Prediction of metabolic syndrome by a high intake of energy-dense nutrient-poor snacks in Iranian children and adolescents

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BACKGROUND: Our aim was to investigate the relationship between metabolic syndrome (MetS) and energy-dense nutrient-poor solid snacks intakes during 3.6 y of follow-up among children and adolescents.

METHOD: This population-based longitudinal study was conducted within the framework of the Tehran Lipid and Glucose Study, on 424 MetS free subjects, aged 6–18 y. Data on consumption of energy-dense nutrient-poor solid snacks, sweet and salty snacks, were collected at baseline (2006–2008). Logistic regression, adjusted for age, sex, total energy intake, physical activity, dietary fiber, family history of diabetes, and body mass index, was used to assess the relationship between snacks and incident MetS.

RESULTS: After adjustment for confounders, compared with the lowest quartile of total energy-dense nutrient-poor solid snacks, odds ratio of incident MetS in the highest quartile was 3.04 (95% confidence interval (CI): 1.11–8.49); for sweet snacks this was 2.88 (95% CI: 1.00–8.32), and for salty ones it was 2.85 (95% CI: 1.09–7.43). The risk of incident hypertension in the highest, compared with the lowest quartile of total and salty snacks, was 2.99 (95% CI: 1.00–8.93) and 3.35 (95% CI: 1.10–10.17), respectively.

CONCLUSION: Energy-dense nutrient-poor solid snacks, both salty and sweet, may have undesirable effects on the incidence of MetS, with salty snacks having the potential to increase risk of incident hypertension in children and adolescents as well.

Children and adolescents with metabolic syndrome (MetS) are at increased risk of many clinical conditions in adulthood, including chronic low-grade inflammation, oxidative stress, hypertension, dyslipidemia, polycystic ovary syndrome, nonalcoholic fatty liver disease, and certain forms of cancer (1). According to the International Diabetes Federation, the global prevalence of MetS in children is increasing (2), which has been attributed mainly to nutrition transition, i.e., a shift of dietary habits from the traditional, toward a more Western way of life (3). Major changes in snacking patterns have been observed, highlighting the marked increase in the contribution of snacks to total energy and saturated fat intake, in particular among children and adolescents (4).

Snacking patterns are usually identified based on the type of snack or the time when the snack was eaten (5). A recent review of current evidence on snack consumption and weight status reported data available to the controversial due to use of different definitions for snacking patterns and types of food that constituted snacks (4). According to their type, snack foods are categorized into two food groups, including energy-dense nutrient-poor (e.g., potato chips, chocolates, cakes, or biscuits) and low-energy high-nutrient (e.g., fruit or milk) snacks (6). Based on the snacking definition, energy-dense nutrient-poor snacks were associated with increased risk of obesity (7), whereas, in adolescents from Greece, no relationship was found between different levels of consumption and MetS and cardiovascular risk factors (8). Unlike previous studies, when snacking pattern was defined as any food consumed between regular meals, both (healthy and unhealthy) has been reported to be inversely associated with overweight and abdominal obesity (9).

Energy-dense nutrient-poor snacks, which are rich sources of simple sugars, sodium, and saturated and trans fatty acids, are associated with MetS in adults (10). Excessive amounts of sweeteners, such as sucrose in snacks, may contribute to increased energy intake, raise the glycemic indices, induce lipogenesis and β-cell dysfunction, and increase obesity and metabolic disorders (11,12).

Although recent review has addressed the potential implications of snacking patterns for weight status (4), the contribution of energy-dense nutrient-poor snacks to metabolic abnormalities among child and adolescent populations in a longitudinal design study has not yet been fully elucidated. Therefore, this study was designed to describe the quantities of energy-dense nutrient-poor solid snacks among Iranian children and adolescents, aged 6–18 y, and to examine whether consumption of snacks, salty and sweet, was associated with incident MetS and its components after a mean follow up of 3.6 y.

