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ORIGINAL ARTICLE

Case Control Study

Egg consumption and risk of non-alcoholic fatty liver disease

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Abstract

AIM

To evaluate the association between egg consumption and risk of non-alcoholic fatty liver disease (NAFLD) development.

METHODS

This case-control study was conducted on individuals who were referred to two hepatology clinics in Tehran, Iran in 2015. The study included 169 patients with NAFLD and 782 controls. Egg consumption was estimated using a validated food frequency questionnaire. The participants were categorized according to the frequency of their egg consumption during the previous year: Less than two eggs per week, two to three eggs per week, and four or more eggs per week.

RESULTS

In the crude model, participants who consumed 2 to 3 eggs per week, were 3.56 times more likely to have NAFLD in comparison to those who consumed less than 2 eggs per week (OR: 3.56; 95%CI: 2.35-5.31). Adjustment for known risk factors of NAFLD strengthened

this significant association so that individuals have consumed two to three eggs per week had 3.71 times higher risk of NAFLD than those who have eaten less than two eggs per week (OR: 3.71; 95%CI: 1.91, 7.75).

CONCLUSION

Our data indicate that higher egg consumption in common amount of usage is associated with higher risk of NAFLD.

Key words: Egg; Diet; Non-alcoholic fatty liver disease; Dietary cholesterol

Core tip: The data indicate that egg consumption in common amount of usage is associated with risk of non-alcoholic fatty liver disease. According to the case-control design of this study, it can not show the causality effect; thus, these findings should be confirmed in future prospective studies with separate parts of eggs to find the etiological relationships.

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INTRODUCTION

Non-alcoholic fatty liver disease (NAFLD) includes a spectrum of liver disordersfrom simple steatosis to non-alcoholic steatohepatitis (NASH), fibrosis, cirrhosis, and even hepatocellular carcinoma[1]. NAFLD is the most common cause of chronic liver diseases around the world[2] and may be considered as hepatic manifestation of metabolic syndrome[3]. The increasing prevalence of obesity, together with insulin resistance, hypertension, dyslipidemia, and eventually the metabolic syndrome dispose many people to the risk of NAFLD development in the futureyears[4].

Increasing evidence showed that dietary factors contribute to the pathophysiology and treatment of NAFLD[5-7]. Among the known dietary factors that involved in the development of NAFLD, dietary cholesterol has drown a great deal of attention. Current studies of animal models propose that excess dietary cholesterol is regarded as the key factorrelated to the riskof steatohepatitis and hepatic inflammation[8-10]. Addition of cholesterol to the diet of obese, diabetic mice increasedthe accumulation of hepatic free cholesterol, hepatocyte apoptosis, and liver fibrosis[11]. Moreover, an association between raised cholesterol intake and the risk or severity of NAFLD has been addressed by epidemiological studies[12-14].

Among single foods, eggs are regarded as a main source of dietary cholesterol, with one large egg containing almost 210 mg of cholesterol; on the other hand, eggs are rich in proteins, and other nutrients[15], which can improve human health. There is limited evidence on the relationship between egg consumption and NAFLD and its risk factorswith controversial results[16-18]. Therefore, the present study was designed to examine the association between egg consumption and risk of NAFLD development.

MATERIALS AND METHODS

Participants

The present case-control study was conducted on individuals who were undertaken a liver Ultrasound, and were referred to two Hepatology clinics in Tehran, Iran in 2015. The study included 169 patients with NAFLD and 782 controls. The cases were patients with NAFLD, which was diagnosed by a gastroenterologistaccording to the presence of hepatic steatosis in Ultrasound exam within previous month, and referred to our clinics to be examined by Fibroscan®, and the Fibroscan resultsshowed a Controlled Attenuation Parameter score of more than 263, and fibrosis score of more than 7. These patients were selected with the convenience-sampling procedure. Controls were randomly selected age- and sex-matched subjects from the sameclinic among patients with pancreatobiliay disorders who had been undertaken an Ultrasound showing no hepatic steatosis. The age ranges for matching were 20-40, 40-60 and > 60 years old. Data on each pair of cases and controls were collected at the same time. The participation rate in the study was 94% for cases and 98% for controls. Written informed consent was obtained from all the participants. The study protocol was approved by the local Ethics Review Committee.

