The association between low-carbohydrate diet score and metabolic syndrome among Iranian adults

Zohreh Sadat Sangsefidi[1,2,3] , Elnaz Lorzadeh[1,2], Azadeh Nadjarzadeh[1,2], Masoud Mirzaei[4] and Mahdieh Hosseinzadeh[1,2,*]

[1]Nutrition and Food Security Research Center, Shahid Sadoughi University of Medical Sciences, Yazd, Iran: [2]Department of Nutrition, School of Public Health, Shahid Sadoughi University of Medical Sciences, Yazd, Iran: [3]Department of Nutrition and Public Health, School of Public Health, North Khorasan University of Medical Sciences, Bojnurd, Iran: [4]Yazd Cardiovascular Research Centre, Shahid Sadoughi University of Medical Sciences, Yazd, Iran

Abstract

Objective: Assessing the relationship between low-carbohydrate diet (LCD) score and metabolic syndrome (Mets) in Iranian adults.
Design: Cross-sectional study
Setting: Yazd Health Study and Taghzieh Mardom-e-Yazd study.
Participants: Data of 2074 participants were used. Dietary intakes were assessed by a validated semi-quantitative FFQ. LCD score was calculated for each person by summing up the assigned scores to deciles of energy percentages from macronutrients. Mets was evaluated using National Cholesterol Education Program Adult Treatment Panel III. Eventually, association between LCD score and Mets was examined using logistic regression.
Results: Total Mets prevalence was approximately 40·5 %. After adjustment for confounders, subjects in the higher quartile of LCD score had a significant lower chance of Mets than lower quartile among all participants (Q4 *v.* Q1: OR: 0·68, 95 % CI (0·50, 0·92)) and separately in men (Q4 *v.* Q1: OR: 0·54, 95 % CI (0·34, 0·86)) and women (Q2 *v.* Q1: OR: 0·53, 95 % CI (0·34, 0·82)). Furthermore, more LCD adherence in men reduced abdominal obesity by 47 % (Q3 *v.* Q1: OR: 0·53, 95 % CI (0·28, 0·99)). A significant inverse relation was also observed between low HDL cholesterol and LCD score in all participants (Q4 versus Q1 OR: 0·74, 95% CI: 0·56–0·99) and separately in men (Q4 versus Q1 OR: 0·63, 95% CI: 0·40–0·98).
Conclusions: More adherence to LCD might be related to lower chance of Mets and some of its components such as low HDL-cholesterol and abdominal obesity specially in men. Further studies are required to confirm the findings.

Metabolic syndrome (Mets) clusters a number of metabolic complications which is characterised by obesity, hypertension, dyslipidemia, glucose intolerance and insulin resistance[1,2]. The prevalence of Mets in the developed and developing countries is growing. It is reported that Mets is present in 40 % of the adult population in the USA[3] and less than 25 % in European nations[4]. Various modifiable factors such as diet can be effective in preventing and management of Mets[5,6].

Carbohydrate is the main source of energy intake in the middle-eastern region including Iran and is being consumed through foods such as rice, potato and grains. Increasing in carbohydrate consumption is associated with the risks of CVD or other components of Mets by high intakes of energy and glycemic load[4,7]. However, most of these outcomes are controversial, for instance in a study, sugar and sweetened beverage consumption did not have any significant effect on Mets[8]. Therefore, investigating the effect of macronutrients intake within a dietary pattern can help evaluate the association between diet and diseases[9,10].

Dietary pattern assessment takes both the complexity and synergistic effect of the foods and nutrients that make up a diet into account[11–13]. Low-carbohydrate diet (LCD) is a diet with lower intakes of carbohydrate and higher consumption of fat and protein[9,10,14]. Studies suggest that higher carbohydrate intake is followed by lower HDL, hypertriglyceridemia and hyperinsulinemia[4,15,16]. Therefore, LCD may have protective effect against chronic diseases including MetS[7]. Limited

Corresponding author: Email hoseinzade.mahdie@gmail.com

studies have been conducted assessing the relation between LCD and Mets, or its components and the outcomes are inconsistent[1,7,17–21]. For example, it has been suggested in Shirani *et al.* study that LCD was not significantly associated with Mets in Iranian women[1] which is similar to the results of a recent Korean study that observed no significant relationship between this dietary pattern and Mets[22]. Furthermore, another study among Tehranian adults by Mirmiran *et al.* reported that LCD may in fact be associated with decreased risk of Mets and its components[7]. According to several studies, Iranians traditionally consume high portions of carbohydrate foods, especially refined grains (which have a high glycemic load and increase the energy intake) such as rice and potatoes or foods that consist of a lot of simple sugars; this high-carbohydrate diet could be the possible reason for the incidence or development of many cardiovascular risk factors[7,23–27].

As a conclusion, considering the growth in Mets prevalence, limited investigations assessing the association between LCD and Mets and inconsistencies in the achieved outcomes, this study aims to investigate the association between LCD and Mets in a sample of adult population in Yazd city, Iran.

Materials and methods

Study population and data collection

We used Yazd Health (YaHS) and Taghzieh Mardom-e-Yazd (TAMIZ) studies data in the current cross-sectional survey. These population-based cohort studies have been conducted in a large sample of adults (20–69 years old) in Yazd city, Iran. Adults (*n* 10 000) from 200 clusters were randomly selected from Yazd population based on residential postal codes via cluster sampling method. Yazd Nutrition Survey (locally known as TAMYZ in Persian) has evaluated dietary and supplements intakes of participants of YaHS by a validated FFQ. More details of these studies have been previously published[28]. Information on socio-demographic characteristics, smoking status, history of chronic disease, biochemical and physical activity evaluations and dietary assessment was collected using a validated questionnaire. Furthermore, anthropometric examinations were performed. In the current study, out of 3443 available cases with data on dietary intakes, biochemical assessment and Mets, some individuals were excluded according to the following exclusion criteria: having under- or over-reporting (total daily energy intake less than 800 or higher than 6500 kcal)[29], pregnancy, following a special diet, having a history of chronic disease such as CVD, diabetes and cancer. Eventually, 2074 participants were entered in the present research. This study was approved by the logical Ethics Committee. Written informed consents were also taken from all subjects.

