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The Relationship between Nutrients Pattern and Hypercholesterolemia

Maryam Sadat Amirkalali; MD Student [1], Sayyed Saeid Khayyatzadeh; MSc [1], Mohammad Baghernyia; MSc [1], Seyed Mohammad Reza Parizadeh; PhD [1], Mohammad Safarian; MD, PhD [1] & Majid Ghayour-Mobarhan; MD, PhD [1,2*]

[1] *Biochemistry of Nutrition Research Center, School of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran.*
[2] *Department of Modern Sciences and Technologies, School of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran.*

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Corresponding author:
ghayourmobarhan@yahoo.com
MD, PhD, Metabolic syndrome Research Center, School of Medicine, Mashhad University of Medical Sciences, 99199 - 91766, Mashhad, Iran.

Postal code: 91779-84564
Tel: +98 5138002288

ABSTRACT

Background: The prevalence of hypercholesterolemia is increasing globally. It is associated with a significant risk of developing type 2 diabetes mellitus and cardiovascular diseases. The aim of the current study was to explore the relationship of nutrients patterns and other lifestyle-related factors with the presence of hypercholesterolemia in a representative population of Iran. **Methods:** Dietary information was collected using a 24-h recall from male and female adults in the age range of 35-65 years. The relationship between adherence to different nutrients patterns and hypercholesterolemia was explored in 5700 participants from Mashhad, Iran. **Results:** Among the participants (n = 5700), 2195 (38.51%) were men and 3505 (61.49%) of them were women. Furthermore, 722 (32.89%) male and 1434 (40.91%) female participants had hypercholesterolemia. The group with hypercholesterolemia had significantly higher intake rates of fiber, lactose, vitamin C, potassium, calcium, and phosphorus, however, they had lower total energy intake than the control group ($P < 0.05$). **Conclusions:** The results showed that consumption of nutrients patterns high in lactose, calcium, phosphor, iodine, retinol, riboflavin, and cobalamin is associated with the likelihood of hypercholesterolemia. Prospective studies are required to examine the association between nutrient patterns and hypercholesterolemia.

Keywords: *Hypercholesterolemia; Nutrient patterns; Factor analysis*

Introduction

Cardiovascular diseases (CVDs) are the cause for 30% of all deaths in the world (Thabane *et al.*, 2015). These diseases have an increasing prevalence in many countries all around the world. This elevation is caused by many factors such as population aging and adoption of predisposing lifestyles like sedentary behaviors and changes in eating habits (do Prado Junior *et al.*, 2015, Md, 2000). CVDs have also been known as the cause of 38% of all deaths in

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Iran (Shadmani and Karami, 2013). Primary risk factors that play a significant role in the incidence of CVDs include hypercholesterolemia, hypertension, hyperglycemia, smoking, and overweight (Lloyd-Jones *et al.*, 2010, Yang *et al.*, 2011). The World Health Organization (WHO) declared that hypercholesterolemia is involved in more than half of the coronary heart disease cases annually all over the world (Churilla *et al.*, 2012). It was previously reported that the prevalence of hypercholesterolemia was 42.9% among 15-64 years Iranian citizens (Esteghamati *et al.*, 2009).

There are several factors associated with serum cholesterol level, such as age, gender, body weight, body mass index (BMI), lifestyle, amount of activity, and dietary intake (Veghari *et al.*, 2013). Management of diets is known as a key strategy for reducing the lipid disorders (Anderson, 2003, Chitra *et al.*, 2012). Some studies reported a negative correlation of dietary fiber intake and plant sterols with the prevalence of hypercholesterolemia and higher levels of low density lipoprotein (LDL) (Narayan *et al.*, 2014, Shinozaki *et al.*, 2015). In addition, some other researchers showed that dietary glycemic load is associated with serum total cholesterol concentrations and the other lipid profile markers (Cocate *et al.*, 2014a, Lin *et al.*, 2012). Moreover, it has been shown that consumption of some micronutrients like selenium, calcium, iron, and zinc may affect the cholesterol levels (Christensen *et al.*, 2015, Lorenzen and Astrup, 2011).

