International Journal of Preventive Medicine

Brief Communication Open Access

Dairy Consumption and Risk of Stroke: A Case-control Study

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How to cite this article: Khosravi-Boroujeni H, Saadatnia M, Shakeri F, Keshteli AH, Saneei P, Esmaillzadeh A. Dairy consumption and risk of stroke: A case-control study. Int J Prev Med 2016;7:2.

ABSTRACT

Background: It remains controversial if dairy product intake is associated with risk of stroke. Limited information is available from Middle East countries in this regard. This case-control study was conducted to assess the relationship between dairy consumption and risk of stroke in Iranian adults.

Methods: In this study, 195 stroke patients (recognized based on clinical findings and computed tomography scan) hospitalized in neurology ward of Alzahra University Hospital were enrolled. Controls (n = 195) were selected with convenience nonrandom sampling procedure from other wards of this hospital. A validated food frequency questionnaire was used to assess participants' usual dietary intakes. Data on other variables were collected by the use of questionnaires.

Results: Patients with stroke were older (P < 0.001), had lower weight and body mass index (P < 0.05) and were more likely to be male (P < 0.05) and less likely to be obese (P < 0.001). After adjustment for age, sex and total energy intake, Individuals with the highest consumption of low-fat dairy had a significantly decreased risk of stroke (odds ratio [OR]: 0.58; 95% of confidence interval [CI]: 0.34–0.99), while those with the highest intake of high-fat dairy had a 2-fold increased risk of stroke. The association between high-fat dairy consumption and stroke even persisted after additional adjustments for physical activity, smoking and dietary variables (OR: 2.02; 95% CI: 1.02–4.02); but the association between low-fat dairy intake and stroke disappeared after these adjustments (OR: 0.84; 95% CI: 0.44–1.58).

Conclusions: We found a significant positive association between high-fat dairy consumption and risk of stroke. Further prospective studies are required to confirm this finding.

Keywords: Dairy intake, diet, food frequency questionnaire, stroke

Access this article online	
Quick Response Code:	Website: www.ijpvmjournal.net/www.ijpm.ir
	DOI: 10.4103/2008-7802.173792

INTRODUCTION

Stroke is a main cause of death in developed countries, and it is expected to become a rising health problem in developing countries as well.[1] The reported incidence of stroke in Iran is higher than in some Western societies (139/100,000).[2] Recognition of risk factors

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may have a significant role in preventing the incidence of stroke.[3] Diet has long been considered as a main contributing factor to the incidence of stroke.[4] It has been well-established that intake of high dietary cholesterol and saturated fatty acid (SFA) would result in higher risk of stroke,[5] while dietary intake of calcium and potassium have been associated with lower risk.[6]

Both prospective studies[7,8] and controlled trials[9,10] have shown an inverse association between milk and dairy consumption and stroke, but not consistently.[6,11,12] On the other hand, a meta-analysis of cohort studies on milk and cardiovascular disease risk have suggested that milk drinking might be associated with a small but worthwhile reduction in heart disease and stroke risk.[13] In the Middle-Eastern countries the incidence of stroke occurs in younger ages than that in western societies. Thus, this study aimed to assess the relationship between dairy consumption and stroke in Iranian adults.

METHODS

Participants

This case-control study was conducted in Alzahra University Hospital. Totally, 195 cases and 195 controls with convenience nonrandom sampling procedure participated in this study. We tried to match cases and control in terms of sex and age; however, due to having difficulties getting enough patients in the hospital, we were not successful in doing this. Written informed consent was obtained from each participant.

Assessment of dietary intake

Usual dietary intakes of participants in both groups were assessed using a food frequency questionnaire (FFQ) containing 168 food items usually consumed by Iranians.[14] Low-fat dairy (<2.5%) intakes were defined as consumption of skim milk, low-fat milk, and low-fat yogurt. High-fat dairy category was computed by summing up dietary intakes of high-fat milk, cocoa milk, chocolate milk, regular yogurt, condensed yogurt, and cheese. Total dairy consumption was calculated by summing up the consumption of these dairy items.