Dietary assessment

Dietary intakes were evaluated via a validated FFQ consisting of 178 food items which was a modified version of a previously validated 168-item FFQ[28,30]. Ten additional questions relating to the consumption of Yazd-specific food items were added to the original 168-item FFQ[28,30]. Frequency and usual amount of food items intake were answered by participants, and eventually amounts of consumptions were converted to grams based on the guidelines of household scales[31].

Calculation of the low-carbohydrate diet score

For computing LCD score, first the participants were classified based on deciles of percentages of energy from carbohydrates, proteins and fats. For carbohydrate consumption, individuals in the lowest decile received 9 points, adults in the second decile received 8 points, and so on down to the subjects in the highest decile received 0 point. For fats and proteins intake, the assigned points to deciles were reversed so that individuals in the highest decile received 9 points and those in the lowest decile received 0 point. Finally, the assigned points to all macronutrients were summed up and LCD score was obtained. After calculation, LCD score ranged from 0 to 27 and the higher score showed more adherence to LCD dietary pattern (the lower carbohydrate intake and the higher protein and fat intake)[1,9]. Eventually, participants were classified according to quartiles of LCD score.

Metabolic syndrome definition

Mets definition was based on National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III)[32]. Subjects who had at least three of following criteria were considered as those with Mets: serum TAG ≥150 mg/dl, serum HDL-cholesterol <40 mg/dl for men and HDL-cholesterol < 50 mg/dl for women, fasting blood glucose ≥ 100 mg/dl, blood pressure ≥130/85 mmHg, and waist circumference ≥102 cm for men and >88 cm for women.

Anthropometric measurements

Weight was measured by Omron BF511 portable digital scale with the accuracy of 0·1 kg. Height was measured in a standing position by a tape measure on a straight wall to the nearest centimetre according to the standard method. BMI was also calculated by dividing the body weight (kg) by the square of height (m).

Physical activity assessment

Physical activity was examined via the Persian translated short form of the International Physical Activity Questionnaire (IPAQ). Eventually, the physical activity levels presented as metabolic equivalent (MET)[33,34].

Statistical analysis

Statistical analysis was performed by Statistical Package for Social Sciences (SPSS Corp., version 18). Kolmogorov–Smirnov test was used for assessing the normality of data. For the description of data, frequency and percent or median and interquartile range were performed. Comparing categorical and continuous variables were conducted via χ^2 or Kruskal–Wallis tests, respectively, based on the categories of LCD score.

Examination of relationship between adherence to LCD with Mets and its components among all participants and separately in men and women was performed by logistic regression analysis in various models. In the first model, we carried out the adjustments for history of chronic disease (hypercholesterolemia, brain disease, asthma, thyroid disorders, depression, Alzheimer's disease, blood coagulation disorders, arthritis and osteoporosis; yes/no); age (20–29, 30–39, 40–49, 50–59 and 60–69 years); marital status (single, married, widowed or divorced); education level (illiterate, high school, diploma and associated diploma, bachelors, masters and PhD); smoking status (never smoker, current smoker and ex-smoker); total energy intake (continues, kcal/d) and physical activity level (continues, MET/min/week). Further adjustment was conducted for BMI (continues, kg/m^2). P-value less than 0·05 was considered as statistical significant level.

Results

As demonstrated in Table 1, the general characteristics of participants across the quartiles of LCD scores are provided. Mets prevalence was estimated as 40·5 % among total population, and the prevalence across the quartiles of LCD was reported in Table 1. Those with higher LCD score were less likely to have Mets and more likely to be more active ($P < 0.05$). No other significant difference has been observed across the quartiles of LCD scores.

Table 2 provides selected food groups and nutrient intake across the quartiles of LCD scores. Participants in the highest quartile of the LCD score had increased intakes of vegetables, legumes, dairy products, red meat, poultry, fish, eggs, nuts and nutrients such as protein and fat in comparison to the lowest quartiles ($P < 0.05$). A significant difference was found across the quartiles of LCD scores for consumption of fruit, whole and refined grains and carbohydrate ($P < 0.05$), while no significant difference was observed in terms of total energy intake.

LCD score and Mets and its components

The OR for developing Mets and its components according to quartiles of the LCD score is presented in Table 3. After adjustment for various confounders such as history of chronic disease, age, marital status, education level, smoking status, total energy intake and physical activity level, it

was observed that individuals in the highest quartile of LCD score had 31 % significant lower chances of developing Mets than lowest quartile (OR: 0·69, 95 % CI (0·52, 0·92)). It remained significant even after further adjustment for BMI (OR: 0·68, 95 % CI (0·50, 0·92)). Similarly, the results based on the gender showed a significant decrease in odds of Mets in men in the highest quartiles of LCD score than lowest quartile (OR: 0·57, 95 % CI (0·37, 0·90)) after adjusting for potential confounders. Additional adjustment for BMI remained significant (OR: 0·54, 95 % CI (0·34, 0·86)). Moreover, in women, it was observed that the chance of Mets in the second quartile of LCD score was 41 % lower than those in the first quartile (OR: 0·59, 95 % CI (0·38, 0·90)) after adjustment for confounding variables. This association did not change after additional adjustment for BMI (OR: 0·53, 95 % CI (0·34, 0·86)). No other significant association has been found.

Higher LCD score in the third quartile in men reduced abdominal obesity significantly by 47 % after adjustment for all the confounders including BMI (OR: 0·53, 95 % CI (0·28, 0·99)). Furthermore, significant reduction in low HDL-cholesterol was observed in the highest quartile of LCD adherence compared to the first quartile in all participants (OR: 0·74, 95 % CI (0·56, 0·99)) and in men (OR: 0·63, 95 % CI (0·40, 0·98)) after adjusting for all the potential confounder variables.