Assessment of dietary intake

Dietary intake of patients was assessed using a valid and reliablesemi-quantitative food frequency questionnaire (FFQ), which included 168 items of foods with standard servingsizes, as commonly consumed by Iranians[19]. The consumptionfrequency of each food item was questioned ona daily, weekly or monthly basis and converted to dailyintakes. In the case of egg consumption, the participants were categorized according to the frequency of their egg consumptionduring the previous year: Less than two eggs per week, two to three eggs per week, and four or more eggs per week. Dietary nutrients intakes were calculated using NUTRITIONIST V (First Databank, Hearst Corp,San Bruno, CA, United States). The patients who had completed less than 90% of dietary questionnaires and subjects who reported extremely low or high energy intakes (< 500 or > 5000 kcal/d) were excluded from the study[20].

Assessment of other variables

Physical activity was evaluated using the metabolic

Table 1 Baseline characteristics, biochemical parameters and dietary intakes of study participants based on the patients with non-alcoholic fatty liver disease and control group

	Cases (n = 169)	Controls (n = 782)	P value[a]
Age (yr), mean ± SD	42.65 ± 12.21	43.71 ± 14.52	0.373
Male n (%)	81 (47.9)	314 (40.2)	0.063
BMI (kg/m^2), mean ± SD	33.19 ± 8.71	27.74 ± 4.495	< 0.001
Physical activity (MET), mean ± SD	31.89 ± 3.15	34.33 ± 2.85	< 0.001
Current smokers, n (%)	151 (89.9)	145 (18.5)	< 0.001
Drank alcohol in past year, n (%)	22 (13.1)	68 (8.7)	0.077
Diabetes type 2, n (%)	26 (15.6)	53 (6.8)	< 0.001
FBS (mg/dL), mean ± SD	109.29 ± 39.39	90.09 ± 29.24	< 0.001
Total cholesterol (mg/dL), mean ± SD	184.79 ± 54.94	177.72 ± 38.74	0.221
LDL (mg/dL), mean ± SD	121.17 ± 43.04	104.26 ± 31.65	< 0.001
HDL (mg/dL), mean ± SD	41.26 ± 16.72	47.72 ± 10.51	0.001
Triglycerides (mg/dL), mean ± SD	180.40 ± 123.81	131.97 ± 81.59	< 0.001
Total energy (kcal), mean ± SEM	2627.67 ± 61.39	2746.69 ± 27.23	0.068
Carbohydrate (% of total energy), mean ± SEM	58.12 ± 0.95	59.82 ± 0.44	0.001
Protein (% of total energy), mean ± SEM	15.84 ± 0.18	14.07 ± 0.08	< 0.001
Fat (% of total energy), mean ± SEM	29.23 ± 0.30	33.78 ± 0.20	< 0.001
Dietary cholesterol (mg/d), mean ± SEM	315.31 ± 11.50	263.41 ± 5.35	< 0.001
Saturated fat (g/d), mean ± SEM	30.62 ± 5.72	62.67 ± 2.67	< 0.001
Monounsaturated fat (g/d) (mg/d), mean ± SEM	29.85 ± 0.48	32.00 ± 0.23	< 0.001
Polyunsaturated fat (g/d) (mg/d), mean ± SEM	18.51 ± 5.74	59.58 ± 2.67	< 0.001
Dietary fiber (g/d), mean ± SEM	19.21 ± 0.50	14.68 ± 0.23	< 0.001
Red/processed meats (g/d), mean ± SEM	70.95 ± 2.66	36.00 ± 1.24	< 0.001

[a]Independent t-test for quantitative variables and χ^2 test for qualitative variables. Dietary intakes (except total energy) were adjusted for age and total energy intake. BMI: Body mass index; MET: Metabolic equivalent task; FBS: Fasting blood sugar; LDL: Low-density lipoprotein cholesterol; HDL: High density lipoprotein cholesterol.

equivalent task (MET) questionnaire[21,22]. Other covariate information including age, gender, smoking habits, alcohol consumption,medical history, and current use of medications were assessed using questionnaires. Weight and height of all participants were measured.