RESULTS

Mean (SD) age and body mass index (BMI) were 13.6 (3.7) y and 20.0 (3.8) kg/m², respectively, and mean intakes of sweet and salty snacks were 41.2 ± 61.2 and 20.3 ± 31.4 g/d, respectively. Among 424 subjects (180 boys and 244 girls), with a mean follow-up of >3.6 y (range 2.31–4.87), there were 45 documented cases of MetS, respectively, with a cumulative incidence of 11%. There was an eightfold difference in median intake of energy-dense nutrient-poor solid snacks between the highest and lowest quartiles of the study population (12 vs. 104 g/d for total snacks). The contribution of energy-dense nutrient-poor solid snacks to total energy intake was 15% with a mean and median of 61.7 and 39.8 g/d, respectively. Baseline characteristics, except for age, were not significantly different between subjects followed up and those missed to follow-up (data not shown). The mean (SD) age of subjects missed

to follow-up was higher than those followed (14.9 ± 3.4 vs. 13.6 ± 3.6 y, P < 0.05).

Characteristics of study children and adolescent participants according to quartiles of energy-dense nutrient-poor snack consumption are shown in **Table 1**. Participants in higher snack quartiles were younger, had higher waist circumference (WC), systolic blood pressure (SBP), diastolic blood pressure (DBP), and fasting plasma glucose (FPG), and consumed more simple sugars, fructose, total fat, saturated fat, monounsaturated fatty acids, and energy. Consumption of carbohydrates, polyunsaturated fatty acids, and protein decreased by higher quartiles of snacks intake.

The risk of incident MetS and its components according to quartiles of energy-dense nutrient-poor solid snacks are given in **Table 2**. In the fully adjusted model, in comparison with the lowest quartile subjects, those in the highest quartile of

Table 1. Baseline characteristics of children and adolescents according to quartiles of total energy-dense nutrient-poor solid snacks consumption: Tehran Lipid and Glucose Study

	Energy-dense nutrient-poor solid snacks				P for trend[a]
	Q1 (n = 106)	Q2 (n = 106)	Q3 (n = 106)	Q4 (n = 106)	
Median (g/d)	12.4	31.3	55.3	104.4	
Age (y)	14.1 ± 3.73	13.7 ± 3.86	13.4 ± 3.86	13.0 ± 3.36	0.026
Girls (%)	59	63	59	47	0.092
SBP (mm Hg)	96.9 ± 12.4	97.2 ± 11.3	98.3 ± 11.0	99.4 ± 11.9	<0.001
DBP (mm Hg)	63.9 ± 10.62	64.6 ± 8.6	65.8 ± 9.70	66.3 ± 6.67	<0.001
TGs (mg/dl)	82.0 (62.2–100.0)	79.0 (64.0–105.0)	77.0 (63.0–105.0)	87.5 (63.0–111.2)	0.304
FPG (mg/dl)	84.3 ± 6.02	84.5 ± 6.04	85.1 ± 6.51	85.9 ± 5.93	0.035
HDL-C (mg/dl)	45.1 ± 10.5	45.0 ± 10.2	46.4 ± 11.5	46.7 ± 10.1	0.106
WC (cm)	66.7 ± 10.7	68.4 ± 9.1	70.14 ± 11.2	72.25 ± 11.8	0.001
Weight (kg)	50.6 ± 16.5	47.9 ± 14.5	46.6 ± 16.0	48.7 ± 16.1	0.309
BMI (kg/m²)	19.3 ± 3.8	19.5 ± 3.5	20.2 ± 4.1	20.5 ± 4.0	0.320
Low physical activity (%)	65	62	70	58	0.721
Dietary factors					
Total energy intake (kcal)	1959 ± 916	2150 ± 731	2283 ± 1010	2542 ± 1646	<0.001
Energy intake to EER ratio	1.1 ± 0.6	1.2 ± 0.4	1.5 ± 0.6	1.9 ± 1.0	<0.001
Energy-dense nutrient-poor solid snack (% energy)	3.0 ± 1.6	6.6 ± 2.6	9.6 ± 3.8	15.5 ± 9.3	<0.001
Carbohydrate (% energy)	57.6 ± 8.9	57.7 ± 6.3	57.0 ± 7.1	55.9 ± 6.8	0.016
Simple sugar (g)	87.6 ± 64.7	105.2 ± 58.7	125.3 ± 85.7	153.9 ± 101.3	<0.001
Fructose (g)	11.1 ± 11.9	14.9 ± 9.0	17.2 ± 9.5	20.0 ± 17.6	<0.001
Dietary fiber (g/1,000 kcal)	14.6 ± 6.7	14.7 ± 6.0	14.7 ± 6.2	13.7 ± 4.2	0.287
Total fat (% energy)	30.0 ± 8.1	31.2 ± 5.8	32.3 ± 6.4	34.8 ± 6.7	<0.001
SFA (% energy)	9.5 ± 3.6	10.3 ± 3.4	10.8 ± 3.1	11.9 ± 2.7	<0.001
MUFA (% energy)	10.3 ± 3.3	10.4 ± 2.1	11.2 ± 2.5	11.9 ± 2.8	<0.001
PUFA (% energy)	7.3 ± 2.5	6.3 ± 2.0	6.0 ± 1.7	5.5 ± 2.4	<0.001
Protein (% energy)	13.5 ± 3.1	13.3 ± 1.7	12.9 ± 2.6	12.0 ± 2.3	<0.001
Sodium (mg)	4430 ± 629	5817 ± 499	5700 ± 583	5809 ± 1488	0.329