Assessment of stroke

Patients aged >45 years with first ever symptomatic acute stroke (arterial) confirmed by brain computed tomography or magnetic resonance imaging were included. Ischemic stroke was defined as an episode of focal neurologic deficit with acute onset due to a vascular cause and lasting more than 24 h.[15] The study protocol was approved by local Ethics Review Committee (No. 187028 IUMS).

Statistical methods

Independent samples Student's *t*-test or Chi-square test were used for comparing variables among cases and controls. General characteristics and dietary intakes of participants across tertiles of dairy intake were compared by the use of analysis of variance, Chi-square and analysis of covariance, where appropriate. To explore the associations between dairy intake and stroke, we applied logistic regression method in different models. The overall trend across tertiles of dairy consumption was examined through the use of Mantel-Haenszel extension Chi-square test.

RESULTS

Patients with stroke were older ($P < 0.001$), had lower weight and body mass index (BMI) ($P < 0.05$) and were more likely to be male ($P < 0.05$) and less likely to be obese ($P < 0.001$) [Table 1]. There were significantly differences in dietary intake of high-fat dairy, low-fat dairy, fruits, pulses and nonhydrogenated vegetable oils (non-HVOs) between cases and controls. High consumption of total dairy was significantly associated with higher intakes of total energy, fruits and vegetables [Table 2]. Individuals in the highest category of high-fat dairy consumption had lower age, were more likely to be male and less likely to be obese [Table 3].

Multivariate associations between total-, high- and low-fat dairy consumption and stroke are indicated

Table 1: General characteristics and dietary intakes of study participants separately by case and control groups[a]

	Cases ($n=195$)	Controls ($n=195$)	P[d]
Age (year)	68.0±1.0	61.5±0.8	<0.001
Weight (kg)	69.5±1.0	72.4±1.1	0.048
BMI (kg/m^2)	25.2±0.3	28.5±1.0	0.004
Male (%)	60.0	46.7	0.006
Female (%)	40.0	53.3	0.006
Physical activity (MET-min/day)	681.0±98.0	564.5±110.7	0.43
Obesity[b] (%)	11.3	29.2	<0.001
Dietary intakes			
Total energy (kcal)	2076±71	2110±63	0.71
Total dairy (g)	402.4±17.2	413.4±20.9	0.68
Low-fat dairy (g)	270.3±14.9	339.9±20.1	0.006
High-fat dairy (g)	132.2±15.0	73.6±8.9	<0.001
Fruits (g)	358.6±29.6	280.5±17.2	0.023
Pulses (g)	34.6±2.3	25.0±1.8	<0.001
HVO (g)[c]	18.8±2.6	18.7±2.1	0.96
Non-HVO (g)	10.4±0.8	19.2±1.3	<0.001
Meats (g)	81.9±16.2	57.1±4.9	0.14
Vegetables (g)	247.7±12.3	289.9±16.0	0.07
Grains (g)	316.3±12.7	344.6±13.9	0.13

[a]Data are means±SE unless indicated. Data for dietary intakes are adjusted for age and total energy intake, [b]BMI ≥30, [c]HVO=Hydrogenated vegetable oil, [d]Obtained by the use of student *t*-test and Chi-square, where appropriate. SE=Standard error, BMI=Body mass index, MET=Metabolic equivalent of task

Table 2: General characteristics and dietary intakes of study participants by tertiles of total dairy consumption[a]

	Tertiles of total dairy intake (n=130)			P^d
	T1 (<279 g/day)	T2 (279-490 g/day)	T3 (>490 g/day)	
Age (year)	63.6±1.0	64.5±1.1	66.1±1.2	0.25
Weight (kg)	70.6±1.3	71.6±1.2	70.8±1.4	0.83
BMI (kg/m^2)	26.9±0.5	26.3±0.4	27.7±1.6	0.59
Male (%)	50.0	56.9	53.1	0.53
Female (%)	50.0	43.1	46.9	0.53
Physical activity (MET-min/day)	700.2±148.8	607.5±127.3	560.6±104.7	0.74
Obesity[b] (%)	21.5	20.8	18.5	0.81
Dietary intakes				
Total energy (kcal)	1830.3±77.2	1981.6±66.8	2463.0±90.0	<0.001
Total dairy (g)	166.2±6.8	371.0±5.1	686.7±22.7	<0.001
Low-fat dairy (g)	124.3±7.1	275.5±10.7	515.5±25.8	<0.001
High-fat dairy (g)	41.9±4.8	95.5±10.6	171.2±22.5	<0.001
Fruits (g)	266.7±24.3	292.0±17.8	399.7±41.0	0.003
Pulses (g)	30.5±2.9	31.0±2.6	28.0±2.3	0.68
HVO (g)[c]	18.0±2.7	14.9±2.3	23.3±3.5	0.12
Non-HVO (g)	15.4±1.1	15.0±1.7	14.0±1.1	0.73
Meats (g)	77.2±24.3	66.4±6.9	65.1±4.6	0.82
Vegetables (g)	218.4±12.0	236.6±13.0	342.9±23.2	<0.001
Grains (g)	325.2±15.7	341.0±18.3	324.9±14.8	0.73

