Original Article

Healthy Dietary Pattern Reduces Risk of Gallstones: Results of a Case-Control Study in Iran

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Abstract

Background: Nutrition-related factors have been of great interest as one of risk factors of biliary stones. This study evaluated the association of dietary patterns with biliary stone among Iranians. **Methods:** This is a hospital-based case-control study, which was conducted in a general hospital in Tehran, Iran. A total of 110 patients with gallstone or common bile duct (CBD) stone confirmed by Ultrasonography within the last 6 months before collecting data were recruited. Controls were age-matched patients admitted to the other wards of the same hospital for a broad spectrum of disorders including traumas and orthopedic conditions, or elective surgeries, or throat/ear/nose disease and had no gallbladder disorders, participated in this study. We used a valid and reliable food frequency questionnaire to assess dietary intakes of participants. Dietary patterns were determined by factor analysis. **Results:** By design, age was similar in both groups (57.66 ± 16.39 years vs. 56.00 ± 10.64 years in cases and controls, respectively). Two dietary patterns were extracted; "Unhealthy" (high consumption of artificial juice, processed meats, refined grains, sweets and desserts, pickles, snacks, and red meats), and "Healthy" (high consumption of vegetable oils, vegetables, fruits, fish, legumes, and nuts, as well as low consumption of hydrogenated fats and salt). Participants in the highest tertile of "Healthy" dietary pattern were significantly less likely to have the gallstones disease (OR: 0.33, 95% CI = 0.120.89) compared to the reference group (low tertile of "Healthy" dietary pattern) (P = 0.02). **Conclusions:** High consumption of vegetable oils, vegetables, fruits, fish, legumes, and nuts, as well as low consumption of hydrogenated fats and salt in context of healthy dietary pattern are inversely associated with risk of gallstones.

Keywords: *Cholecystectomy, dietary, gallbladder diseases, gallstones, Iran, patterns*

Introduction

Gallstones disease is a prevalent health issue among gastrointestinal diseases worldwide,[1-4] with ~1520% prevalence rate in the western populations.[3,5] Old age, female gender, ethnicity (Western Caucasian, Native Americans and Hispanics), genetic component and family history, obesity and rapid weight loss, pregnancy, reduced physical activity and history of total parenteral nutrition are known risk factors that closely linked with gallstones formation.[3,4,6]

Cholesterol and pigment gallstones are two main types of gallstones. In western countries in contrast to Asian ones, there are higher prevalence of cholesterol gallstones than pigment ones.[7] Saturation of cholesterol in bile and subsequently cholesterol crystallization and gallbladder stasis is associated with cholesterol form development of gall stone,[8] whereas release of β-glucuronidase from bacterial infections triggers the pigment stones formation.[9]

Diet and nutrition related factors have been of great interest as one of risk factors of gallstones.[10] Nutritional epidemiologic studies propose that dietary patterns assessment instead of focusing on a single dietary component can clarify the association between diet and health status more completely[11] because dietary patterns provide a snapshot of dietary habits including the interactions among dietary nutrients. Using a multivariate approach like dietary patterns might reduce concerns about confounding factors and interactions of foods and nutrients. Thus, we designed this study to assess the association between dietary patterns and risk of gallstones.

How to cite this article: Naseri K, Saadati S, Asadzadeh-Aghdaei H, Hekmatdoost A, Sadeghi A, Sobhani SR, *et al.* Healthy dietary pattern reduces risk of gallstones: Results of a case-control study in Iran. Int J Prev Med 2022;13:66.

Access this article online

Website: www.ijpvmjournal.net/www.ijpm.ir

DOI: 10.4103/ijpvm.IJPVM_455_19

Quick Response Code:

Methods

Study design

This case-control study was carried out in Taleghani hospital (Tehran, Iran) from November 2017 to October 2018. Case subjects (aged 2191 years) were recruited from patients with gallstone or common bile duct (CBD) stone confirmed by Ultrasonography within the past 6 months before collecting data. Control subjects (aged 2384 years) were patients admitted to the other wards of the same hospital for a broad spectrum of disorders including traumas and orthopedic conditions, or elective surgeries, or throat/ear/nose disease and have no gallbladder disorders, participated in this study. Controls were matched to cases based on age (±5 years) and sex. Overall, after excluding 5 cases whose reported energy intakes were outside the range of ± 3 SD from mean energy intakes of population and those with missing data, 110 cases and 230 controls (n = 340) remained in final analysis. This protocol of study was approved by Research Institute of Gastroenterology and Liver Diseases Ethics Committee (IR.SBMU.RIGLD.REC.1396.159) and a written informed consent was obtained from each individual before the interview.