An individual's diet is composed of different kinds of food which have complex relationships with nutrients (Hu, 2002, Jacobs and Steffen, 2003). Although many studies have been conducted on single nutrients, food intake status, and the risk of hypercholesterolemia, some correlations among these factors might be ignored due to limited evaluations (Castellanos-Jankiewicz *et al.*, 2014, Christensen *et al.*, 2015, Cocate *et al.*, 2014a, Cocate *et al.*, 2014b, Gunasekara *et al.*, 2011, Lin *et al.*, 2012, Narayan *et al.*, 2014, Shinozaki *et al.*, 2015). Furthermore, the effects of a single nutrient or food may be too small to be recognized (Salehi-Abargouei *et al.*, 2015). Dietary pattern analysis has recently emerged as an epidemiological method to investigate the relationship between diet and the risk of diseases. In this approach, the effects of overall diet instead of individual nutrients and foods were measured to predict the risk of diseases (Hu, 2002). Nutrients patterns can give us a good insight about correlation of nutrients and the risk of diseases in a universal scale and for different people living in various climates with different cultures and eating behaviors. Variations in foods and the way they are cooked or prepared are not due to nutrients since they are global and consumed by people with different cultural and behavioral background. Instead, such variations are caused by difference within populations (Freisling *et al.*, 2010, Salehi-Abargouei *et al.*, 2015).

Monitoring of elevated levels in total serum cholesterol concentration is one of the most important strategies to reduce the risk of CVDs (Hovsepian *et al.*, 2015). So, it is necessary to find and clarify the relationship of macronutrients and micronutrients consumption with the risk of hypercholesterolemia. Therefore, this comprehensive study was carried out in a large scale to investigate the correlation of nutrition patterns and other lifestyle-related factors with hypercholesterolemia in Mashhad city in north east of Iran.

Materials and Methods

Study design and participants: In this case-control study, 5700 individuals participated, out of whom 2156 (37.82%) had hypercholesterolemia. They were recruited from an urban population of Mashhad, a city in northeastern part of Iran, using a stratified-cluster method. Participants were selected from the Mashhad Stroke Heart Atherosclerosis Disorder (MASHAD) study (Ghayour-Mobarhan *et al.*, 2015).

Households with individuals from 35 to 65 years were identified and the local population authorities provided these families with an information brochure of the study. Exclusion

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criteria were pregnancy and lactation, established cardiovascular disease or diabetes, as well as consumption of dietary supplements. All participants signed the informed written consent to contribute in the survey.

This case-control study was a part of MASHAD study, the comprehensive prospective cohort study which is currently being implemented (Ghayour-Mobarhan *et al.*, 2015, Mirhafez *et al.*, 2015a). This study was funded and supported by Mashhad University of Medical Sciences.

Measurements: The lifestyle, demographic and anthropometric data were collected and recorded by two certified health care professionals and a nurse. The health-related questionnaires included demographic data, physical exercise, tobacco and alcohol use, as well as smoking status. Physical activity was assessed using James and Schofield human energy requirements equations. Physical activity level was further calculated as the total energy expenditure (TEE) and ratio of basal metabolic rate (BMR) over a 24-hour period. Questions on physical activity were based on James and Schofield equations, and were selected from those used in the Scottish Heart Health Study (SHHS)/MONICA questionnaire. Questions assessed the time spent on activities during work (including housework), outside work, and in bed (resting and sleeping). The physical activity levels of individuals were defined in 4 levels scored from 1 to 4; inactive, low active, active, and very active. Smoking status was determined by describing two groups: current smoker and non-smoker groups. Current smokers were those who smoked at least one cigarette per day, while non-smoker group contained individuals who had never smoked or were former smokers.

Participants' body weight and height were measured with light clothing and without shoes. Body mass index (BMI) was calculated as weight (kg) divided by height in meters squared. Waist circumference (WC) was then measured at the mid-point between the lowest rib margin and the iliac crest during minimal respiration. Resting blood pressure was assessed three times by a trained technician using the standardized protocol. The average of three recorded measurements was then used in all data analyses. For blood pressure measurements, participants remained seated for 15 min and the minimum of two readings were taken using a standard mercury sphygmomanometer. Later, the mean values of the closest two readings were calculated (Emamian *et al.*, 2015, Mirhafez *et al.*, 2014).

