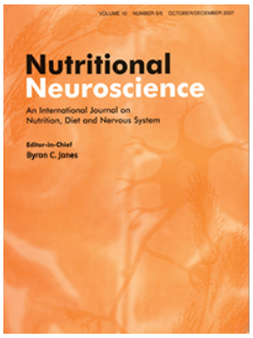

Taylor & Francis
Taylor & Francis Group

Nutritional Neuroscience

An International Journal on Nutrition, Diet and Nervous System

ISSN: 1028-415X (Print) 1476-8305 (Online) Journal homepage: https://www.tandfonline.com/loi/ynns20

Refined grains consumption is associated with a greater odds of glioma

Seyed Mohammad Mousavi, Somaye Rigi, Mehdi Shayanfar, Minoo Mohammad-Shirazi, Giuve Sharifi & Ahmad Esmaillzadeh

To cite this article: Seyed Mohammad Mousavi, Somaye Rigi, Mehdi Shayanfar, Minoo Mohammad-Shirazi, Giuve Sharifi & Ahmad Esmaillzadeh (2020): Refined grains consumption is associated with a greater odds of glioma, Nutritional Neuroscience, DOI: 10.1080/1028415X.2020.1758889

To link to this article: https://doi.org/10.1080/1028415X.2020.1758889

Published online: 07 May 2020.

Submit your article to this journal

Article views: 14

View related articles

View Crossmark data

Full Terms & Conditions of access and use can be found at
https://www.tandfonline.com/action/journalInformation?journalCode=ynns20

NUTRITIONAL NEUROSCIENCE
https://doi.org/10.1080/1028415X.2020.1758889

Taylor & Francis
Taylor & Francis Group

Check for updates

Refined grains consumption is associated with a greater odds of glioma

Seyed Mohammad Mousavi[a,b], Somaye Rigi[a], Mehdi Shayanfar[c], Minoo Mohammad-Shirazi[c], Giuve Sharifi[d] and Ahmad Esmaillzadeh [a,e,f]

[a]Department of Community Nutrition, School of Nutritional Sciences and Dietetics, Tehran University of Medical Sciences, Tehran, Iran; [b]Students' Scientific Research Center (SSRC), Tehran University of Medical Sciences, Tehran, Iran; [c]Department of Clinical Nutrition and Dietetics, National Nutrition and Food Technology Research Institute, Shahid Beheshti University of Medical Sciences, Tehran, Iran; [d]Department of Neurosurgery, Loghman Hakim Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran; [e]Obesity and Eating Habits Research Center, Endocrinology and Metabolism Molecular Cellular Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran; [f]Food Security Research Center, Department of Community Nutrition, Isfahan University of Medical Sciences, Isfahan, Iran

ABSTRACT

Objective: Grain consumption has been associated with brain carcinogenesis in earlier studies, however, no data are available examining the association between refined grains consumption and risk of glioma. The current study was done to investigate the association between refined grains consumption and risk of glioma in Iranian adults.

Methods: This hospital-based case-control study was performed on 128 pathologically confirmed cases with glioma and 256 age- and sex-matched controls in Tehran, Iran. Dietary intakes of participants including refined grains consumption were collected using a validated Block-format 123-item detailed food frequency questionnaire (FFQ). Refined grains were considered as the sum of white breads, pasta, rice, boiled and fried potato, sweets, and cookies.

Results: A significant positive association was found between refined grains consumption and glioma (OR: 3.51, 95% CI: 1.97–6.26, $P_{trend} < 0.001$). This association did not change after adjustment for energy intake (OR: 4.30, 95% CI: 2.27–8.15, $P_{trend} < 0.001$). After controlling for potential confounders, those in the top tertile of refined grains consumption were significantly more likely to have glioma than those in the bottom tertile (OR: 2.92, 95% CI: 1.38–6.17, $P_{trend} = 0.007$). This significant association remained unchanged, even after further adjustment for other dietary variables (OR: 2.54, 95% CI: 1.15–5.63, $P_{trend} = 0.02$) and BMI (OR: 2.49, 95% CI: 1.12–5.53, $P_{trend} = 0.03$).

Conclusion: We found a significant positive association between refined grains consumption and odds of glioma. Further prospective cohort studies are needed to confirm these findings.