Discussion

The present research showed a significant protective association between LCD score and odds of Mets after adjustment for potential confounding variables. Higher LCD score was also associated with lower chance of HDL-cholesterol in all participants and specifically men. Moreover, these health benefit effects were observed for abdominal obesity only in the male population.

Previous researches on the association of LCD score and the risk of Mets are limited[35–37]. Studies suggest that consumption of diets with high carbohydrate and less fat in patients with non-alcoholic fatty liver disease is associated with higher risk of Mets, obesity and type 2 diabetes in men[36,38,39]. Furthermore, observational studies in Korean[40,41], Japanese[42] and Chinese populations[43] show that high carbohydrate intake is associated with high levels of Mets and type 2 diabetes. In line with our results, a recent study among Iranian adults reported a significant association between LCD and Mets risk[7]. However, in contrast to our study, a study by Eslamian et al. did not report any significant relation between LCD score and Mets[44], and also Shirani et al. did not find any significant association between scores of LCD and Mets among Iranian women[1].

Our study found a significant inverse relation between LCD and abdominal obesity only in men. Similar to our results, one cross-sectional study by Jafari-Maram et al. in Iranian women showed no significant relationship

Table 1 General characteristics of participants according to quartiles of LCD score

		Quartiles of LCD score (total n 2074)				
	All (n) (n 2074)	Q1 (n 563)	Q2 (n 443)	Q3 (n 567)	Q4 (n 501)	
	n	%	%	%	%	P-value
Age (year)						
20–29	448	26·3 %	20·8 %	29·0 %	23·9 %	0·14
30–39	487	28·1 %	21·6 %	25·9 %	24·4 %	
40–49	521	22·8 %	22·3 %	29·9 %	25·0 %	
50–59	379	32·5 %	18·2 %	25·9 %	23·5 %	
60–69	227	28·2 %	26·4 %	22·9 %	22·5 %	
Gender						
Male	996	28·2 %	20·8 %	27·2 %	23·8 %	0·71
Female	1069	26·1 %	22·1 %	27·3 %	24·5 %	
Education						
Illiterate	415	29·4 %	21·0 %	23·4 %	26·3 %	0·16
Lower than high school diploma	632	27·4 %	21·4 %	29·1 %	22·2 %	
High school diploma or college	653	26·8 %	20·2 %	29·7 %	23·3 %	
University	355	24·2 %	24·2 %	24·2 %	27·3 %	
Smoking status						
Never smoker	1805	26·9 %	21·3 %	27·4 %	24·4 %	0·96
Current smoker	175	28·6 %	21·1 %	26·3 %	24·0 %	
Ex-smoker	37	18·9 %	24·3 %	29·7 %	27·0 %	
Marital status						
Single	224	26·8 %	21·0 %	28·6 %	23·7 %	0·86
Married	1775	27·3 %	21·5 %	26·8 %	24·3 %	
Widowed or divorced	69	24·6 %	17·4 %	34·8 %	23·2 %	
Mets						
Yes	840	29·0 %	20·6 %	28·5 %	21·9 %	*0·04
No	1138	25·2 %	22·4 %	26·2 %	26·2 %	
Abdominal obesity						
Yes	852	29·0 %	21·1 %	27·3 %	22·5 %	0·29
No	1201	25·7 %	21·7 %	27·1 %	25·4 %	
High blood pressure						
Yes	1386	27·3 %	27·8 %	23·4 %	0·46	
No	607	26·0 %	21·6 %	25·9 %	26·5 %	
Hyperglycemia						
Yes	594	28·4 %	18·8 %	26·9 %	25·9 %	0·25
No	1479	26·6 %	22·4 %	27·5 %	23·5 %	
Hypertriglyceridemia						
Yes	1293	27·4 %	20·3 %	28·5 %	23·8 %	0·32
No	781	26·8 %	23·0 %	25·5 %		
Low HDL-cholesterol						
Yes	729	28·0 %	21·4 %	28·3 %	22·4 %	0·52
No	1336	26·6 %	21·5 %	26·7 %	25·1 %	
BMI (kg/m²)						
Median	26·5	26·7	26·5	26·6	26·1	0·44
IQR	23·5–29·9	23·0–30·0	23·6–30·1	23·3–29·8	23·4–29·4	
Physical activity level (Met/h/week)						
Median	106·1	99·0	102·8	106·1	125·7	*0·04
IQR	35·4–183·1	31·3–166·4	35·4–184·3	41·3–191·1	42·4–192·9	

LCD, low-carbohydrate diet; IQR, interquartile range.
*Comparisons were performed using χ^2 or Kruskal–Wallis tests for categorical and continues variables, respectively.
$P < 0.05$ was considered as a significance level.
Data were presented as n (%) for categorical variables or median and IQR for continues variables.

between LCD and obesity[9]. However, contrary to our finding, a meta-analysis reported that carbohydrate intake did not have any effect on the risk of obesity[45]. Mixed results regarding the association between LCD and obesity are also reported[46–49] A limited number of studies have assessed the effects of LCD on abdominal fat loss and, therefore, the improvement in cardiovascular factors in both obese and none obese individuals[50]. As suggested by Brinkworth et al., LCD can decrease abdominal fat mass by approximately 30 %[51].