Data are represented as mean and SD or median (IQR 25–75) for continuous variables and as percentages for categorically distributed variables.
BMI, body mass index; DBP, diastolic blood pressure; EER, estimated energy requirement; FPG, fasting plasma glucose; HDL-C, high-density lipoprotein cholesterol; IQR, interquartile range; MUFA, monounsaturated fatty acid; PUFA, polyunsaturated fatty acid; SBP, systolic blood pressure; SFA, saturated fatty acid; TG, triglyceride; WC, waist circumference.
[a]Linear regression and chi-square test were used for continuous and categorical variables, respectively.

Table 2. Multivariable-adjusted ORs (95% CIs) for incidence of MetS and its component by quartiles of energy-dense nutrient-poor solid snack intakes in children and adolescents during a 3.6-y follow-up

	Energy-dense nutrient-poor solid snacks				P for trend[a]
	Q1	Q2	Q3	Q4	
Median (g/d)	12.4	31.3	55.3	104.4	
MetS (n)	106	106	106	106	
Model 1	1.00	1.00 (0.34–2.98)	1.98 (0.74–5.29)	3.03 (1.10–8.30)	0.023
Model 2	1.00	1.04 (0.34–3.01)	2.04 (0.76–5.47)	3.04 (1.11–8.49)	0.034
Low HDL-C (n)	72	73	73	72	
Model 1	1.00	0.84 (0.29–2.49)	0.70 (0.23–2.16)	0.58 (0.17–2.01)	0.327
Model 2	1.00	0.83 (0.28–2.45)	0.71 (0.22–2.17)	0.49 (0.14–1.76)	0.288
Abdominal obesity (n)	82	82	81	82	
Model 1	1.00	1.32 (0.55–3.15)	1.82 (0.79–4.21)	1.67 (0.69–4.05)	0.271
Model 2	1.00	0.93 (0.36–2.37)	1.85 (0.76–4.51)	1.28 (0.50–3.28)	0.262
Hypertension (n)	110	110	109	110	
Model 1	1.00	1.24 (0.36–4.29)	2.31 (0.76–6.95)	3.14 (1.07–9.23)	0.057
Model 2	1.00	1.18 (0.34–4.12)	2.54 (0.83–7.68)	2.99 (1.00–8.93)	0.045
High FPG (n)	119	119	119	119	
Model 1	1.00	0.54 (0.22–1.31)	0.73 (0.31–1.71)	0.95 (0.38–2.37)	0.505
Model 2	1.00	0.54 (0.22–1.32)	0.74 (0.32–1.75)	0.96 (0.38–2.38)	0.445
High TGs (n)	86	87	87	87	
Model 1	1.00	1.03 (0.39–2.68)	0.88 (0.32–2.42)	0.69 (0.21–2.30)	0.220
Model 2	1.00	1.03 (0.39–2.71)	0.92 (0.34–2.60)	0.72 (0.22–2.42)	0.214

Model 1: Adjusted for age, sex, total energy intake, physical activity, dietary fiber, and family history of diabetes.
Model 2: Adjusted for model 1 variables plus BMI.
BMI, body mass index; CI, confidence interval; FPG, fasting plasma glucose; HDL-C, high-density lipoprotein cholesterol; MetS, metabolic syndrome; OR, odds ratio; TG, triglyceride.
[a]Based on logistic regression model using the median values for quartile of snack estimates as a continuous variable

snacks consumption had increased risk of incident MetS (odds ratio (OR): 3.04; 95% confidence interval (CI): 1.11–8.49, P for trend = 0.034) and hypertension (OR: 2.99; 95% CI 1.00–8.93, P for trend = 0.045).