Dietary assessment

To evaluate the dietary intake of subjects during 1 year before gallstones diagnosis in cases or hospital admission in controls, we used a valid and reproducible semi-quantitative food frequency questionnaire (FFQ).[12] Interviewer asked subjects to clarify the frequency of consumption on a daily, weekly, monthly or yearly for each food item and data from the questionnaire were converted to daily frequency. For calculating daily intake of each food group, intakes of food items within that group was summed. Food items of the questionnaire were categorized into 28 food groups with respect to similarity of their nutrient contents [Table 1].

Data collection

Trained interviewer carried out all measurements and filled out the questionnaires, including socio-demographic data, anthropometric measurements, physical activity, comorbidities, smoking status, and consumption of alcohol in last year by face-to-face interview. Physical activity was assessed by interviewer, using a questionnaire that was previously validated and represented as metabolic equivalents hour/day (METs h/d) in which 9 different MET levels were ranged from sleep/rest (0.9 METs) to high intensity physical activities (>6 METs).[13,14]

Measurement of weight was done, whereas participants standing on digital scales (Soehnle, Berline, Germany) with accuracy of 100g.[15] Height was measured using tape-meter fixed to a wall to the nearest 0.5 cm weight in kg divided by the square of height in meter to calculate body mass index (BMI) [Table 2].

Statistical analysis

Statistical analysis was conducted using SPSS software version 16 (SPSS Inc., Chicago, Illinois). Major dietary patterns were determined on 24 food groups using principal components analysis (PCA) with Varimax rotation. By taking relevant criteria into consideration, such as changing process of scree plot, the percentage of attended variance and the ability of the identified factors to be interpreted by two main factors out of 9 factors that had an Eagain value greater than 1, were identified as the major dietary patterns.[16] Each participant's score was obtained based on consumption value and the load factor of 24 different food groups for each of the two major dietary patterns. Individuals were classified based on tertiles of dietary patterns. Baseline characteristics, biochemical parameters, and dietary intakes of study participants between case and control group were compared t-test for quantitative variables and Chi-square test for qualitative variables. Logistic regression was used to calculate the odds ratio of gallstones disease as the dependent variable in relation to the different dietary patterns as independent variables. Physical activity and total energy intake were adjusted in the model. When the first tertile of the dietary patterns was considered as the reference, the odds ratios of the outcomes were determined with 95% confidence interval.

Results

A total of 110 cases and 230 controls (n = 340) remained in final analysis. By design, age was similar in both groups (57.66 ± 16.39 years vs. 56.00 ± 10.64 years in cases and controls, respectively).

Two dietary patterns were determined. "Unhealthy" dietary pattern (high consumption of Artificial juice, Processed meats, Refined grains, Sweets and desserts, Pickles, Snacks, and Red meats) and "Healthy" dietary pattern (high consumption of Vegetable oils, Vegetables, Fruits, Fish, Legumes, and Nuts, as well as low consumption of Hydrogenated fats and salt) were identified after performing the principal components analysis [Table 3]. In total, these two factors explained 18.36% of the total variance.

Baseline characteristics, biochemical parameters, and dietary intakes of study participants were shown based on case and control group [Table 2]. Individuals in the case group as compared with those in the control group were higher in total energy intake and prevalence of type-2 diabetes and lower in physical activity, protein intake, dietary cholesterol, and dietary fiber (P value <0.05).

Table 4 shows the odds ratios for the gallstones disease for male, female, and both sex together. There was a significant relationship between gallstones disease and "Healthy" dietary pattern when both sexes analyzed together. Participants in the highest tertile of "Healthy" dietary pattern were significantly less likely to have the gallstones

Table 1: Food groups

Food group	Food item(s)
Refined grains	White breads, pasta, rice, toasted bread, milled barley, sweet bread, white flour, starch, biscuits
Whole grains	Dark breads, barley bread
French fries	French fries
Baked potato	Potatoes
Dairy products	milk, yoghurt cream, cheese, ice cream
Red meats	Beef, lamb
Processed meats	Sausages
Eggs	Eggs
Poultry	Chicken with or without skin
Artificial juice	Soft drinks, Artificial juice
Vegetables	Cucumbers, mixed vegetables, eggplant, green peas, green beans, green peppers, squash, onions, lettuce, Tomatoes, Carrots, Cabbage, cauliflower, Brussels sprouts, kale, Olives
Legumes	Beans, peas, lima beans, broad beans, lentils, soy
Fruits	Pears, apricots, cherries, apples, raisins or grapes, bananas, cantaloupe, oranges, grapefruit, kiwi, grapefruits, peaches, nectarines, tangerines, mulberries, plums, pomegranates, lemons, pineapples, natural fruit juices
Dried fruits	dried dates, dried mulberries, other dried fruits
Vegetable oils	Vegetable oils
Fish	Canned tuna fish, other fish
Hydrogenated fats	Hydrogenated fats, animal fats, Mayonnaise
Spice	Pepper, turmeric, saffron, ginger, thyme Salt
Salt	
Snacks	Potato chips, puffs, crackers
Pickles	Pickles
Tea and Coffee	Tea, coffee
Nuts	Peanuts, almonds, pistachios, hazelnuts, roasted seeds, walnuts
Sweets and desserts	Chocolates, cookies, cakes, confections, Sugars, candies, Jam, jelly, honey