This study found a significant relationship between LCD score and OR of low HDL-cholesterol in all the participants and in men. Just like what has been mentioned above, previous investigations have shown controversial results. Several studies reported that despite a low-fat intake, a high-carbohydrate diet can positively associate with a low HDL-cholesterol level and an increased risk of Mets[20,41]. These findings similar to our results are also in accordance with previous Randomized clinical trial that indicated an improvement in levels of HDL-cholesterol after the

Table 2 Dietary intakes of participants according to quartiles of LCD score

	Quartiles of LCD score										
	All (*n* 2074)		Q1 (*n* 563)		Q2 (*n* 443)		Q3 (*n* 567)		Q4 (*n* 501)		
*Dietary intakes	Median	IQR	Median	IQR	Median	IQR	Median	IQR	Median	IQR	**P-value
Total energy (kcal/d)	2479·5	1868·3–3613·4	2412·8	1865·6–3744·0	2294·4	1800·1–3595·0	2431·8	1862·1–3514·1	2810·9	2037·2–3695·6	0·07
Carbohydrates (g/d)	337·6	257·7–496·2	380·4	289·5–634·1	331·5	260·3–541·6	330·1	250·3–463·7	304·6	219·0–403·4	**$P < 0.001$
Proteins (g/d)	98·7	73·9–136·9	82·1	65·5–113·8	90·7	70·9–123·0	101·9	79·6–134·9	129·8	93·3–180·5	**$P < 0.001$
Fats (g/d)	89·0	61·1–145·7	65·8	52·7–113·8	74·0	58·8–140·3	93·9	67·5–146·3	120·5	83·6–167·7	**$P < 0.001$
Whole grains (g/d)	60·1	25·2–93·4	82·7	26·9–122·2	74·4	30·2–95·7	56·6	23·0–92·3	44·2	20·4–87·1	**$P < 0.001$
Refined grains (g/d)	180·1	114·2–289·2	241·1	128·3–307·1	166·3	99·0–289·0	174·5	116·7–277·2	167·5	104·6–273·9	**$P < 0.001$
Vegetables (g/d)	210·8	146·5–340·6	193·8	133·3–322·7	196·0	142·2–317·0	230·1	155·2–339·0	239·2	154·5–383·3	**$P < 0.001$
Fruits (g/d)	420·4	272·7–705·6	496·7	315·7–833·4	413·9	293·3–667·6	401·9	255·6–654·6	373·7	226·3–655·2	**$P < 0.001$
Legumes (g/d)	32·5	22·2–51·7	27·3	20·0–46·1	33·2	23·2–53·7	33·7	23·1–52·0	34·6	24·4–53·4	**$P < 0.001$
Dairy products (g/d)	191·2	126·0–302·1	175·8	110·1–265·2	193·9	120·8–294·2	194·2	132·0–312·7	216·8	146·8–346·9	**$P < 0.001$
Red meat (g/d)	39·0	20·2–66·6	31·0	14·1–54·5	35·3	17·7–61·0	41·6	23·3–69·9	61·0	34·7–97·0	**$P < 0.001$
Poultry (g/d)	27·3	14·7–19·9	23·7	11·1–39·2	27·3	14·7–51·0	39·2	15·4–74·8	62·9	27·3–146·0	**$P < 0.001$
Fish (g/d)	9·4	3·5–19·9	5·6	2·4–14·3	7·0	3·6–15·2	10·6	3·7–28·6	10·0	3·5–24·1	**$P < 0.001$
Eggs (g/d)	17·2	8·0–51·5	17·2	4·0–25·7	17·2	4·0–51·5	25·7	8·6– 51·5	25·7	8·0–51·5	**$P < 0.001$
Nuts (g/d)	12·1	6·4–26·2	10·8	5·5–18·8	12·7	99·0–289·0	13·0	7·3–29·2	11·7	6·2–32·5	**$P < 0.001$

LCD, low-carbohydrate diet; IQR, interquartile range.
*Data were presented as median and IQR.
**Comparisons were performed using Kruskal–Wallis test.
P < 0·05 was considered as a significance level.

Table 3 Multivariable-adjusted OR for metabolic syndrome and its components across quartiles low-carbohydrate diet (LCD) score

	Quartiles of LCD score						
	Q1 (n 563)	Q2 (n 443)		Q3 (n 567)		Q4 (n 501)	
	OR (95 % CI)	OR	95 % CI	OR	95 % CI	OR	95 % CI
Metabolic syndrome							
Model 1							
All	Reference	0·81	0·61–1·09	0·95	0·72–1·26	*0·69	0·52–0·92
Men	Reference	0·94	0·60–1·46	0·84	0·56–1·27	*0·57	0·37–0·90
Women	Reference	*0·59	0·38–0·90	0·96	0·64–1·46	0·69	0·46–1·05
Model 2							
All	Reference	0·74	0·54–1·01	0·90	0·67–1·21	*0·68	0·50–0·92
Men	Reference	0·91	0·57–1·45	0·80	0·52–1·24	*0·54	0·34–0·86
Women	Reference	*0·53	0·34–0·82	0·94	0·62–1·44	0·74	0·48–1·12
Abdominal obesity							
Model 1							
All	Reference	0·94	0·70–1·27	0·98	0·74–1·30	0·83	0·62–1·12
Men	Reference	0·69	0·42–1·	0·72	0·45–1·15	0·82	0·51–1·32
Women	Reference	0·92	0·59–1·42	1·07	0·71–1·62	0·70	0·46–1·06
Model 2							
All	Reference	0·80	0·55–1·17	0·89	0·611·23	0·82	0·57–1·17
Men	Reference	0·61	0·31–1·20	*0·53	0·28–0·99	0·73	0·39–1·38
Women	Reference	0·79	0·46–1·33	1·07	0·65–1·77	0·79	0·48–1·29
High blood pressure							
Model 1							
All	Reference	0·96	0·70–1·32	1·14	0·85–1·54	0·80	0·59–1·09
Men	Reference	1·18	0·70–1·99	0·99	0·62–1·59	0·78	0·49–1·26
Women	Reference	0·80	0·52–1·23	1·28	0·84–1·94	0·86	0·57–1·29
Model 2							
All	Reference	0·92	0·66–1·27	1·12	0·83–1·53	0·82	0·60–1·11
Men	Reference	1·11	0·64–1·87	0·94	0·58–1·54	0·75	0·46–1·23
Women	Reference	0·77	0·50–1·20	1·29	0·85–1·97	0·91	0·60–1·39
Hyperglycemia							
Model 1							
All	Reference	0·84	0·61–1·16	0·86	0·63–1·16	1·11	0·78–1·43
Men	Reference	0·82	0·51–1·32	0·83	0·53–1·28	0·96	0·61–1·49
Women	Reference	0·85	0·54–1·34	0·91	0·59–1·40	1·14	0·74–1·76
Model 2							
All	Reference	0·82	0·59–1·14	0·86	0·63–1·16	1·09	0·80–1·49
Men	Reference	0·82	0·50–1·34	0·85	0·55–1·33	0·98	0·63–1·54
Women	Reference	0·82	0·52–1·30	0·89	0·57–1·38	1·19	0·77–1·84
Hypertriglyceridemia							
Model 1							
All	Reference	0·94	0·70–1·26	1·03	0·78–1·37	0·95	0·71–1·26
Men	Reference	1·06	0·70–1·61	0·96	0·65–1·41	0·81	0·54–1·20
Women	Reference	0·77	0·50–1·19	1·06	0·69–1·61	1·04	0·68–1·60
Model 2							
All	Reference	0·99	0·74–1·35	1·06	0·80–1·41	0·94	0·70–1·25
Men	Reference	1·10	0·72–1·70	0·98	0·66–1·47	0·82	0·55–1·24
Women	Reference	0·82	0·52–1·28	1·06	0·69–1·64	0·99	0·64–1·53
Low HDL-cholesterol							
Model 1							
All	Reference	0·86	0·64–1·15	0·91	0·69–1·19	*0·75	0·57–0·99
Men	Reference	0·82	0·53–1·29	1·01	0·67–1·52	0·64	0·41–1·01
Women	Reference	0·84	0·56–1·24	0·83	0·57–1·21	0·80	0·55–1·17
Model 2							
All	Reference	0·82	0·62–1·10	0·89	0·68–1·17	*0·74	0·56–0·99
Men	Reference	0·78	0·49–1·22	0·97	0·64–1·47	*0·63	0·40–0·98
Women	Reference	0·81	0·54–1·20	0·83	0·57–1·21	0·81	0·55–1·20