The ORs for incidence of MetS and its components according to quartiles of sweet and salty snack consumption are shown in **Table 3**; subjects in the highest quartile of sweet and salty snack consumption had increased risk of incident MetS, compared with those in the lowest, after adjustment for confounders ((OR: 2.88; 95% CI: 1.00–8.32, P for trend = 0.024) and (OR: 2.85; 95% CI: 1.09–7.43, P for trend = 0.013), respectively). Participants in the highest quartile of salty snacks showed an increased risk of incident hypertension (OR: 3.35; 95% CI: 1.10–10.17; P for trend = 0.046), in comparison with those in the lowest.

DISCUSSION

In this study, energy-dense nutrient-poor solid snack consumption, both sweet and salty, increased the risk of incident MetS, whereas intake of salty snacks was accompanied by increased risk of incident hypertension in children and adolescents, associations, which both remained significant after considering potential confounders, i.e., age, sex, total energy intake, physical activity, dietary fiber, family history of diabetes, and BMI.

Studies conducted in pediatrics investigating the relationship between dietary snacks and cardiometabolic risk factors are limited and their results are debatable (7–9,13); some indicate that snacks are associated with unfavorable cardiovascular disease risk factors (7,13), while others failed to establish any correlation or showed inverse correlations (8,9). A positive association between blood pressure and the frequency of consumption of salty snack foods was found with 50% of daily salt intake from salty snacks (13). Middle-school Italian adolescents also showed higher prevalence of overweight and obesity with higher frequencies and calorie intakes of daily snacks (7), findings in contrast to those among Greek adolescents with an average consumption of 90 g/d snacks, showing no significant association with MetS (8). In Australia, a study extracting dietary patterns of adolescents showed that participants with high scores of a Western dietary pattern, including sweet and salty snacks, were significantly associated with a greater risk of MetS (14). In our study, in particular salty snack consumption was positively associated with hypertension, even after controlling for BMI, results supported by observational and interventional studies showing that higher intakes of salt increase hypertension (13,15).

The association between energy-dense nutrient-poor solid snack consumption and MetS in adolescents can be explained by several factors. Associations of snack intakes with MetS and

Table 3. Multivariable-adjusted ORs (95% CIs) for incidence of MetS by quartiles of sweet and salty snacks intake in children and adolescents during a 3.6-y follow-up