Biochemical factors including total cholesterol (TC), high density lipoprotein cholesterol (HDL-c), low density lipoprotein cholesterol (LDL-c), and triglyceride (TG), C-reactive protein (CRP), and fasting blood glucose (FBG) were measured, as reported earlier (Mirhafez *et al.*, 2015b, Oladi *et al.*, 2015, Zomorrodian *et al.*, 2015).

Dietary information was collected using a 24-h recall, administered by well -trained dietary interviewers in a face-to-face interview. Participants were supposed to recall and describe every item of food and beverage consumed over the 24 h period (Motamed *et al.*, 2013). Individual nutritional intakes were assessed using Dietplan6 software (Forest field Software Ltd., UK). The variables selected for this study were total energy, protein, total fat, cholesterol, minerals, and vitamins. All nutrient intake values were adjusted for total energy intake using the residual method.

Ethic consideration: Ethic Committee of Mashhad University of Medical Sciences approved the study.

Data analysis: All data were analyzed using SPSS software (version 20, SPSS Inc., IL, USA). P-value < 0.05 was considered as statistically significant. Values were expressed as a mean± standard deviation (SD) for normally distributed data and analyzed by Student *t*-test. Non-normally distributed data were expressed by median and analyzed through Kruskal-Willis test. Qualitative data were finally tested using the chi-square test. Participants were categorized into two groups of case patients with hypercholesterolemia and control participants without hypercholesterolemia. Factor analysis was used to identify nutrient groups and determine factor loadings. The

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association between nutrient patterns and odds of hypercholesterolemia was assessed. Principal component factor analysis (PCFA) was used to calculate dietary nutrient patterns and determine factor loadings. Varimax rotation was also applied to retain uncorrelated factors and enhance interpretability (Jae-On and Mueller, 1978). The number of factors to maintain was selected based on an Eigen value > 1, scree plot test, and factor interpretability. The quartile cut-offs of dietary nutrient pattern scores were classified based on the factor scores of the controls. Nutrients were found to have rotated factor loadings ≥0.32 (Norman and Streiner). The odds ratio (OR) and 95% confidential intervals (CI) were assessed using the logistic regression models for each quartile. These analyses were adjusted for different variables in 3 models. Crude was not adjusted for any variable. Model A was adjusted for age and gender (male/female). Model B included adjustment for BMI in addition to the variables adjusted in model A. In this model, BMI was included as a covariate to isolate the independent effects caused by central adiposity measured by WC.

Results

A total of 5700 participants were enrolled in the study, 2195 (38.51%) of them were men and 3505 (61.49%) were women. Among the male participants, 722 individuals (32.89%) and 1434 of females (40.91%) had hypercholesterolemia. General characteristics of participants are shown in **Table 1**. Gender and age were significantly different between the hypercholesterolemia and control groups ($P < 0.001$). But there was no significant difference in physical activity between the two groups. The number of hypercholesterolemic females was more than hypercholesterolemic males ($P < 0.001$). The mean age of hypercholesterolemic patients was higher than the control group ($P < 0.001$). It was also found that participants with hypercholesterolemia were more likely to smok ($P = 0.008$). Dietary intakes status is presented in **Table 2**. According to dietary nutrient intake status, intakes of fiber ($P = 0.009$), lactose ($P = 0.004$), vitamin C ($P = 0.016$), potassium ($P = 0.007$), calcium ($P < 0.001$), and phosphor ($P = 0.013$) were significantly higher but total energy intake was lower in the hypercholesterolemia than the control group ($P < 0.001$). Factor loading scores and dietary nutrients are shown in **Table 3**. Factor 1, classified as "the first nutrient pattern" was defined by high levels of protein, thiamin, niacin, potassium, magnesium, iron, zinc, selenium, and fiber. Factor 2, identified as "the second nutrient pattern" had the greatest loading of total fat, cholesterol, saturated fat, monounsaturated fat, polyunsaturated fat, trans fat, carbohydrate, maltose, and sucrose. Factor 3 was associated with greater level of consumption of lactose, calcium, phosphor, iodine, retinol, riboflavin, and cobalamin which was named "the third nutrient pattern". All 3 patterns demonstrated 45.79% of variance in dietary nutrient intake (16.80% for factor 1, 16.52% for factor 2, and 12.47% for factor 3). The adjusted ORs (95% CIs) of dietary nutrient pattern quartiles and hypercholesterolemia were also investigate (**Table 4)**. The highest quartile (Q4) of "the first nutrient pattern" (OR: 1.17; 95% CI: 1.01-1.37; P for trend = 0.02) was associated with the likelihood of hypercholesterolemia in crude model; but no significant association was observed between the first nutrient pattern and odds of hypercholesterolemia in adjusted models.