Model 1: Adjusted for history of chronic disease, age, marital status, education level, smoking status, total energy intake and physical activity level (MET/min/week).
Model 2: Model 1 + BMI.
*$P < 0.05$ was considered as a significance level.

administration a LCD[15,52]. Additionally, the recent Japanese[53] and Korean studies[22] have found that higher LCD scores had positive effects on HDL-cholesterol and dyslipidemia level, regardless of the food source. However, in contrast to our findings, in some studies that were conducted among Iranian adults, no significant association was reported between HDL-cholesterol and LCD score[1,7].

In the light of what has been mentioned above, multiple systematic review studies have shown that LCD score is negatively related to hypertension and low HDL-cholesterol[54,55].

Even though we did not observe any significant association between hypertension or any of the other components of Mets with LCD score in the present study which might be due to different study design (randomised clinical trial $v.$ cross-sectional study), carbohydrate proportion and population characteristics, most of the studies included in these systematic reviews were conducted in Western countries in which a LCD is defined differently[15,52].

In Iranian population, consuming a large portion of food with carbohydrate base such as grains, rice and potatoes accompanied by food containing simple sugar is very common which contribute to the incident or development of the cardiovascular risk factors[23–27]. In this study, LCD is defined as a relatively lower percentage of carbohydrate intake, accompanied by higher percentage of protein and fat intake, in which each macronutrient may affect the risk of Mets differently[33,34]. Subjects with high scores of LCD consume more food groups such as vegetables, legumes, dairy products, red and white meat (poultry and fish), and eggs and generally have higher intakes of protein and fat. This could be another possible explanation for the null association outcomes, since the high protein portion which consists of healthy foods such as poultry and fish inversely associates with Mets. On the other hand, the high amount of red and processed meat consumption has direct effects on the incident and development of Mets[37,56,57] and this can lead to neutral results. Therefore, our results are similar to Mediterranean dietary pattern which is rich in vegetables, fish, nuts and legumes and is indicated to reduce the risk of Mets[58]. In contrast, Western dietary pattern is characterised by the high consumption of carbohydrate such as sweet beverage and sugar that is majorly associated with greater odds of increased Mets components[59]. Moreover, the present study reports that participants in high quartiles of LCD score consume less amount of carbohydrate (which consist of whole and refined grains and fruit) in general. This outcome is similar to the findings of multiple studies that suggest individuals with lower intake of simple sugars such as fructose are less susceptible to cardiometabolic disorders including dyslipidemia, insulin resistance, high BP and obesity[60,61]. We also observed that higher scores of LCD were associated with increased intakes of dairy products as well which has further been suggested to be associated with lower risk of Mets[62]. Overall, it seems that participants with higher scores of LCD are less prone to various chronic diseases such as Mets.

With what has been mentioned above, it is reported that Mets is highly carbohydrate-intolerant[63]. Over consumption of carbohydrate is related to high plasma levels of glucose and insulin which is followed by insulin resistance and symptoms of Mets. Since dietary carbohydrate not only serves as a source of energy but also serves as a control element whether directly through glucose or fructose or indirectly as an insulin signalling agent, its decrease can ameliorate markers of Mets more efficiently than a low-fat diet[64]. Low-fat and high-carbohydrate diet are reported to exacerbate Mets[65]. Dietary fat has also a passive role in insulin resistance that contributes to down-regulation due to hyperinsulinemia[66]. Low intake of dietary carbohydrates resulted in decreased carbohydrates-induced insulin and causes the impaired regulation goback to normal levels[64]. Furthermore, LCD diet may be generally associated with lower fructose intake. Fructose consumption has a major role in epidemics of obesity, Mets and type 2 diabetes and is known to be the cause of hypertension, de novo lipogenesis, hepatic insulin resistance and adiposity[67–70]. Additionally, it is worth mentioning that high-carbohydrate diets and consumptions of foods with high glycemic index, especially fructose, can conduct rapid stimulation of lipogenesis, TAG accumulation, adipocyte hypertrophy and macrophage accumulation in adipose tissues that is associated with obesity[18,71]. High blood glucose, a result of high glycemic index foods consumption, is followed by an enhanced need to insulin secretion and consequently impairment in beta cells function and glucose metabolism which accompanied by counter-regulatory insulin secretion and then a number of metabolic disorders and chronic diseases such as Mets[70].