	Intakes				P for trend[a]
	Q1	Q2	Q3	Q4	
Median sweet snacks (g/d)	7	19.1	34.6	72.8	
MetS (n)	106	106	106	106	
Model 1	1.00	1.42 (0.46–4.30)	2.29 (0.81–6.50)	2.72 (0.96–7.73)	0.031
Model 2	1.00	1.42 (0.46–4.32)	2.35 (0.82–6.73)	2.88 (1.00–8.32)	0.024
Low HDL-C (n)	72	73	73	72	
Model 1	1.00	1.10 (0.54–2.24)	1.15 (0.55–2.41)	1.06 (0.48–2.41)	0.133
Model 2	1.00	1.11 (0.54–2.26)	1.17 (0.55–2.44)	1.08 (0.49–2.37)	0.156
Abdominal obesity (n)	82	82	81	82	
Model 1	1.00	0.57 (0.26–1.26)	1.03 (0.50–2.13)	0.56 (0.25–1.27)	0.215
Model 2	1.00	0.54 (0.22–1.31)	1.04 (0.45–2.39)	0.59 (0.24–1.45)	0.307
Hypertension (n)	110	110	109	110	
Model 1	1.00	1.27 (0.38–4.23)	2.49 (0.82–7.50)	2.05 (0.67–6.30)	0.126
Model 2	1.00	1.17 (0.35–3.93)	2.49 (0.82–7.59)	2.18 (0.70–6.81)	0.141
High FPG (n)	119	119	119	119	
Model 1	1.00	0.70 (0.30–1.63)	1.19 (0.52–2.69)	0.87 (0.35–2.15)	0.814
Model 2	1.00	0.70 (0.30–1.62)	1.18 (0.52–2.68)	0.87 (0.35–2.16)	0.836
High TGs (n)	86	87	87	87	
Model 1	1.00	0.93 (0.37–2.32)	0.47 (0.15–1.47)	0.78 (0.27–2.27)	0.336
Model 2	1.00	0.92 (0.37–2.28)	0.49 (0.16–1.52)	0.87 (0.29–2.58)	0.520
Median Salty snacks (g/d)	2.6	6.6	16.8	41.4	
MetS (n)	106	106	106	106	
Model 1	1.00	1.04 (0.37–2.80)	1.73 (0.53–5.65)	2.52 (1.00–6.35)	0.012
Model 2	1.00	1.02 (0.37–2.77)	1.71 (0.52–5.62)	2.85 (1.09–7.43)	0.013
Low HDL-C (n)	72	73	73	72	
Model 1	1.00	0.73 (0.22–2.34)	0.80 (0.27–2.40)	0.68 (0.20–2.24)	0.421
Model 2	1.00	0.77 (0.23–2.50)	0.83 (0.23–2.50)	0.70 (0.21–2.32)	0.452
Abdominal obesity (n)	82	82	81	82	
Model 1	1.00	0.63 (0.29–1.37)	0.88 (0.43–1.82)	0.99 (0.46–2.16)	0.215
Model 2	1.00	0.61 (0.26–1.46)	0.78 (0.34–1.76)	0.72 (0.30–1.74)	0.307
Hypertension (n)	110	110	109	110	
Model 1	1.00	1.72 (0.53–5.59)	2.17 (0.71–6.61)	3.32 (1.10–10.04)	0.046
Model 2	1.00	1.84 (0.56–5.99)	2.27 (0.74–6.96)	3.35 (1.10–10.17)	0.046
High FPG (n)	119	119	119	119	
Model 1	1.00	0.47 (0.19–1.15)	0.89 (0.40–1.94)	1.16 (0.50–2.66)	0.200
Model 2	1.00	0.47 (0.19–1.16)	0.88 (0.40–1.93)	1.15 (0.50–2.66)	0.209
High TGs (n)	86	87	87	87	
Model 1	1.00	0.76 (0.27–2.09)	1.01 (0.39–2.62)	1.71 (0.62–4.70)	0.125
Model 2	1.00	0.78 (0.28–2.17)	1.02 (0.39–2.68)	1.76 (0.63–4.90)	0.117

Model 1: Adjusted for age, sex, total energy intake, physical activity, dietary fiber, and family history of diabetes.
Model 2: Adjusted for variables in model 1 plus BMI.
CI, confidence interval; FPG, fasting plasma glucose; HDL-C, high-density lipoprotein cholesterol; MetS, metabolic syndrome; OR, odds ratio; TG, triglyceride.
[a]Based on logistic regression model using the median values for quartile of sweet and salty snack estimates as a continuous variable.

its components were independent of energy intake and BMI, implying the potential of other snack constituents (fat, sugar, and salt) to predict MetS beyond BMI. Considering isocaloric levels, higher intakes of total simple sugars, fructose, total fat, and lower intakes of polyunsaturated fatty acids and protein may explain the observed associations, indicating that not only

is the quantity of dietary intake important but quality of dietary intake and the source of calorie intake are also crucial. Evidence has confirmed the individual roles of different types of fat and carbohydrate on cardiometabolic risk factors (16,17); He *et al.* (15) reported that British children, aged 4–18 y, showed an increase of 0.4 mm Hg in SBP with each 1 g/d intake of salt. A systematic review of environmental determinants of dietary behaviors, including attitudes, revealed that parental intake and parental education are undoubtedly associated with adolescents' intake (18). Physical, sociocultural, economic, and political factors in the school environment (school food policy and food prices) and neighborhood (availability and accessibility of foods in shops) are among other notable influential factors (18). Also, focusing on environmental level factors indicates that the major driving force for increases in noncommunicable diseases is a lifestyle encouraging unhealthy eating while overlooking physical activity (19,20).