[a]Data are means±SE unless indicated. Data for dietary intakes are adjusted for age and total energy intake, [b]BMI ≥30, [c]HVO=Hydrogenated vegetable oil, [d]Obtained by the use of ANOVA and Chi-square, where appropriate. SE=Standard error, BMI=Body mass index, MET=Metabolic equivalent of task

Table 3: General characteristic and dietary intake of study participants by tertiles of dairy consumption separated by low and high fat dairy[a]

	Tertiles of low fat dairy intake (n=130)			P	Tertiles of high fat dairy intake (n=130)			P^d
	T1 (<157 g/day)	T2 (157-362 g/day)	T3 (>362 g/day)		T1 (<15 g/day)	T2 (15-55 g/day)	T3 (>55 g/day)	
Age (year)	64.2±1.0	64.2±1.1	65.8±1.2	0.42	67.2±1.0	63.7±1.1	63.4±1.2	0.025
Weight (kg)	68.9±1.3	72.1±1.1	71.9±1.4	0.14	68.7±1.2	75.4±1.3	68.8±1.2	≤0.001
BMI (kg/m^2)	26.3±0.5	26.5±0.4	26.1±1.6	0.38	26.0±0.4	29.2±1.5	25.5±0.5	0.014
Male (%)	55.4	57.3	47.3	0.23	50.8	46.2	63.1	0.006
Female (%)	44.6	42.7	52.7		49.2	53.8	36.9	0.006
Physical activity (MET-min/day)	771.7±152.7	670.7±127.7	423.9±95.7	0.14	550.3±138.3	476.5±79.4	841.4±152.8	0.10
Obesity[b] (%)	17.7	21.4	21.7	0.67	16.9	30.0	13.8	0.02
Dietary intake								
Total energy (kcal)	1981.7±84.2	2042.2±78.9	2257.7±81.7	0.04	1876.2±83.4	1865.5±51.9	2533.1±91.5	≤0.001
Total dairy (g)	247.2±18.4	336.2±9.7	642.8±23.7	≤0.001	388.2±22.1	323.8±15.4	511.8±28.0	≤0.001
Low fat dairy (g)	71.3±4.2	271.4±5.0	574.9±20.2	≤0.001	383.2±22.1	291.4±15.5	240.6±25.1	≤0.001
High fat dairy (g)	175.9±19.5	64.8±9.7	67.9±13.0	≤0.001	5.1±0.4	32.3±1.0	271.2±19.3	≤0.001
Fruits (g)	288.0±32.3	300.2±16.6	371.3±36.7	0.10	270.5±21.3	292.2±19.1	394.6±42.0	0.007
Pulses (g)	35.0±3.4	28.1±1.9	26.3±2.2	≤0.05	26.9±2.5	25.3±2.2	37.2±2.9	0.002
HVO (g)[c]	21.0±3.0	14.2±2.1	21.0±3.4	0.16	19.6±2.9	13.7±2.0	22.9±3.5	0.08
Non-HVO (g)[c]	13.7±1.1	14.1±1.2	16.7±1.7	0.24	16.4±1.7	15.8±1.1	12.2±1.1	0.06
Meats (g)	60.0±6.4	88.7±24.3	59.8±4.2	0.27	71.2±23.8	57.0±4.1	80.2±8.2	0.53
Vegetables (g)	340.6±15.9	241.9±12.8	316.2±21.9	0.005	222.0±12.7	246.3±13.4	330.4±23.1	≤0.001
Grains (g)	317.5±16.1	353.9±19.0	319.2±13.1	0.20	306.7±18.9	337.4±13.1	347.3±16.4	0.19