KEYWORDS
Refined grains; glioma; cancer; brain tumor; case-control study; cereal; FFQ; grain products

Introduction

Glioma is a general term that is used for all malignancies rooting in neuroglial cells of central nervous system [1]. Gliomas account for up to 70% of all tumors in the brain [2]. The universal incidence rate of glioma is 3.7 and 2.6 per 100,000 in males and females, respectively [3]. In Iran, a recent national report has demonstrated a mortality rate of 2.92 per 100,000 in males and 2.46 per 100,000 in females [4]. It is worth mentioning that glioma is considered as cancer with poorest survival rate among diverse types of cancers so that 5-year survival rate is just 0.05–4.4% after diagnosis [5]. As a result, recognition of contributing factors in the occurrence and development of this type of cancer is vital.

In the etiology of impaired proliferation of glial cells, diverse environmental, occupational, dietary and genetic factors seem to have a pivotal role [6,7]. Dietary intakes are the most important contributing factors to cancers, including glioma [8]. With respect to diet and glioma risk, global investigations have shown that fish intake, antioxidants intake, consumption of fruits and vegetables as well as use of vitamin supplements are protective agents against brain tumors [9–13], while total energy intake [14], protein intake [12] and intake of nitrate [10] or nitrite [15] have been identified as risk factors in the incidence of glioma. By far, most studies that have assessed the link between dietary components and glioma, have largely paid attention to specific foods and food groups. However, unlike whole grains, refined grains have received limited attention. Refined grains refer to grain products consisting of grains or flours that have been considerably altered from their normal composition [16]. Several studies found a positive correlation between consumption of refined grains and risk of several cancers including cancers of the upper digestive

CONTACT Ahmad Esmaillzadeh a-esmaillzadeh@tums.ac.ir Department of Community Nutrition, School of Nutritional Sciences and Dietetics, Tehran University of Medical Sciences, Tehran, P.O. Box 14155-6117, Iran

© 2020 Informa UK Limited, trading as Taylor & Francis Group

and respiratory tract [17,18], stomach [19], colorectal [20–23], breast [24] and endometrium [18].

Refined grains digest quickly and have high glycemic index. This means that they increase fasting blood sugar and insulin after meals [25]. Through their effects on hyperinsulinemia, refined grains intake results in high circulating insulin-like growth factor-I (IGF-I), which in turn acts as a proliferative, cell differentiate, and anti-apoptotic agent [26,27].

To the best of our knowledge, no study has reported the association between refined grains consumption and risk of glioma. Investigating the association of refined grains consumption with risk of glioma is especially relevant for the Middle-Eastern countries, where more than 60% of total energy intake is taken from carbohydrates, most of them are refined grains [28]. Given the lack of evidence in this area, the present study aimed to assess the association between refined grains consumption and risk of glioma in Iranian adults.

Materials and methods

Study population

The recruitment of case and control subjects for this case–control study was done between November 2009 and September 2011, in Tehran, Iran. By using the convenience-sampling method, both cases and controls were elected. The hospitals affiliated to Shahid Beheshti University of Medical Sciences were the origin of sampling. Considering 5% type I error and 80% of study power, we needed 115 cases and 230 controls for the current study. To reduce errors, we recruited 128 cases and 256 age- and sex-matched controls in the study. Cases were pathologically confirmed (ICD-O-2, morphology codes 9380-9481) glioma patients referring to the Neurosurgery department. Controls were individuals attending to other wards (orthopedic and surgical department) of the same hospital. The age of both cases and controls were between 20 and 75-years-old. The exclusion criteria of our study were having a history of pathologically confirmed cancers or a history of chemotherapy or radiotherapy. All Participants gave written informed consent. Ethical approval of the study was taken from the Medical Ethics Committee of the Tehran University of Medical Sciences, Tehran. Iran.