In "the third nutrient pattern", the highest quartile (Q4) (OR: 1.18; 95%CI: 1.01-1.37; P for trend = 0.02) was correlated with the odds of developing hypercholesterolemia without any adjustments and even after adjustment for age and gender (OR: 1.14; 95% CI: 0.98-1.33; P for trend = 0.04). However, no significant association was found in further adjustments in model B. Moreover, "the second nutrient pattern" was not significantly associated with the odds of developing hypercholesterolemia in crude and adjusted models.

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Table 1. General and clinical characteristics of study participants

Variables	Healthy participants (n = 3544)	Hypercholesterolemic participants (n = 2156)	P-value[a]
Age (y)	48.00 ± 8.13	50.39 ± 7.81	<0.001
Gender (Male)	1473 (41.56)	722 (33.48)	<0.001
Current smoker	791 (22.31)	418 (19.38)	0.008
Physical activity			0.21
Inactive	907 (15.9)	518 (9.1)	
Low active	971 (17.1)	631 (11.1)	
Active	1307 (23.0)	812 (14.3)	
Very active	349 (6.1)	192 (3.4)	
Body mass index (kg/m^2)	27.74 ± 4.63	28.58 ± 4.56	<0.001
Systolic blood pressure (mmHg)	120.97 ± 18.47	125.50 ± 19.53	<0.001
Diastolic blood pressure (mmHg)	78.60 ± 11.74	81.20 ± 11.95	<0.001
Waist circumference (cm)	94.71 ± 11.78	97.17 ± 11.98	<0.001
Total Cholesterol (mg/dL)	167.34 ± 22.91	229.82 ± 25.99	<0.001
Triglycerides (mg/dL)	108 ± 39	152 ± 44	<0.001
High density lipoprotein (mg/dL)	39.86 ± 9.00	44.96 ± 9.37	<0.001
Low density lipoprotein (mg/dL)	100.26 ± 22.83	147.86 ± 30.03	<0.001
Fasting blood glucose (mg/dL)	87.33 ± 31.81	96.17 ± 42.59	<0.001
Uric acid (mg/dL)	4.50 ± 1.32	4.87 ± 1.34	<0.001

[a]: ANOVA for continuous variables and chi-square test for categorical variables

Table 2. Daily dietary intakes of study participants

Variables	Healthy participants	Hypercholesterolemia participants	P-value[a]
Energy (kcal)	1905.58 ± 665.00	1838.67 ± 633.97	<0.001
Protein (g)	68.54 ± 21.25	69.33 ± 20.51	0.171
Carbohydrate (g)	241.98 ± 53.66	239.54 ± 51.50	0.092
Total fat (g)	70.04 ± 21.67	70.72 ± 20.40	0.232
Cholesterol (mg)	225.32 ± 166.70	231.24 ± 211.26	0.241
Saturated fat (g)	18.28 ± 7.03	18.50 ± 7.13	0.257
Monounsaturated fat (g)	19.52 ± 6.75	19.70 ± 6.42	0.357
Polyunsaturated fat (g)	23.73 ± 12.76	23.90 ± 12.26	0.628
Trans fat (g)	1.77 ± 0.65	1.78 ± 0.66	0.486
Fiber (g)	17.04 ± 9.04	17.68 ± 8.96	0.009
Maltose (mg)	3.39 ± 2.52	3.35 ± 2.22	0.579
Sucrose (mg)	34.51 ± 26.93	33.55 ± 23.18	0.157
Lactose (mg)	11.36 ± 12.56	12.37 ± 13.16	0.004
Retinol (µg)	422.72 ± 2030.09	414.69 ± 2035.36	0.885
Thiamin (mg)	1.79 ± 0.56	1.82 ± 0.52	0.122
Riboflavin (mg)	2.09 ± 0.78	2.13 ± 0.78	0.062
Niacin (mg)	16.90 ± 9.22	16.74 ± 8.66	0.516
Cobalamin (µg)	2.92 ± 8.16	2.98 ± 7.87	0.783
Vitamin C (mg)	91.79 ± 86.93	97.63 ± 91.54	0.016
Vitamin D (µg)	2.02 ± 2.37	1.99 ± 2.16	0.681
Sodium (mg)	3157.49 ± 7711.06	3077.99 ± 6378.49	0.688