[a]Data are means±SE unless indicated. Data for dietary intakes are adjusted for age and total energy intake. [b]BMI ≥30, [c]HVO=Hydrogenated vegetable oil, [d]Obtained by the use of ANOVA and Chi-square, where appropriate. SE=Standard error, BMI=Body mass index, MET=Metabolic equivalent of task

in Table 4. In crude model, no significant associations were found between consumption of total-, high- or low-fat dairy with the stroke risk. After adjustment for age, sex and total energy intake, individuals with the

Table 4: Multivariable-adjusted OR and 95% CI for stroke across tertiles of total-, low- and high-fat dairy consumption

	Tertiles of total dairy intake (*n*=130)			P_{trend} [f]	Tertiles of low-fat dairy intake (*n*=130)			P_{trend} [f]	Tertiles of high-fat dairy intake (*n*=130)			P_{trend} [f]
	T1 (<279 g/day)	T2 (279-490 g/day)	T3 (>490 g/day)		T1 (<157 g/day)	T2 (157-362 g/day)	T3 (>362 g/day)		T1 (<15 g/day)	T2 (15-55 g/day)	T3 (>55 g/day)	
Stroke												
Crude	1.00	1.40 (0.86-2.28)[e]	1.03 (0.63-1.68)	0.38	1.00	0.90 (0.55-1.46)	0.64 (0.39-1.04)	0.09	1.00	1.00 (0.61-1.63)	1.59 (0.98-2.60)	0.08
Model 1[a]	1.00	1.32 (0.78-2.22)	0.86 (0.50-1.48)	0.54	1.00	0.88 (0.52-1.47)	0.58 (0.34-0.99)	0.04	1.00	1.36 (0.81-2.31)	2.28 (1.29-4.00)	0.03
Model 2[b]	1.00	1.33 (0.78-2.26)	0.86 (0.49-1.48)	0.57	1.00	0.89 (0.53-1.51)	0.61 (0.35-1.04)	0.07	1.00	1.28 (0.75-2.19)	2.19 (1.24-3.88)	0.02
Model 3[c]	1.00	1.20 (0.67-2.15)	0.88 (0.47-1.67)	0.63	1.00	0.96 (0.52-1.76)	0.84 (0.44-1.58)	0.13	1.00	1.55 (0.85-2.83)	2.02 (1.02-4.02)	0.04
Model 4[d]	1.00	1.32 (0.72-2.41)	0.95 (0.49-1.84)	0.51	1.00	1.08 (0.58-2.01)	0.98 (0.51-1.91)	0.27	1.00	1.77 (0.95-3.31)	1.84 (0.90-3.45)	0.17

[a]Adjusted for age, sex and energy, [b]Adjusted for age, sex, energy, physical activity and smoking, [c]Adjusted for age, sex, energy, physical activity, smoking and dietary intakes (fruits, pulses, HVO, non-HVO, meats, vegetables, nuts and grains), [d]Adjusted for age, sex, energy, physical activity, smoking, dietary intakes (fruits, pulses, HVO, non-HVO, meats, vegetables, nuts and grains) and BMI, [e]OR (95% CI), [f]Obtained by the use of tertiles of dairy intake as an ordinal variable in the model. OR=Odds ratio, CI=Confidence interval, BMI=Body mass index, HVO=Hydrogenated vegetable oil

highest consumption of low-fat dairy had a significantly decreased risk of stroke (odds ratio [OR]: 0.58; 95% confidence interval [CI]: 0.34–0.99), while those with the highest intake of high-fat dairy had a 2-fold increased risk of stroke (OR: 2.28; 95% CI: 1.29–4.00). The association between high-fat dairy consumption and stroke even persisted after additional adjustment for dietary intake (including, meat, fruit, vegetable, pulses, non-HVO, HVO, nuts and grains); however, further adjustment for BMI made the association disappeared, indicating an obesity-dependent association between high-fat dairy intake and risk of stroke.

DISCUSSION

In this case-control study, we found a significant positive association between high-fat dairy consumption and risk of stroke among Iranian adult population. The associations persisted in multivariate models adjusting for potential confounders; however, after further control for BMI the associations disappeared, indicating an obesity-dependent association between high-fat dairy intake and stroke.