Several key strengths are needed to be taken into consideration. To the best of our knowledge, this is the first study that evaluated the association between LCD and Mets in a larger sample of Iranian adults with various confounders being controlled in different models. In the present study, a validated FFQ was also used which was based on a list of food items and list of specific foods that are commonly consumed in the study population. Moreover, dietary assessments were achieved by professional interviewers. Our study has several limitations: (i) the cross-sectional design does not show a causal relationship between LCD and Mets; therefore, more prospective studies are needed to be done to truly examine the effect of LCD on Mets in the Iranian population. Moreover, the subjects with Mets may have modified their diet towards improvement for reduction of disease complications due to cross-sectional nature of the study. However, we excluded the individuals with chronic disease history to decrease this issue; (ii) despite controlling for various confounders in our analyses, other confounding factors due to unknown or unmeasured confounders cannot be ignored; (iii) since dietary assessments in this study were based on FFQ, misclassification of study participants might be occurred; (iv) although socio-demographic characteristics of the population including age, gender, education, marital status and smoking status were evaluated, we did not assess economic status; and (v) it should be considered that the study participants were selected from municipal areas of Yazd city. Thus, the findings generalisation may be done with caution.

In conclusion, our findings suggest that adherence to LCD may be associated with lower chances of Mets and some of its component such as HDL-cholesterol levels and abdominal obesity in men. Further large-scale

researches, especially cohort studies, are highly recommended to clarify the nature of the observed associations.

Acknowledgements

References

1. Shirani F, Esmaillzadeh A, Keshteli AH *et al.* (2015) Low-carbohydrate-diet score and metabolic syndrome: an epidemiologic study among Iranian women. *Nutrition* **31**, 1124–1130.
2. Dandona P, Aljada A, Chaudhuri A *et al.* (2005) Metabolic syndrome: a comprehensive perspective based on interactions between obesity, diabetes, and inflammation. *Circulation* **111**, 1448–1454.
3. Ford ES, Li C & Zhao G (2010) Prevalence and correlates of metabolic syndrome based on a harmonious definition among adults in the US. *J Diabetes* **2**, 180–193.
4. Shirani F & Azadbakht L (2011) The association between carbohydrate intake and metabolic syndrome. *J Isfahan Med Sch* **29**, 1–11.
5. Kimokoti R & Brown L (2011) Dietary management of the metabolic syndrome. *Clin Pharmacol Ther* **90**, 184–187.
6. Reaven GM (2000) Diet and syndrome X. *Curr Atheroscler Rep* **2**, 503–507.
7. Mirmiran P, Asghari G, Farhadnejad H *et al.* (2017) Low carbohydrate diet is associated with reduced risk of metabolic syndrome in Tehranian adults. *Int J Food Sci Nutr* **68**, 358–365.
8. Lorzadeh E, Sangsefidi ZS, Mirzaei M *et al.* (2020) Dietary habits and their association with metabolic syndrome in a sample of Iranian adults: a population-based study. *Food Sci Nutr* **8**, 6217–6225.
9. Jafari-Maram S, Daneshzad E, Brett NR *et al.* (2019) Association of low-carbohydrate diet score with overweight, obesity and cardiovascular disease risk factors: a cross-sectional study in Iranian women. *J Cardiovasc Thorac Res* **11**, 216.
10. Hite AH, Berkowitz VG & Berkowitz K (2011) Low-carbohydrate diet review: shifting the paradigm. *Nutr Clin Pract* **26**, 300–308.
11. Kant AK (1996) Indexes of overall diet quality: a review. *J Am Diet Assoc* **96**, 785–791.
12. Millen BE, Quatromoni PA, Pencina M *et al.* (2005) Unique dietary patterns and chronic disease risk profiles of adult men: the Framingham nutrition studies. *J Am Diet Assoc* **105**, 1723–1734.
13. Millen BE, Quatromoni PA, Copenhafer DL *et al.* (2001) Validation of a dietary pattern approach for evaluating nutritional risk: the Framingham nutrition studies. *J Am Diet Assoc* **101**, 187–194.
14. Sangsefidi ZS, Salehi-Abarghouei A, Sangsefidi ZS *et al.* (2021) The relation between low carbohydrate diet score and psychological disorders among Iranian adults. *Nutr Metabol* **18**, 1–9.
15. Hu T, Mills KT, Yao L *et al.* (2012) Effects of low-carbohydrate diets *v.* low-fat diets on metabolic risk factors: a meta-analysis of randomized controlled clinical trials. *Am J Epidemiol* **176**, S44–S54.
16. Volek JS, Sharman MJ & Forsythe CE (2005) Modification of lipoproteins by very low-carbohydrate diets. *J Nutr* **135**, 1339–1342.
17. Ainsworth BE, Haskell WL, Whitt MC *et al.* (2000) Compendium of physical activities: an update of activity codes and MET intensities. *Med Sci Sports Exerc* **32**, S498–S504.
18. Yang EJ, Chung HK, Kim WY *et al.* (2003) Carbohydrate intake is associated with diet quality and risk factors for cardiovascular disease in US adults: NHANES III. *J Am Coll Nutr* **22**, 71–79.
19. Silva FM, Steemburgo T, de Mello VD *et al.* (2011) High dietary glycemic index and low fiber content are associated with metabolic syndrome in patients with type 2 diabetes. *J Am Coll Nutr* **30**, 141–148.
20. Choi H, Song S, Kim J *et al.* (2012) High carbohydrate intake was inversely associated with high-density lipoprotein cholesterol among Korean adults. *Nutr Res* **32**, 100–106.
21. Hu T, Mills KT, Yao L *et al.* (2012) Effects of low-carbohydrate diets *v.* low-fat diets on metabolic risk factors: a meta-analysis of randomized controlled clinical trials. *Am J Epidemiol* **176**, S44–S54.
22. Ha K, Joung H & Song Y (2018) Low-carbohydrate diet and the risk of metabolic syndrome in Korean adults. *Nutr Metabol Cardiovasc Dis* **28**, 1122–1132.
23. Liu S, Willett WC, Stampfer MJ *et al.* (2000) A prospective study of dietary glycemic load, carbohydrate intake, and risk of coronary heart disease in US women. *Am J Clin Nutr* **71**, 1455–1461.
24. Khosravi-Boroujeni H, Mohammadifard N, Sarrafzadegan N *et al.* (2012) Potato consumption and cardiovascular disease risk factors among Iranian population. *Int J Food Sci Nutr* **63**, 913–920.
25. Hosseinpour-Niazi S, Sohrab G, Asghari G *et al.* (2013) Dietary glycemic index, glycemic load, and cardiovascular disease risk factors: Tehran lipid and glucose study. *Arch Iran Med* **16**, 401–407.
26. Bahadoran Z, Mirmiran P, Delshad H *et al.* (2014) White rice consumption is a risk factor for metabolic syndrome in Tehrani adults: a prospective approach in Tehran lipid and glucose study. *Arch Iran Med* **17**, 435–440.
27. Mirmiran P, Bahadoran Z, Delshad H *et al.* (2014) Effects of energy-dense nutrient-poor snacks on the incidence of metabolic syndrome: a prospective approach in Tehran lipid and glucose study. *Nutrition* **30**, 538–543.
28. Mirzaei M, Salehi-Abargouei A, Mirzaei M *et al.* (2018) Cohort Profile: the Yazd Health Study (YaHS): a population-based study of adults aged 20–70 years (study design and baseline population data). *Int J Epidemiol* **47**, 697h–698h.