A study in the United States evaluating snacking trends in children (21) reported that during the last three decades, snacking behavior has increased in children of all age groups, constituting 27% of the daily caloric intake. In the current study, energy-dense nutrient-poor solid snacks comprised >15% of total calorie intake, which was accompanied by higher intakes of total fat, simple sugars, and saturated fatty acids. A rise of energy-dense nutrient-poor solid snack consumption can have a number of reasons, such as environmental factors, including incorrect eating habits, family nutritional knowledge, TV publicizing, and their easy availability at school (22), all mainly attributed to the changes of dietary habits and a shift from the traditional toward a more Western way of life (23). In addition to their increased consumption, snacks are often also substituted for fruit and vegetable intakes, which are a part of low-energy high-nutrient diet (24).

During the cooking process of sweet snacks, large amounts of simple sugars are added, because of which these foods constitute rich sources of saturated and trans fatty acids; the high glycemic index of these sweet snacks hence causes a rise in blood sugar levels (25). Dietary glycemic index is associated with some cardiovascular disease risk factors, obesity, insulin resistance, and some components of MetS (11,26). Saturated and trans fatty acids cause an increase in expression and secretion of inflammatory cytokines, such as interleukin-6 and C-reactive protein (27,28). Persistent inflammation in the circulation disrupts metabolic homeostasis of the body and thus contributes to a family of disorders, including insulin resistance, glucose intolerance, hyperlipidemia, and hypertension, collectively known as metabolic syndrome (29).

Of our study limitations, the following need to be mentioned. First, data on the puberty status of the participants were not recorded, and we were not able to adjust puberty stage. Second, although research continues on determining a perfect site for WC assessment, for prediction of cardiovascular risk factors, WC was measured at the umbilicus level, however, almost all sites of WC measurements were accurate in predicting in general populations of children and adolescents (30,31). Third, since household measures were not available

for all food items in the food frequency questionnaire (FFQ), the standard US Department of Agriculture (USDA) serving sizes were applied as an alternative. Fourth, recall bias was also an inevitable problem when asking children to remember and report dietary intakes. Compared with the regular meals, children have more potential to forget the snacks they consumed may due to misreporting, food and drink items perceived as unhealthy are underreported more often than other foods, especially if the children are overweight (32–34). However, using well-trained interviewers, who are skilled in asking questions help subjects recall what they ate and also asking mothers about the type and quantity of meals and snacks, when children were unable to recall may help minimizing the memory limitations. Furthermore, we compensated for miss-reporting by using a valid and reliable FFQ and excluding over- and underreporters of energy intake. Again, we could not determine how many times per day the adolescents snacked, how much energy they consumed in each snack, when precisely they consumed snacks (during meals, e.g., potato chips and caramels, or between meals), and the setting, e.g., at home, at school, or in school neighborhoods, schools in which they snacked. The fifth limitation is that sugar sweetened beverages, including sugar sweetened carbonated soft drinks and fruit juice drinks, were not considered as energy-dense nutrient-poor snack in the analysis. Therefore, analysis focused only on energy-dense nutrient-poor solid snacks. Finally, despite controlling for various confounders in our analysis, residual confounding due to unknown or unmeasured confounders cannot be excluded. Our study had a prospective design and a population-based sample of participants and was adjusted for confounders such as lifestyle factors.

Conclusion

We found that high energy-dense nutrient-poor solid snack intakes, both salty and sweet, are associated with higher incidence of MetS and hypertension in children and adolescents, findings emphasizing the impact of consumption of large amounts and the composition of simple sugars, fructose, and fatty acids on the development of morbidity, independent of BMI.

METHODS
Subjects

Children and adolescents were selected from among participants of the Tehran Lipid and Glucose Study (TLGS), an ongoing prospective community-based investigation being conducted to determine the risk factors and prevent noncommunicable diseases by implementing and promoting healthy lifestyle (35). To summarize, 15,005 participants, aged ≥3 y, residents under the coverage of three medical health centers in District No. 13 of Tehran, underwent baseline examinations between 1999 and 2002. Every 3 y, TLGS study participants are invited to come to the "Lipid and Glucose Research Unit" to update their data on demographic, lifestyle, biochemical, clinical, and dietary measurements using pretested questionnaires and standard protocols. The baseline survey was a cross-sectional study conducted from 1999 to 2001, and surveys 2 (2002–2005), 3 (2006–2008), and 4 (2009–2011) were prospective follow-up surveys.

