *Am J Clin Nutr.* 2000; **72**: 15 – 21.
  48. Gazzaniga JM, Burns TL. Relationship between diet composition and body fatness, with adjustment for resting energy expenditure and physical activity, in preadolescent children. *Am J Clin Nutr.* 1993; **58**: 21 – 28.
  49. Hassapidou M, Fotiadou E, Maglara E, Papadopoulou SK. Energy intake, diet composition, energy expenditure, and body fatness of adolescents in northern Greece. *Obesity (Silver Spring).* 2006; **14**: 855 – 862.
  50. Seneff S, Wainwright G, Mascitelli L. Is the metabolic syndrome caused by a high fructose, and relatively low fat, low cholesterol diet? *Arch Med Sci.* 2011; **7**: 8 – 20.