29. Food & Nutrition Board (2005) *Dietary Reference Intakes for Energy, Carbohydrate, Fiber, Fat, Fatty Acids, Cholesterol, Protein, and Amino Acids (Macronutrients)*. Washington, DC: National Academy Press.

30. Esfahani FH, Asghari G, Mirmiran P *et al.* (2010) Reproducibility and relative validity of food group intake in a food frequency questionnaire developed for the Tehran lipid and glucose study. *J Epidemiol* **20**, 150–158.

31. Ghaffarpour M, Houshiar-Rad A & Kianfar H (1999) The manual for household measures, cooking yields factors and edible portion of foods. *Tehran Nashre Olume Keshavarzy* **7**, 213.

32. Alberti KGMM, Eckel RH, Grundy SM *et al.* (2009) 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* **120**, 1640–1645.

33. Committee IR (2005) Guidelines for data processing and analysis of the International physical activity questionnaire (IPAQ)-short and long forms. http://wwwipaqkise/scoringpdf (accessed April 2004).

34. Moghaddam MB, Aghdam FB, Jafarabadi MA *et al.* (2012) The Iranian version of international physical activity questionnaire (IPAQ) in Iran: content and construct validity, factor structure, internal consistency and stability. *World Appl Sci J* **18**, 1073–1080.

35. Brunner E, Wunsch H & Marmot M (2001) What is an optimal diet? Relationship of macronutrient intake to obesity, glucose tolerance, lipoprotein cholesterol levels and the metabolic syndrome in the Whitehall II study. *Int J Obes* **25**, 45–53.

36. Kang H, Greenson JK, Omo JT *et al.* (2006) Metabolic syndrome is associated with greater histologic severity, higher carbohydrate, and lower fat diet in patients with NAFLD. *Am J Gastroenterol* **101**, 2247–2253.

37. Kim J & Jo I (2011) Grains, vegetables, and fish dietary pattern is inversely associated with the risk of metabolic syndrome in South Korean adults. *J Am Diet Assoc* **111**, 1141–1149.

38. De Koning L, Malik VS, Rimm EB *et al.* (2011) Sugar-sweetened and artificially sweetened beverage consumption and risk of type 2 diabetes in men. *Am J Clin Nutr* **93**, 1321–1327.

39. Liu S, Manson J, Stampfer MJ *et al.* (2000) A prospective study of whole-grain intake and risk of type 2 diabetes mellitus in US women. *Am J Public Health* **90**, 1409.

40. Park S-H, Lee K-S & Park H-Y (2010) Dietary carbohydrate intake is associated with cardiovascular disease risk in Korean: analysis of the third Korea National Health and Nutrition Examination Survey (KNHANES III). *Int J Cardiol* **139**, 234–240.

41. Song S, Lee JE, Song WO *et al.* (2014) Carbohydrate intake and refined-grain consumption are associated with metabolic syndrome in the Korean adult population. *J Acad Nutr Diet* **114**, 54–62.

42. Nanri A, Mizoue T, Noda M *et al.* (2010) Rice intake and type 2 diabetes in Japanese men and women: the Japan public health center–based prospective study. *Am J Clin Nutr* **92**, 1468–1477.

43. Villegas R, Liu S, Gao Y-T *et al.* (2007) Prospective study of dietary carbohydrates, glycemic index, glycemic load, and incidence of type 2 diabetes mellitus in middle-aged Chinese women. *Arch Intern Med* **167**, 2310–2316.

44. Eslamian G, Mirmiran P, Asghari G *et al.* (2014) Low carbohydrate diet score does not predict metabolic syndrome in children and adolescents: Tehran lipid and glucose study. *Arch Iran Med* **17**, 417–422.