Table 2: Baseline characteristics, biochemical parameters and dietary intakes of study participants based on the patients with biliary stone disease and control group

	Cases (*n*=110)	Controls (*n*=230)	*P*[a]
Age (yr), mean±SD	57.66±16.39	56.00±10.64	0.072
Male *n* (%)	53 (48.2)	129 (56.1)	0.172
BMI (kg/m^2), mean±SD	27.04±5.46	26.70±4.01	0.884
Physical activity (MET), mean±SD	29.47±3.33	40.00±9.35	<0.001
Current smokers, *n* (%)	29 (26.4)	41 (17.8)	0.069
Drank alcohol in past year, *n* (%)	6 (5.2)	5 (2.2)	0.190
Diabetes type 2, *n* (%)	18 (16.4)	20 (8.7)	0.036
Total energy (kcal), mean±SEM	2448.28±61.48	2302.27±38.11	0.034
Carbohydrate (% of total energy), mean±SEM	48.27±0.80	49.00±0.44	0.079
Protein (% of total energy), mean±SEM	12.59±0.25	13.19±0.14	0.004
Fat (% of total energy), mean±SEM	41.53±0.86	40.91±0.46	0.682
Dietary cholesterol (mg/d), mean±SEM	203.30±8.50	236.99±6.58	0.001
Saturated fat (g/d), mean±SEM	25.49±0.85	24.42±0.38	0.142
Monounsaturated fat (g/d) (mg/d), mean±SEM	29.22±1.21	29.74±0.56	0.376
Polyunsaturated fat (g/d) (mg/d), mean±SEM	21.95±0.93	22.79±0.44	0.201
Dietary fiber (g/d), mean±SEM	36.08±2.01	40.33±0.74	0.001

T test for quantitative variables and χ^2 test for qualitative variables. Dietary intakes (except total energy) were adjusted for total energy intake. BMI: Body mass index; MET: Metabolic equivalent task

disease (OR: 0.33, 95% CI = 0.120.89) compared with the reference group (low tertile of "Healthy" dietary pattern) (*P* for trend = 0.02). Physical activity and total energy intake were adjusted in the model.

Discussion

In the present study, we identified two major dietary patterns named as "healthy" and "unhealthy". Our results revealed that healthy or prudent dietary pattern with high intake of vegetable oils, vegetables, fruits, fish, legumes, and nuts, as well as low intake of hydrogenated fats and salt, inversely associated with risk of all types of gallstones and this significance after adjusting for total energy intake and physical activity permanently existed. Unhealthy dietary pattern including high intake of artificial juice, processed meats, refined grains, sweets and desserts, pickles, snacks, and red meats appeared to increase the incident cases of gallstones.

Table 3: Factor loading matrix for the two dietary patterns identified in the study population

Food groups	Dietary patterns	
	Unhealthy	Healthy
Artificial juice	**0.57**	0.241
Processed meats	**0.55**	
Refined grains	**0.55**	
Sweets and desserts	**0.49**	
Pickles	**0.48**	
Snacks	**0.45**	
Red meats	**0.45**	0.203
Baked potato	0.39	
French fries	0.28	
Dairy product	0.23	
Tea and coffee		
Poultry		
Vegetable oils		**0.63**
Vegetables		**0.57**
Hydrogenated fats	0.27	**-0.55**
Fruits		**0.48**
Fish		0.39
Legumes		0.36
Nuts		0.32
Salt		-0.27
Eggs		0.22
Dried fruits		0.21
Spices		
Whole grains		
Percentage variance explained by each pattern	9.80	8.56

Total variance explained by all of the patterns is 18.36%. Loadings >0.4 are given in bold