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Potassium (mg)	2816.00 ± 939.10	2885.32 ± 932.36	0.007
Calcium (mg)	844.94 ± 331.90	877.37 ± 342.12	<0.001
Magnesium (mg)	246.99 ± 93.24	251.51 ± 88.50	0.071
Phosphor (mg)	1308.02 ± 342.56	1330.99 ± 329.56	0.013
Iron (mg)	10.83 ± 5.01	10.93 ± 5.08	0.468
Zinc (mg)	9.18 ± 2.90	9.21 ± 2.78	0.665
Selenium (µg)	37.03 ± 25.35	36.62 ± 27.23	0.562
Iodine (µg)	110.21 ± 85.52	113.88 ± 86.58	0.118

[a]: Obtained from ANOVA

Table 3. Factor loading matrix and explained variance for nutrient patterns identified by factor analyses

Variables	First pattern	Second pattern	Third pattern
Carbohydrate (g)	-0.069	-0.959	-0.007
Maltose (mg)	-0.067	-0.402	0.006
Sucrose (mg)	-0.183	-0.349	-0.011
Lactose (mg)	0.074	-0.189	0.684
Total fat (g)	-0.208	0.883	-0.112
Cholesterol (mg)	-0.069	0.447	0.276
Saturated fat (g)	-0.153	0.674	0.181
Monounsaturated fat (g)	-0.151	0.870	-0.073
Polyunsaturated fat (g)	-0.180	0.635	-0.255
Trans fat (g)	0.111	0.450	0.091
Retinol (µg)	0.003	0.097	0.482
Thiamin (mg)	0.712	-0.181	0.027
Riboflavin (mg)	0.189	0.025	0.864
Niacin (mg)	0.500	0.225	0.063
Cobalamin (µg)	0.058	0.168	0.538
Vitamin C (mg)	0.293	-0.117	-0.035
Vitamin D (µg)	-0.058	0.282	0.064
Sodium (mg)	0.077	0.106	0.097
Potassium (mg)	0.709	-0.158	0.257
Calcium (mg)	0.119	-0.253	0.727
Magnesium (mg)	0.834	-0.123	0.110
Phosphor (mg)	0.551	0.039	0.588
Iron (mg)	0.720	-0.110	-0.020
Zinc (mg)	0.719	0.243	0.126
Selenium (µg)	0.374	0.126	0.097
Iodine (µg)	-0.044	0.184	0.675
Proportion of explained variance (%)	16.801	16.521	12.470
Cumulative explained variance (%)	16.801	33.322	45.792

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Table 4. Multivariable-adjusted odds ratios (95% CIs) for hypercholesterolemia across quartile (Q) categories of nutrient pattern scores

Nutrient patterns	Quartile of dietary nutrient pattern score				P-trend
	Q1	Q2	Q3	Q4	
First nutrient pattern					
Crude	1	1.09 (0.93-1.27)	1.14 (0.98-1.32)	1.17 (1.01-1.37)	0.02
Model A	1	1.01 (0.86-1.21)	1.04 (0.89-1.21)	1.1 (0.94-1.28)	0.21
Model B	1	1.00(0.86-1.17)	1.03 (0.9-1.2)	1.07 (0.91-1.2)	0.29
Second nutrient pattern					
Crude	1	1.02 (0.86-1.17)	1.07 (0.92-1.25)	1.03 (0.89-1.20)	0.49
Model A[a]	1	0.96 (0.82-1.13)	1.02 (0.88-1.19)	1.04 (0.89-1.21)	0.46
Model B	1	0.98 (0.84-1.12)	1.03 (0.88-1.21)	1.05 (0.90-1.22)	0.39
Third nutrient pattern					
Crude	1	1.02 (0.88-1.19)	1.09 (0.94-1.27)	1.18 (1.01-1.37)	0.02
Model A	1	0.99 (0.85-1.16)	1.07 (0.92-1.25)	1.14 (0.98-1.33)	0.04
Model B	1	1.01 (0.85-1.16)	1.06 (0.89-1. 25)	1.11 (0.93-1.3)	0.08