45. Sartorius K, Sartorius B, Madiba TE *et al.* (2018) Does high-carbohydrate intake lead to increased risk of obesity? A systematic review and meta-analysis. *BMJ Open* **8**, e018449.

46. Hu T & Bazzano L (2014) The low-carbohydrate diet and cardiovascular risk factors: evidence from epidemiologic studies. *Nutr Metabol Cardiovasc Dis* **24**, 337–343.

47. Foster GD, Wyatt HR, Hill JO *et al.* (2003) A randomized trial of a low-carbohydrate diet for obesity. *N Engl J Med* **348**, 2082–2090.

48. Trichopoulou A, Psaltopoulou T, Orfanos P *et al.* (2007) Low-carbohydrate–high-protein diet and long-term survival in a general population cohort. *Eur J Clin Nutr* **61**, 575–581.

49. Lagiou P, Sandin S, Weiderpass E *et al.* (2007) Low carbohydrate–high protein diet and mortality in a cohort of Swedish women. *J Intern Med* **261**, 366–374.

50. Miyashita Y, Koide N, Ohtsuka M *et al.* (2004) Beneficial effect of low carbohydrate in low calorie diets on visceral fat reduction in type 2 diabetic patients with obesity. *Diabetes Res Clin Pract* **65**, 235–241.

51. Brinkworth GD, Noakes M, Buckley JD *et al.* (2009) Long-term effects of a very-low-carbohydrate weight loss diet compared with an isocaloric low-fat diet after 12 mo. *Am J Clin Nutr* **90**, 23–32.

52. Mansoor N, Vinknes KJ, Veierød MB *et al.* (2016) Effects of low-carbohydrate diets v. low-fat diets on body weight and cardiovascular risk factors: a meta-analysis of randomised controlled trials. *Br J Nutr* **115**, 466–479.

53. Nakamura Y, Ueshima H, Okuda N *et al.* (2016) Relationship of three different types of low-carbohydrate diet to cardiometabolic risk factors in a Japanese population: the INTERMAP/INTERLIPID study. *Eur J Nutr* **55**, 1515–1524.

54. Santos FL, Esteves SS, da Costa Pereira A *et al.* (2012) Systematic review and meta-analysis of clinical trials of the effects of low carbohydrate diets on cardiovascular risk factors. *Obes Rev* **13**, 1048–1066.

55. Hu T & Bazzano LA (2014) The low-carbohydrate diet and cardiovascular risk factors: evidence from epidemiologic studies. *Nutr Metabol Cardiovasc Dis* **24**, 337–343.

56. Radhika G, Van Dam RM, Sudha V *et al.* (2009) Refined grain consumption and the metabolic syndrome in urban Asian Indians (Chennai urban rural epidemiology study 57). *Metabolism* **58**, 675–681.

57. Micha R, Wallace SK & Mozaffarian D (2010) Red and processed meat consumption and risk of incident coronary heart disease, stroke, and diabetes mellitus: a systematic review and meta-analysis. *Circulation* **121**, 2271–2283.

58. Esposito K, Kastorini C-M, Panagiotakos DB *et al.* (2013) Mediterranean diet and metabolic syndrome: an updated systematic review. *Rev Endocr Metabol Disord* **14**, 255–263.

59. Amini M, Esmaillzadeh A, Shafaeizadeh S *et al.* (2010) Relationship between major dietary patterns and metabolic syndrome among individuals with impaired glucose tolerance. *Nutrition* **26**, 986–992.

60. Tappy L & Lê K-A (2010) Metabolic effects of fructose and the worldwide increase in obesity. *Physiol Rev* **90**, 23–46.

61. Sackner-Bernstein J, Kanter D & Kaul S (2015) Dietary intervention for overweight and obese adults: comparison of low-carbohydrate and low-fat diets. A meta-analysis. *PloS One* **10**, e0139817.

62. Azadbakht L, Kimiagar M, Mehrabi Y *et al.* (2007) Soy inclusion in the diet improves features of the metabolic syndrome: a randomized crossover study in postmenopausal women. *Am J Clin Nutr* **85**, 735–741.

63. Volek JS & Feinman RD (2005) Carbohydrate restriction improves the features of metabolic syndrome. Metabolic syndrome may be defined by the response to carbohydrate restriction. *Nutr Metabol* **2**, 31.

64. Feinman RD & Volek JS (2008) Carbohydrate restriction as the default treatment for type 2 diabetes and metabolic syndrome. *Scand Cardiovasc J* **42**, 256–263.

65. Paoli A, Rubini A, Volek JS *et al.* (2013) Beyond weight loss: a review of the therapeutic uses of very-low-carbohydrate (ketogenic) diets. *Eur J Clin Nutr* **67**, 789–796.

Public Health Nutrition

66. Sears B & Perry M (2015) The role of fatty acids in insulin resistance. *Lipids Health Dis* **14**, 121–121.

67. Lê K-A & Tappy L (2006) Metabolic effects of fructose. *Curr Opin Clin Nutr Metabol Care* **9**, 469–475.

68. Rutledge AC & Adeli K (2007) Fructose and the metabolic syndrome: pathophysiology and molecular mechanisms. *Nutr Rev* **65**, S13–S23.

69. Zammit VA (2002) Insulin stimulation of hepatic triacylglycerol secretion in the insulin-replete state: implications for the etiology of peripheral insulin resistance. *Ann N Y Acad Sci* **967**, 52–65.

70. Barclay AW, Petocz P, McMillan-Price J *et al.* (2008) Glycemic index, glycemic load, and chronic disease risk—a meta-analysis of observational studies. *Am J Clin Nutr* **87**, 627–637.

71. Blades B & Garg A (1995) Mechanisms of increase in plasma triacylglycerol concentrations as a result of high carbohydrate intakes in patients with non-insulin-dependent diabetes mellitus. *Am J Clin Nutr* **62**, 996–1002.

Public Health Nutrition