High consumption of dairy fat, due to its saturated fat content, positively and dietary calcium intake negatively are associated with the stroke.[5,6] It must be kept in mind that besides fat content, dairy consumption would result in several nutrients intake which, in turn, might play different roles in the development of stroke. Several studies have reported the association of dairy consumption and risk of stroke albeit with inconsistent results. Some studies[16,17] have demonstrated that dairy's fatty acids are associated with greater risk of stroke. However, an inverse association between dairy intake, stroke and vascular disease has been documented by other studies.[7,12,18] In this study, the association between low-fat dairy intake and stroke did not persist after controlling all potential variables. Larsson *et al*.[19] have also reported no significant association between either total- or low-dairy consumption and stroke. Such findings have also been reached in other studies.[11] In contrast, some studies have suggested an inverse association between total dairy intake and risk of stroke.[6,8] Different findings might be explained by study designs, control for confounders and different sample sizes. The differences in dietary calcium intake might also provide additional reason for conflicting findings. In addition, these studies varied in terms of population characteristics, dietary assessment methods, which may explain the inconsistencies.

Milk, yoghurt and cheese are the most common dairy products which are consumed in Iran. Although consumption of traditionally full-fat dairy products is common, consumption of low fat dairy products has recently given particular attention.[20] Consumption of dairy products, especially high-fat choices, as a

contributing risk factor for coronary disease and stroke has been doubtful.[21] Several mechanisms have been stated to explain the logic behind this hypothesis. The first nutrient to be blamed in high-fat dairy products is high amounts of SFAs which have long been identified as a risk factor for coronary artery disease and stroke. Based on this hypothesis, authorities have recommended the use of skim or low-fat dairy.[21] Some studies have also expressed the high dietary calcium content of dairy products as a risk factor for arterial calcification and myocardial ischemia.[22] Other investigators believe that consumption of dairy products would result in lowering blood pressure and reduces risk of stroke, due to their high calcium content.[6,8,23] However, another study showed no association between stroke and total calcium intake.[24] Furthermore, calcium could reduce platelet aggregation and total cholesterol levels via creating insoluble complexes with fatty acids and decreasing fatty acids absorption.[6] Moreover people who choose to drink low-fat milks, always pay attention to other healthy behavior and these factors may be responsible for their health situation. Not all of these factors are known and removable so they could be responsible for biases.

Several limitations should be considered in interpreting the findings of this study. The major one is the case-control design of the study which would prohibit causal inferences. Another limitation was the lack of estimation of nutrient intakes in the current study; because there is no specific food composition table for Iranian foods. Also, the study was a hospital-based case-control, not a community-based; therefore, controls might not be representative of the general population. Total number of population in the study was relatively small, which might reduce statistical power. Possible misclassifications of participants due to using FFQ for assessing dietary intakes, which increase the risk of recall bias, should also be considered. This is particularly relevant for inclusion of cheese and other dairy products in the same category. Unfortunately, our database did not include fat intake contributed from dairy products and it just had a variable on total fat intake. It must also be taken into account that the controls were not strictly matched to cases and several differences between these two groups might contribute to the associations reported. Finally, known lifestyle variables associated with dairy consumption were controlled; however, residual confounding of other variables, such as intake of medicine and socioeconomic status, was inevitable.

CONCLUSIONS

Given the aforementioned limitations, we have found evidence indicating a marginally significant positive association between high-fat dairy consumption and the risk of stroke. However, this association might be obesity-dependent. Further prospective large-scale studies are required to confirm this finding.

ACKNOWLEDGEMENTS

This study was financially supported by Research Council of the Food Security Research Center (No. 292081), Isfahan University of Medical Sciences, Isfahan, Iran.

Received: 24 Jun 15 **Accepted:** 22 Sep 15
Published: 11 Jan 16

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Source of Support: This study was supported by a grant from the Isfahan University of Medic Sciences, Islamic Republic of Iran. The financial support for conception, design, data analysis and manuscript drafting comes from Food Security Research Center, Isfahan University of Medical Sciences, Isfahan, Iran. **Conflict of Interest:** None declared.