Statistical analysis

Baseline characteristics and dietary intakes were compared between cases and controls using t-test for continuous variables and χ^2 for categorical variables. Egg consumptionwas dividedinto three ascending categories on an ordinal scale. Mean or prevalence of baseline characteristics wascomputed for each category. Baseline characteristicswere also compared using ANOVA for continuous variables and χ^2 categorical variables. The relationship between NAFLDand egg consumptionwas assessed using multipleregression analysis. Estimates were presented inthree models; the first model was adjusted for age (continuous),and total energy intake (kcal/d). In thesecond model, we further controlled for body mass index (BMI), history of diabetes and smoking (non-smoker, current smoker). Finally, we further adjusted for physical activity (MET) and gender. All models were conducted by treating thefirstcategory of egg consumption (< 2/wk) as a reference. All the statistical analyses were done using SPSS for Windows (version 19; SPSS Inc., Chicago, IL).

RESULTS

Baseline characteristics, biochemical parametersand dietary intakes of the cases and controls are shown in Table 1. Mean age of the total study population was 43.54 ± 14.13 years and 41.5% (395) of participants were male. By design, cases and controls had the similar age and sex distribution. Patients with NAFLD had significantly more BMI, lower physically activity, lowerconsumption of alcohol, and were more likely to be smoker, and have diabetes in comparison to controls. Furthermore, the cases had elevatedfasting blood glucose (FBS), low-density lipoprotein cholesterol (LDL), Triglycerides, and reduced high density lipoprotein cholesterol (HDL) levels and increasedintake of protein, cholesterol, fiber and red/processed meats compared with the controls (Table 1).

Basic characteristics and dietary intakes of the studied participants by categories of egg consumption are presented in Table 2. Compared to egg consumption of lower than two per week, higher egg consumption was associated with a lower average age, male sex, current smoking, higher energy intake, lower percent of total energy from carbohydrate and fat. Additionally, the subjects with higher egg consumption tended toconsume more protein, cholesterol, monounsaturated fat and red/processed meats, but less saturated and polyunsaturated fatty acids (Table 2).

In secondary analysis, there wasa similar egg-NAFLD associationsin women (P-trend 0.001) and men (P-trend 0.048) (Table 3).

Multivariate adjusted odds ratios for NAFLD based on egg consumption categories are indicated in Figure 1. In the crude model, participants that consumed 2 to 3 eggs per week, were 3.56 times more likely to have NAFLD in

Table 2 Basic characteristics and dietary intakes of study participants by frequency of egg consumption *n* (%)

	Egg consumption categories			*P* value[a]
	< 2/wk (*n* = 589)	2-3/wk (*n* = 142)	⩾ 4 /wk (*n* = 220)	
Age (yr)	45.65 ± 12.26	39.73 ± 13.18	40.35 ± 13.30	< 0.001
Male gender	218 (37.0)	56 (39.4)	121 (55)	< 0.001
BMI (kg/m^2), mean ± SD	28.58 ± 5.44	29.60 ± 7.34	28.51 ± 5.87	0.150
Physical activity (MET), mean ± SD	33.99 ± 3.05	33.42 ± 3.21	33.94 ± 2.95	0.136
Current smokers	155 (26.3)	59 (41.8)	82 (37.3)	< 0.001
Total energy (kcal), mean ± SEM	2580.59 ± 30.68	2744.94 ± 57.45	3101.07 ± 51.20	< 0.001
Carbohydrate (% of total energy), mean ± SEM	60.44 ± 0.67	59.48 ± 0.63	58.14 ± 0.85	0.001
Protein (% of total energy), mean ± SEM	14.09 ± 0.10	14.71 ± 0.20	14.95 ± 0.17	0.001
Fat (% of total energy), mean ± SEM	33.06 ± 0.24	32.56 ± 0.49	32.97 ± 0.40	< 0.001
Dietary cholesterol (mg/d)	226.40 ± 5.75	291.95 ± 11.60	383.90 ± 9.53	< 0.001
Saturated fat (g/d)	56.70 ± 3.16	64.70 ± 6.38	52.57 ± 5.24	< 0.001
Monounsaturated fat (g/d) (mg/d), mean ± SEM	31.20 ± 0.26	31.32 ± 0.53	32.91 ± 0.44	< 0.001
Polyunsaturated fat (g/d) (mg/d), mean ± SEM	53.10 ± 3.20	57.26 ± 6.45	46.71 ± 5.30	< 0.001
Dietary fiber (g/d)	15.65 ± 0.28	16.25 ± 0.57	14.60 ± 0.47	< 0.001
Red/processed meats (g/d)	37.76 ± 1.53	47.79 ± 3.10	50.51 ± 2.54	< 0.001

[a]Dietary intakes (except total energy) were adjusted for age and total energy intake. BMI: Body mass index; MET: Metabolic equivalent task.