In the third survey of the TLGS (2006–2008), from among 12,523 participants examined, 4,920 were randomly selected for completing dietary assessments, based on their age and sex; of these, 3,462 agreed to participate and completed the FFQ. Of participants who agreed to

participate, 45.9, 15.8, 9.5, and 18.3% were males, were ≤18 y, were smokers, and had academic education, in comparison with 43.4, 18.9, 11.4, and 16.5% of participants who refused to complete the FFQ, respectively.

For the current study, from among 3,462 participants with completed dietary assessment, 621 individuals, aged 6–18 y, were included. We excluded 29 subjects who did not have complete data on physical activity and anthropometric and biochemical variables. Furthermore, six subjects who were over- or underreported were also excluded. To define over- and underreports, the reported energy intake was divided by the estimated energy requirement (EER; calculated according to equations proposed by the Institute of Medicine (36), who were not within the ±3SD range (those in the top and bottom 1% of the energy intake to EER ratio). Depending on the outcome variables under analysis, subjects who had MetS (*n* = 69), hypertension (*n* = 53), high triglycerides (TGs; *n* = 168), low high-density lipoprotein cholesterol (HDL-C; *n* = 242), high fasting glucose (*n* = 12), or abdominal obesity (*n* = 145) were also excluded at baseline for determining the incidence of MetS and its components. Some individuals fell into more than one exclusion category. After a mean 3.6 y of follow-up (2009–2011), eventually data of 424, 439, 347, 290, 476, and 327 participants remained for occurrence of MetS, hypertension, hypertriglyceridemia, low HDL-C, high FPG, and abdominal obesity, respectively (response rate was 86%).

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

Measurements

Using the Modifiable Activity Questionnaire, information on physical activity to calculate metabolic equivalent task minutes per week was collected. High reliability (97%) and moderate validity (49%) have been ascertained previously for the Persian translated Modifiable Activity Questionnaire in adolescents (37). Low level of physical activity was considered as metabolic equivalent task <600 min/wk.

Weight was measured, while participants were minimally clothed without shoes, using digital scales (Seca 707, Seca, Hanover, MD; range 0.1–150 kg) and was recorded to the nearest 100 g. Height was measured in a standing position without shoes, using a stadiometer, with shoulders in normal alignment. BMI was calculated as weight (kg) divided by square of height (m^2). WC was measured at the umbilicus, using a measuring tape without pressure to body surfaces and was recorded to the nearest 0.5 cm.

To measure blood pressure, the participants remained seated for 15 min when 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 documented.

Blood samples, at baseline and follow-up, were drawn between 7:00 and 9:00 AM from all study participants after 12–14 h of overnight fasting. All the blood analyses were done at the TLGS research laboratory on the day of blood collection. 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 TGs were assayed using an enzymatic colorimetric method with glycerol phosphate oxidase. These analyses were performed using commercial kits (Pars Azmoon, 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, 2.0 and 0.5% for HDL-C, and 1.6 and 0.6% for TGs, respectively.

Dietary Assessment

A valid and reliable 168-item semiquantitative FFQ (38–40) was used by trained dietitians, during face-to-face interviews, to evaluate the usual dietary intakes of participants at baseline. Participants were asked to report their consumption frequency of food items during the previous year on a daily, weekly, or monthly basis, and data were then converted to mean daily intakes. Portion sizes of consumed foods, which were reported in household measures, were specified according to the USDA standard portion sizes (e.g., apple, 1 medium; bread, 1 slice; dairy, 1 cup) and were then converted to grams. When using USDA portion sizes was not possible, household measures (e.g., beans, 1 tablespoon; chicken meat, 1 leg or wing; rice, 1 large or small plate) were used alternatively.

To study the reproducibility of the FFQ, 132 subjects completed a 168-item FFQ (FFQ1 and FFQ2) twice with a 14-month interval between FFQ1 and FFQ2, and to assess the validity, 12 dietary recalls were collected (1 each month) over the 1-y interval. Age- and energy-adjusted and deattenuated Spearman correlation coefficients used to assess validity of the FFQ for food groups were 0.44 and 0.37 in males and females, respectively; age- and energy-adjusted intraclass correlation coefficients, which reflect the reproducibility of food groups in the FFQ, were 0.52 and 0.57 in males and females, respectively (39).