Few studies have addressed the association between dietary patterns and risk of gallstones in different populations.[1,2,10] In Mexican-American men, a traditional Mexican diet including high consumption of beans, corn tortillas, and chili peppers was associated with reduced prevalence of gallbladder diseases.[10] Jessri *et al*.[1] reported that among Iranian women, unhealthy dietary pattern including high consumption of high-fat dairy products, solid fats, baked potatoes, red and processed meats, eggs, snacks and refined grains was positively linked with the risk of gallstones. In a study that conducted among Korean population, association between dietary patterns with cholesterol and pigment gallstone has been investigated separately. In this study, increased risk of gallstone was related to dietary pattern consuming pork, beef and fried foods, although there was not any relation between dietary pattern and risk of pigment stone.[2] All of these studies were cross sectional, but they were conducted on different populations with heterogeneous sample sizes. In Mexican-American study, both sexes were evaluated but association of dietary patterns with incidence cases of GBD were considerable only among men.[10] Assessed dietary patterns in Iranian population were among women only, as well.[1] In Korean study,[2] dietary factors evaluated with two types of gallstone distinctly. It is important and considerable to note that results of a large prospective cohort study showed that vegetarian diet did not have any protective association with risk for symptomatic gallstones, but after adjusting for BMI, this association became significant.[17] There are some differences among these dietary patterns but all of them focused on this outcome that unhealthy dietary pattern including fried foods, red and processed meats can raise the risk of gallstones disease.

Other studies reported evidence for protective effect of fruits,[1,2] vegetables,[2,18] and vegetable oil[19] against risk

Table 4: Odds ratios of biliary stone disease for dietary patterns[a]

Dietary patterns	Men		Women		Both sexes	
	OR	95% CI	OR	95% CI	OR	95% CI
Tertiles of Unhealthy dietary pattern						
Low	1.00		1.00		1.00	
Medium	1.48	0.366.18	0.72	0.105.08	0.41	0.141.24
High	2.74	0.58 12.87	2.29	0.38 13.61	0.40	0.521.11
P value for trend	0.20		0.34		0.10	
Tertiles of Healthy dietary pattern						
Low	1.00		1.00		1.00	
Medium	0.34	0.091.25	0.71	0.134.01	0.44	0.161.19
High	0.29	0.081.11	0.32	0.061.74	0.33	0.120.89
P value for trend	0.06		0.19		0.02	

[a]Adjusted for physical activity and total energy intake

of gallbladder disease. Findings from the woman's health initiative prospective cohort showed that vegetable protein consumption inversely associated with risk of gallbladder diseases.[20] As well as, among women aged 48-60 years, intake of fruit and vegetables reduced the risk of cholecystectomy.[21,22] Magnesium, vitamin C and folate content of fruits and vegetables negatively linked to risk of gall stone.[23-25]

In our study, healthy dietary pattern contained high amounts of fish and vegetable oils. Some of previous studies have brought attention to n-3 fatty acids as protective factors against gallstones.[1,2,26,27] A major mechanism of this effect attributed to the improvement in cholesterol saturation index (CSI) and nucleation time by n-3 fatty acids, which can prevent cholelithiasis.[28] Moreover, the healthy dietary pattern was high in vegetables, fruits, legumes, and nuts, which are the main sources of fiber. It has been shown that dietary fiber can reduce the absorption of cholesterol, which might reduce the risk of cholelithiasis.[29]

In this study we showed that individuals in case group had significantly lower protein intake and dietary cholesterol. There are some studies that proposed dietary cholesterol[30] and animal protein[31] increase the biliary cholesterol saturation and in this way formed cholesterol gallstones.

The present study had several strengths; this study was among the few studies to evaluate the association of dietary patterns with risk of gallstones conducted among Iranian population. Previous studies in this field assessed just gallstone patients, but this was the first evaluation of biliary stone (gallstone and CBD stone and history of last 6 months cholecystectomy). As well as, data was collected by the same interviewer, so interview bias was diminished. To decrease the recall bias, all case subjects were newly diagnosed (within 6 months).

This study has a few limitations. First, the study population was concentrated in capital city of Iran and we could not assess the other cities with different socioeconomic properties. Second, the sample size was small, which could restrict the statistical power to describe differences in the diet. Third, limitations of the using FFQ (such as measurement errors including under- and/or over –reporting of intakes of certain foods, relying on memory and misclassification error) for assessing dietary intakes should be considered.[12]

Conclusions

In conclusion, high consumption of vegetable oils, vegetables, fruits, fish, legumes, and nuts, as well as low consumption of hydrogenated fats and salt in context of healthy dietary pattern are inversely associated with risk of gallstones among Iranian individuals. These findings need to be confirmed in prospective studies.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Acknowledgments

We would like to acknowledge patients who participated in this research and made it possible, and to the colleagues from Research Institute for Gastroenterology and Liver Diseases and staff of Taleghani Hospital, Shahid Beheshti University of Medical Sciences, who provided insight and expertise that greatly assisted the research.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

Received: 12 Dec 19 **Accepted:** 18 May 20
Published: 08 Apr 22

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