[a] Model A was adjusted for age and sex. Model B included additional adjustment for BMI, current smoking and education level.

Discussion

To the best of our knowledge, this study was the first study examining the relationship between three major nutrient patterns and hypercholesterolemia. The same result was also obtained in previous studies (Ahaneku *et al.*, 2015, Doupa *et al.*, 2014). The achieved results suggested that prevalence of hypercholesterolemia is positively associated with age, BMI, systolic, diastolic blood pressure, and WC. Some studies also reported the same results (Ahaneku *et al.*, 2015, Bijari *et al.*, 2015, Lee *et al.*, 2001).

In the current study, a positive association was observed with hypercholesterolemia for the first nutrient group (greater amount of protein, thiamine, niacin, potassium, magnesium, iron, zinc, selenium, and fiber) when it was not adjusted. However, there was no significant association for the adjusted models. A significant correlation was also observed between the third nutrient group (greater amount of lactose, calcium, phosphor, iodine, retinol, riboflavin, and cobalamin) and the odds of hypercholesterolemia in crude model. However, the second nutrient pattern (greater amount of total fat, cholesterol, saturated fat, monounsaturated fat, polyunsaturated fat, trans fat, carbohydrate, maltose, and sucrose) was not significantly associated with presence of hypercholesterolemia.

Our results suggested that the third nutrient pattern (higher amount of lactose, calcium, phosphor, iodine, retinol (vitamin A), riboflavin (vitamin B2) and cobalamin (vitamin B12)) was positively associated with the presence of hypercholesterolemia. Riboflavin and cobalamin are both water soluble vitamins required to be consumed in adequate amounts because the human body cannot synthesize them (Dali-Youcef and Andrès, 2009, Reihl and Stolz, 2005, Watanabe *et al.*, 2010). In this study, dietary intake of riboflavin and cobalamin showed no significant association with hypercholesterolemia. These results are in line with the results of a study conducted in Poland in which the relationship between lipids and vitamin B levels was investigated in persons with elevated risk of atherosclerosis. The results indicated no significant association between lipid profile levels and B vitamins. At last, it was concluded that lipid parameters' levels and B-vitamins may have an independent additional effect on the risk of atherosclerosis (Wasilewska *et al.*, 2003).

In the current study, a non-significant lower level of dietary intake of retinol (vitamin A) was

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observed in individuals with hypercholesterolemia. A study carried out on children with hypercholesterolemia in Slovak republic evaluated parameters of lipid profile, lipophilic vitamins, and antioxidants (retinol, β-carotene, α-tocopherol, γ-tocopherol, xanthophyll and lycopene) as well as markers of oxidative damage to lipids (8-isoprostanes and lipoperoxides). Findings showed no correlation between these lipophilic antioxidants and the total serum's cholesterol in female children with hypercholesterolemia, which confirms findings about retinol (Ondrejovicova *et al.*, 2010). Inconsistent to the results of the present study, Smith et al. reported that serum vitamin A concentration is higher in individuals with hypercholesterolemia than the healthy control group (Smith *et al.*, 1992).

Findings further showed higher levels of iodine in hypercholesterolemic individuals but this difference was not statistically significant in comparison with the control group. A study carried out in China also represented that iodine excess has time- and dose-dependent hypercholesterolemic effects. Authors declared that the hypercholesterolemic effects induced by higher levels of iodine may be due to the role of TRbeta1-mediated down regulation of hepatic LDLr gene (Zhao *et al.*, 2010). Contrary to results of the current study on iodine, the study conducted in Morocco suggested that iodine supplementation in iodine deficient and overweight women may reduce prevalence of hypercholesterolemia (Herter-Aeberli *et al.*, 2015). It should also be noted that these studies were performed in different populations with different geographical, cultural, and behavioral situation, which may explain the different results. Hence, it is worth noting that both deficient and over consumption of iodine may have hypercholesterolemic effects.