As defined by Gregori *et al.* (5), snacks are categorized based on two main criteria: (i) the type of snack and (ii) the time when the snack was eaten (not consumed as part of breakfast, lunch, and dinner); in the current study, snacks were defined according to the first criteria, which included energy-dense nutrient-poor solid foods. Candies, chocolates, cookies, cakes, biscuits, confectionery, caramels, and traditional Iranian confectioneries, such as gaz, sohan, noghl, halva, Yazdi cakes, were all considered sweet snacks, and potato chips, popcorn, and puff (a corn snack or crisp coated with a mixture of cheese or cheese-flavored) were considered as salty ones. Total snack was the sum of sweet and salty snacks. These solid foods have high content of energy, added sugar, saturated fat, and salt. The association between sugar sweetened beverages and MetS among children and adolescents was investigated in another study, published recently (41). Sugar sweetened beverages were not included in snack consumption; nor were foods with high nutritional value, such as fruits, vegetables, and dairy products, considered as snacks.

Definitions

In children and adolescents, MetS was defined according to definition proposed by Cook *et al.* (42) as three or more of the following: WC ≥ 90th percentile for age and sex, according to national reference curves (43); SBP and DBP ≥ 90th percentile for sex, age, and height, from the National Heart, Lung, and Blood Institute's recommended cutoff points (44); FPG ≥ 100 mg/dl, according to the recommendations of American Diabetes Association (45); fasting TGs ≥ 110 mg/dl; and HDL-C < 40 mg/dl. In subjects, aged >18 y after follow-up, MetS was defined according to the joint interim statement (46) as the presence of any three of five risk factors of the following: (i) Abdominal obesity for women WC ≥ 91 cm and for men WC ≥ 89 cm, according to Iranians cutoff point (47); (ii) FPG ≥ 100 mg/dl or drug treatment; (iii) fasting TGs ≥ 150 mg/dl or drug treatment; (iv) fasting HDL-C < 50 mg/dl for women and <40 mg/dl for men or drug treatment; and (v) high blood pressure defined as SBP ≥ 130 mm Hg or DBP ≥ 85 mm Hg, or antihypertensive drug treatment.

Statistical Analysis

EER was calculated according to the equation proposed by Institute of Medicine (36), as follows:

For boys with BMIs between the 5th and 85th percentiles:

$$EER = 88.5 - 61.9 \times \text{age (y)} \times \text{physical activity} + \left[26.7 \times \text{weight (kg)} + 903 \times \text{height (m)} \right] + 25$$

For girls with BMIs between the 5th and 85th percentiles:

$$EER = 135.3 - 30.8 \times \text{age (y)} \times \text{physical activity} + \left[10 \times \text{weight (kg)} + 934 \times \text{height (m)} \right] + 25$$

For boys with BMIs > 85th percentile:

$$EER = 114 - 50.9 \times \text{age (y)} \times \text{physical activity} + \left[19.5 \times \text{weight (kg)} + 1,161.4 \times \text{height (m)} \right]$$

For girls with BMIs > 85th percentile:

$$EER = 389 - 41.2 \times \text{age (y)} \times \text{physical activity} + \left[15 \times \text{weight (kg)} + 701.6 \times \text{height (m)} \right]$$

Characteristics of subjects at baseline, according to quartiles of energy-dense nutrient-poor solid snack intakes, were expressed as mean and SD or median and interquartile range for continuous variables and as percentages for categorical variables. To investigate trend of variables according to the quartiles, linear regression and chi-square test were used for continuous and categorical variables, respectively. We analyzed the data of both the cohort that provided follow-up assessments and that of those lost at baseline. There were no significant differences in mean baseline anthropometric measurements and biochemical assessments.

Energy-dense nutrient-poor solid snacks, both sweet and salty, were divided into quartiles. Multiple logistic regression models were used to examine the association between MetS and its components in each quartile of snacks consumption. The OR and 95% CIs for the incidence of the MetS were calculated. The initial multivariable models were adjusted for age, sex, total energy intake, physical activity, dietary fiber, and family history of diabetes. Multivariable models were further adjusted for BMI. Although categories of snacks intake did not differ significantly with respect to sex and dietary fiber, we adjusted these potential confounding factors, because they significantly altered the risk estimates. Also for consistency to facilitate comparison with previous studies, these variables were adjusted.

Tests of linear trend were conducted by assigning the medians of intakes in quartiles treated as a continuous variable. Statistical analysis was performed using the Statistical Package for Social Sciences (version 15.0; SPSS, Chicago IL).

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