Dietary intake assessment

We assessed each participants' usual dietary intakes using a Block-format-validated 123-item semi-quantitative FFQ [29]. Administration of all FFQs was done by trained interviewers through the face-to-face method. Study participants were asked to report their individual average intake of different dietary items on a daily, weekly or monthly basis during the last year. Daily energy and nutrients intakes were estimated using Nutritionist IV software based on the Iranian foods-modified US Department of Agriculture food composition database [30]. Results from a validation study [29] demonstrated that this questionnaire obtains reasonable estimates of dietary intakes in the long run due to showing proper correlation with 24-h dietary recalls (two 24-h recalls per month) as a gold standard. Estimated correlation coefficients for the reliability between the dietary intakes from the FFQ and those from the several 24-h recalls for b-carotene, vitamin E and vitamin C were 0.84, 0.78 and 0.83, respectively [29].

Refined grains were considered as the sum of white breads (eg, Iranian bread Lavash, Taftoon, and Baguette), pasta, rice, boiled and fried potato, sweets and cookies.

Assessment of glioma

Diagnosis of glioma was done based on pathological findings according to ICD-O-2 morphology codes 9380-9481[31]. Individuals with a maximally one month of diagnosis were recruited in this study to avoid changes in dietary intakes.

Assessment of other variables

All participants were asked to report their information on sociodemographic characteristics (age, the status of marriage, gender, place of residence, job status and education), family history of cancer and glioma, history of head trauma, history of allergy and hypertension in the first degree relatives, exposure to chemicals over the past 10 years, methods of cooking, drug use, hair dye use, duration of cell phone use and history of exposure to the radiographic X-ray; using a pre-examined questionnaire. To assess physical activity of participants, International Physical Activity Questionnaire (IPAQ) was applied. Fulfillment of IPAQ was done through face-to-face interviews by a trained interviewer. IPAQ findings were expressed as Metabolic Equivalents per week (METs/week). Standard methods were applied by a trained dietitian to quantify anthropometric measurements including weight and height. By dividing weight (kg) to height squared (m^2), Body Mass Index (BMI) was calculated. Given that farmers, who either did not clean themselves instantly or did not replace clothes after dealing with pesticides showed a three-fold increased risk of brain tumors [32], we considered farming as a risk factor for glioma. High-risk living areas were defined as those living near electromagnetic fields, cell

phone and broadcast antennas during the last 10 years [33]. Several methods of cooking, including frying, use of barbecue and microwave was also considered as risk factors. Consumption of canned foods was regarded as a risk factor, in case of using at least twice a week.

Statistical analysis

Participants were categorized according to tertiles of refined grains consumption. General characteristics between cases and controls were compared using independent samples' *t*-test for continuous variables and Chi-square for categorical variables. Such comparisons across tertiles of refined grains consumption were done by means of one-way ANOVA and Chi-square, where appropriate. We used ANCOVA to assess dietary intakes between cases and controls as well as across tertiles of refined grains consumption. These analyses were controlled for age, gender, and total energy intake. To evaluate the association of refined grains consumption with glioma, binary logistic regression was applied in different models. First, we controlled for energy intake (kcal/d). In the second model, further adjustments were made for family history of glioma (yes/no), marital status (married/single/divorced), high-risk occupation (farmer/non-farmer), high-risk residential area (yes/no), supplement use (yes/no), history of exposure to the radiographic X-ray (yes/no), smoking (smoker/non-smoker), exposure to chemicals (yes/no), drug use (yes/no), personal hair dye use (yes/no), frequent fried food intake (yes/no), canned foods and microwave (yes/no). We also conducted further controlling for adherence to DASH diet (categorical) and tea and coffee consumption (categorical), based on our earlier findings in these participants [34,35]. Construction of DASH diet score in this study population has been given elsewhere [34]. Finally, adjustments for BMI were performed in the last model. All confounders were selected according to previous studies [32,33,36]. In these analyses, the first tertile of refined grains consumption was considered as the reference category. We considered these tertiles as ordinal variable when trying to obtain the overall trend of odds ratios across tertiles. All statistical analyses were performed using SPSS (version 19.0; SPSS Inc, Chicago IL). *P*-values were considered as significant when they were less than 0.05.

Results

General characteristics and dietary intakes of study participants separately by cases and controls are outlined in Table 1. Compared with individuals in the control group, cases were more likely to have family history of glioma,

Table 1. General characteristics and dietary intakes of study participants separately by cases and controls.