Table 3 Odds ratio for non-alcoholic fatty liver disease-according to egg consumption stratified by gender

	Multivariate adjusted model[a]	
Egg consumption	Female	Male
< 2/wk	1.00	1.00
2-3/wk	5.55 (2.30-13.37)	1.90 (0.50-7.16)
⩾ 4/wk	1.67 (0.68-4.10)	0.25 (0.06-1.01)
P for trend	0.001	0.048

[a]Adjusted for age, energy intake, body mass index, history of diabetes, smoking, and physical activity.

comparison to those who consumed less than 2 eggs per week (OR: 3.56; 95%CI: 2.35-5.31). After controlling for ageand total energy intake, consuming 2 to 3 eggs per week was positively associated with the risk of NAFLD (OR: 3.83; 95%CI: 2.49-5.89). These associations remained significant even after additionally controlling for BMI, history of diabetes and smoking (OR: 3.57; 95%CI: 1.89-6.75). Further adjustment for physical activity, and gender strengthened this significant association so that individuals who have consumed two to three eggs per week had 3.71 times higher risk of NAFLD than those who have eaten less than two eggs per week (OR: 3.71; 95%CI: 1.91-7.75). Egg consumption more than four per week was not significantly associated with the NAFLD risk.

DISCUSSION

The results of the present study showed that the egg consumption increases the risk of NAFLD in common range of its consumption (two tothree eggs per week). This relationship was also significant after adjustment forage, gender, BMI, history of diabetes, smoking, and physical activity.

The role of diet and dietary supplements on the pathogenesis of NAFLD have been shown previously[23-36]; however, to our knowledge, no study has yet evaluated the association of egg consumption and NAFLD risk. It is well established that eggscontain a wide variety of essential nutrients and bioactive compounds that can affecthuman health. Their high quality protein, fats and micronutrients and low price make theman important part of many people's diet[37]; despite the nutritional benefits of egg consumption,there are concerns abouttheir high content of cholesterol and saturatedfat and theirinfluences on metabolic disorders[38]. Thus, one possible explanation for theinverse association between egg consumption and risk of NAFLD development may be due to the highcholesterol content of egg. Previous studieshave shown that a higher consumption of cholesterolis associated with NAFLD and its exacerbation[12,13,39,40]. In addition, the presence of high amount of cholesterol in diet is necessary for development of NAFLD[41]. Baumgartner *et al*[39] have shown that daily egg consumption increases serum cholesterol and LDL-C concentrations inwomen; however, there was no effects on markers for inflammation, endothelial activity, and liver function. Interestingly, the consumption of egg white hydrolyzed with pepsin considerably improved hepatic steatosis[42]. Thus, it seems that the association between egg consumption and NAFLD is mainly due to high cholesterol content of it, and might not be seen when people consume only the white part of it. Therefore, more studies are recommended to evaluate the effects of consumption of different parts of egg on NAFLD risk[13].

An unexpected finding of the present study was that more than 4 eggs consumptionper week was not significantly associated with risk of NAFLD. This may be explained by the fact that nutritional factors are correlated with each other, and determining of the effect of particular nutrients or particular foods on a risk factor is difficult. The effects of egg cholesterol on serum cholesterol concentrations depends on the content of individuals' diet specially the fiber content of it[43,44]. It is possible that those who ate more than 4 eggs per week, consumed it in mixed dishes containing vegetables, which reduces the absorption of cholesterol. Thus, we