Individuals with hypercholesterolemic in this study had higher levels of calcium and lactose in their dietary intake. A double-blind, randomized, placebo-controlled trial was conducted on 190 premenopausal women (30-40 years) and 182 postmenopausal women (50-60 years) with dyslipidemia. The participants received 800 mg Ca/day or a placebo for 2 years. Results suggested that increase in the serum TC is positively associated with calcium supplementation in postmenopausal women (Li *et al.*, 2013). However, opposite results were reported in some other studies demonstrating that high calcium diet decreased the total TC (Jacqmain *et al.*, 2003, Lorenzen and Astrup, 2011). On the other hand, other studies reported no association between Ca consumption and the total TC (Rajpathak *et al.*, 2010, Reid *et al.*, 2010). This seems to be caused by lack of nutritional knowledge. Iranian people consume full fat dairy products as a main dietary calcium source; on the other hand, it was proved that full fat dairy products contribute to the dyslipidemia, which may explain the results of the current study about calcium consumption and hypercholesterolemia.

In the current study, a significant positive association was found between dietary phosphorus intake and the odds of hypercholesterolemia. Overconsumption of phosphor may have harmful effects even in the case of low serum phosphor concentration level. Parathyroid hormone (PTH) and fibroblast growth factor-23 (FGF-23) are two powerful regulators for serum phosphorus concentrations. This hormone increases urinary phosphor excretion. In healthy individuals with high phosphorus dietary intake, serum phosphorus levels are maintained in normal range by increasing parathyroid hormone and FGF-23 physiologically (Chang *et al.*, 2014). Excessive consumption of phosphorus for a long time may be a direct or indirect predisposing factor for diabetes mellitus, cardiovascular disease, hypercholesterolemia, bone problems, chronic kidney disease progression, left ventricular hypertrophy, heart failure, and mortality (Chang *et al.*, 2014, Onufrak *et al.*, 2008, Uribarri and Calvo, 2014). Onufrak et al. carried out a study in US on 13,340 individuals (45–64 years). Participants were selected from the atherosclerosis risk in communities study and did not have any known coronary heart disease, stroke, or renal disease.

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This study demonstrated that rises in serum phosphorus concentration is considerably associated with the chance of having hypercholesterolemia, which I the same line with the current study (Onufrak *et al.*, 2008). It should be considered that most of phosphor sources in the human diet are from animal protein that contain high amount of saturated fat and may cause hypocholesterolemia.

In spite of unique sampling which represented a large adult population of Iran, this study had some limitations. First of all, dietary information was collected using a 24h recall questionnaire by an interviewer to recall and describe every item of food and beverage consumed over the 24h period. But sometime individuals may report wrong dietary information for any reason, mostly because of incomplete remembering and forgetting. Second, in this study individual nutritional intakes were assessed using Dietplan6 software (Forest field Software Ltd., UK), which was designed for European diet assessment. Difference in habitual eating and the ways of foods preparation between Iranian and European people may have affected interpretation of data in this software. Next, individuals with certain anthropometric characteristics may have changed their dietary habit to control the elevated levels of serum TC. Finally, the current study was conducted in cross-sectional design which is unable to deduce causality.

Conclusions

In conclusion, no significant association was found between nutrients patterns and the odds of hypercholesterolemia. Prospective studies are required to examine the nutrient patterns as well as to confirm and clarify the relationships found in this study.

Acknowledgment

This study was approved and founded by Mashhad University of Medical Sciences (MUMS).

Authors' contributions

The paper was drafted by participation of Amirkalali MSA, Khayyatzadeh SS, and Baghernyia M. Ghayour-Mobarhan M, Safarian M and Parizadeh SMR designed the study. Khayyatzadeh SS helped in statistical analyses and Ghayour-Mobarhan M supervised the study. All authors contributed in the development of study, they also read and approved the final version of the manuscript.

Conflict of interest

The authors have no conflict of interest to disclose.

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