	Groups		
	Controls (*n=256*)	Cases (*n=128*)	*P**
Age (years)	42.7 ± 13	43.4 ± 14	0.65
BMI (kg/m^2)	26.1 ± 3.8	26.2 ± 4.3	0.76
Males (%)	58.2	58.6	0.94
Married (%)	80.1	78.9	0.66
University graduated (%)	16.8	11.7	0.004
High-risk jobs[a] (%)	2.7	10.2	0.002
High-risk residential area[b] (%)	21.5	30.5	0.05
Duration of cell phone use (years)	3.7 ± 2.5	2.8 ± 2.9	0.003
History of exposure to the radiographic X-ray (%)	7.4	15.6	0.01
History of dental photography (%)	59	46.1	0.02
History of head trauma (%)	28.9	43.8	0.004
History of allergy (%)	29.3	25	0.37
History of hypertension (%)	5.1	2.3	0.21
Current smoker (%)	25	15.6	0.04
Frequent fried food intake[c] (%)	78.1	90.6	0.002
Frequent use of barbecue[d] (%)	12.1	15.6	0.34
Frequent microwave use (%)	19.1	7.8	0.004
Frequent canned foods intake (%)	5.9	6.3	0.88
Drug use (%)	5.1	7.8	0.29
Personal hair dye use (%)	41	21.9	<0.001
Exposure to chemicals (%)	10.5	19.5	0.01
Family history of glioma (%)	5.5	19.5	<0.001
Family history of cancer (%)	34	32.8	0.82
Supplement use (%)	15.6	7.8	0.03
Physical activity (METs)	33.8 ± 5.5	34.8 ± 6.3	0.12
Energy (kcal/day)	2560 ± 39	2584 ± 55	0.72
Nutrient intakes			
Protein (g/day)	97 ± 0.9	98 ± 1.3	0.76
Fat (g/day)	66 ± 0.9	62 ± 1.3	0.003
Carbohydrate (g/day)	417 ± 2.3	423 ± 3.3	0.02
Dietary fiber (g/day)	23 ± 0.8	23 ± 1.1	0.83
Cholesterol (mg/day)	235 ± 6.7	250 ± 9.5	0.2
SFA (g/day)	20 ± 0.4	19 ± 0.6	0.02
Vitamin B1 (mg/day)	2.4 ± 0.06	2.5 ± 0.08	0.39
Vitamin B2 (mg/day)	2.6 ± 0.06	2.5 ± 0.08	0.22
Vitamin B3 (mg/day)	30.1 ± 0.3	30.8 ± 0.5	0.18
Vitamin B5 (mg/day)	4.7 ± 0.06	4.6 ± 0.09	0.58
Vitamin B6 (mg/day)	2 ± 0.03	1.8 ± 0.04	0.04
Folate (µg/day)	382 ± 15	349 ± 22	0.23
Vitamin B12 (µg/day)	6 ± 0.6	9.7 ± 0.9	0.001
Food groups			
Refined grains (g/day)	424 ± 9	503 ± 13	<0.001
Whole grains (g/day)	150 ± 6	175 ± 9	0.04
Red and processed meats (g/day)	36 ± 1.2	41 ± 1.7	0.01
Vegetables(g/day)	274 ± 8	257 ± 7	0.04
Fruits (g/day)	361 ± 6	324 ± 9	0.001
Fish (g/day)	9.1 ± 0.6	9.2 ± 0.8	0.92
Dairy products (g/day)	355 ± 7	308 ± 10	<0.001
Nuts and legumes (g/day)	46 ± 1.2	40 ± 1.7	0.008
Sugar-sweetened beverage (g/day)	83 ± 4	79 ± 6	0.54

Note: Data are presented as mean ± standard deviations (SDs) or percentages for general characteristics. Data for dietary intakes are as mean ± standard errors (SEs).

[a] Farmers were considered as having a high-risk occupation.

[b] Persons who lived in places nearby electromagnetic fields and cell phone and broadcast antennas in the last 10 years were considered as living in high-risk areas.

[c] Persons who consumed fried food at least twice per week were considered as frequent fried food users.

[d] Persons who used barbecue, microwave and canned foods at least twice per week were considered as frequent users.

* Obtained from ANOVA or Chi-square test. *P*-value for dietary intakes were adjusted for age, sex and energy using ANCOVA.

Table 2. General characteristics and dietary intakes of study participants across tertiles of refined grains consumption.