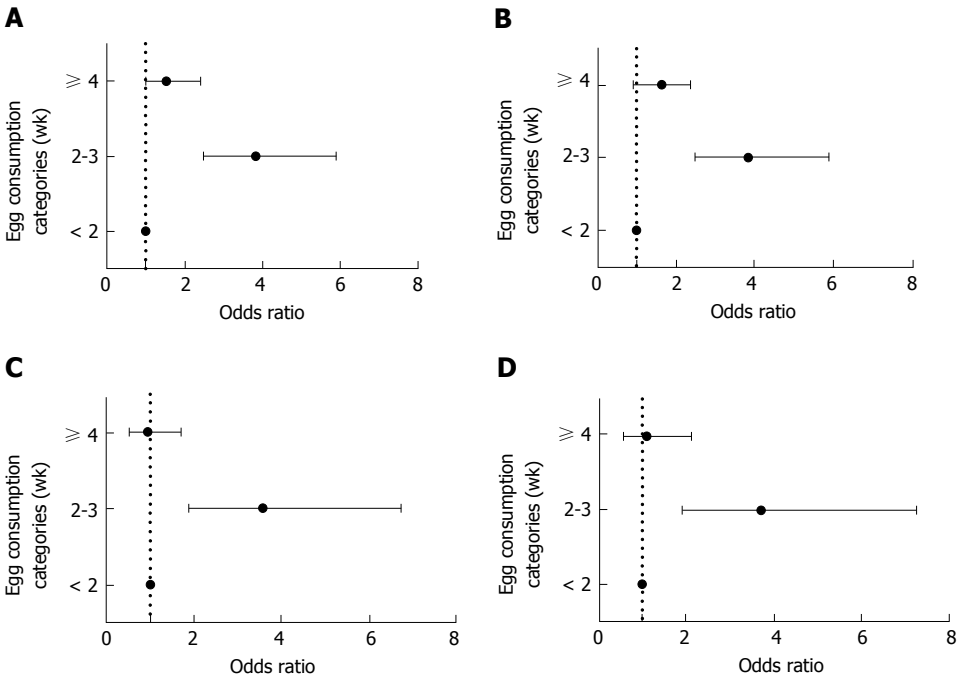

Figure 1 Multivariate-adjusted odds ratio for non-alcoholic fatty liver diseaseaccording to egg consumption. A: Crude model; B: Model 2, multivariate adjusted for age and energy intake; C: Model 3, further controlled for, body mass index, history of diabetes and smoking; D: Model 4, additionally adjusted for physical activity, and gender. Data are presented as the odds ratio (95%CI).

suggest that future studies assess the type of dishes with egg to find the possible interactions of different constituent of them.

It has been reported that dietary intake of patients with NAFLD was richer in saturated fat, cholesterol and was poorer in polyunsaturated fat[12]. Subramanian *et al*[40] have concluded that dietary cholesterol confers in progression of NAFLD to NASH. Furthermore, Zelber-Sagi *et al*[18] found that NAFLD patients have a higher intake of meat, which is another source of dietary cholesterol; however, some other studies only found a significant association between NAFLD and high dietary intake of carbohydrate and simple sugars[45,46], and some studies did find an association only between NAFLD and low intake of n-3 fatty acids and some antioxidants[16]. These dietary habits may accelerate the development of NAFLD by directly affecting steatosis of liver and oxidative injury[12].

This study was the first study that examined the relationship between egg consumption and risk of NAFLD in newly diagnosed patients who have not probably changed their diet due to the disease diagnosis; other strengths of this study includes its relatively large sample size, the high participation rate of participants, and socioeconomic differences of participants, which affects their dietary intakes.

Although we used a validated FFQ for measurement of dietary intakes, measurement error, and recall bias are unavoidable errors. Moreover, there might be some unknown risk factors that affect our results. Therefore, we recommend this analysis to be done in other populations.

In conclusion, our data indicate that egg consumption in common amount of usage is associated with riskof NAFLD. According to the case-control design of this study, it can not show the causality effect; thus, these findings should be confirmed in future prospective studies with separate parts of eggs to find the etiological associations.

ACKNOWLEDGMENTS

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COMMENTS

Background

Among the known dietary factors that affect the pathogenesis of non-alcoholic fatty liver disease (NAFLD), dietary cholesterol has drown a great deal of attention. Current studies propose that excess dietary cholesterol is regarded as the key factor related to the risk of steatohepatitis and hepatic inflammation. Among individual foods, eggs are regarded as a main source of dietary cholesterol; on the other hand, eggs are rich in proteins, and other nutrients. Limited research has assessed therelationship between egg consumption and risk of (NAFLD) development.

Research frontiers

Understanding of the associationbetween egg consumption andrisk of NAFLD developmentcan contribute to clarifyhow intake of special food groups correlate with the disease and could lead to more particularguidelinesfor NAFLD prevention.

Innovations and breakthroughs

This study showed that egg consumption in common amount of usage is associated with risk of NAFLD. It seems that this association is mainly due to

high cholesterol content of it, and might not be seen when people consume only the white part of it.

Applications

According to the results of this study, the authors recommend low intake of eggs specially the yolk part of it for prevention of NAFLD; however, further studies are recommended to reach to a consus in this regard.

Peer-review

This is an interesting paper evaluating the association between egg consumption and NAFLD.

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