	Tertiles of refined grains consumption			
	T1 *n=128*	T2 *n=128*	T3 *n=128*	*P**
Age (years)	46 ± 14	44.7 ± 13	38.2 ± 12	<0.001
BMI (kg/m^2)	25.6 ± 4	26.2 ± 4	26.6 ± 4	0.12
Males (%)	34.4	60.9	79.7	<0.001
Married (%)	81	75	82	0.12
University graduated (%)	21.1	12.6	11.7	0.03
High-risk jobs[a] (%)	4.7	5.5	5.5	0.94
High-risk residential area[b] (%)	17.2	19.5	36.7	<0.001
Duration of cell phone use (years)	3.1±2.7	3.3±2.8	3.8±2.6	0.12
History of exposure to the radiographic X-ray (%)	7	11.7	11.7	0.35
History of dental photography (%)	64.8	50.8	48.4	0.01
History of head trauma (%)	37.5	30.5	33.6	0.71
History of allergy (%)	36.7	23.4	23.4	0.02
History of hypertension (%)	4.7	6.3	1.6	0.16
Current smoker (%)	16.4	26.6	22.7	0.14
Frequent fried food intake[c] (%)	75	85.9	85.9	0.03
Frequent use of barbecue[d] (%)	6.3	9.4	24.2	<0.001
Frequent microwave use (%)	14.8	14.1	17.2	0.77
Frequent canned foods intake (%)	7.8	3.1	7	0.24
Drug use (%)	7	0	11	0.001
Personal hair dye use (%)	54.7	25.8	23.4	<0.001
Exposure to chemicals (%)	11.7	10.9	18	0.19
Family history of glioma (%)	6.2	11.7	12.5	0.05
Family history of cancer (%)	30.5	32.8	37.5	0.18
Supplement use (%)	18.8	14.8	5.5	0.005
Physical activity (METs)	33.8 ± 5.5	34.7 ± 6.3	34.1 ± 5.8	0.12
Energy (kcal/day)	2322 ± 55	2519 ± 56	2861 ± 55	<0.001
Nutrient intakes				
Protein (g/day)	98 ± 1.4	96 ± 1.3	98 ± 1.4	0.50
Fat (g/day)	69 ± 1.3	65 ± 1.2	59 ± 1.3	<0.001
Carbohydrate (g/day)	408 ± 3.5	415 ± 3.3	425 ± 3.6	0.007
Dietary fiber (g/day)	20 ± 1.2	21 ± 1.1	27 ± 1.2	0.001
Cholesterol (mg/day)	248 ± 10	238 ± 9	234 ± 10	0.64
SFA (g/day)	22 ± 0.6	21 ± 0.5	17 ± 0.6	<0.001
Vitamin B1 (mg/day)	2.3 ± 0.09	2.3 ± 0.08	2.6 ± 0.09	0.006
Vitamin B2 (mg/day)	2.6 ± 0.09	2.5 ± 0.08	2.6 ± 0.09	0.51
Vitamin B3 (mg/day)	29 ± 0.5	29 ± 0.4	32 ± 0.5	<0.001
Vitamin B5 (mg/day)	4.5 ± 0.09	4.5 ± 0.09	5 ± 0.09	<0.001
Vitamin B6 (mg/day)	2 ± 0.05	1.8 ± 0.05	1.9 ± 0.05	0.15
Folate (µg/day)	394 ± 24	344 ± 22	373 ± 23	0.28
Vitamin B12 (µg/day)	6 ± 0.9	7 ± 0.8	8 ± 0.9	0.40
Food groups				
Refined grains (g/day)	278 ± 8	433 ± 7	641 ± 8	<0.001
Whole grains (g/day)	219 ± 10	146 ± 9	110 ± 10	<0.001
Red and processed meats (g/day)	38 ± 1.8	39 ± 1.7	36 ± 1.9	0.56
Vegetables(g/day)	288 ± 7	257 ± 7	260 ± 7	0.006
Fruits (g/day)	349 ± 10	342 ± 9	354 ± 10	0.68
Fish (g/day)	10 ± 0.9	9 ± 0.9	9 ± 0.9	0.72
Dairy products (g/day)	366 ± 11	348 ± 10	303 ± 11	0.001
Nuts and legumes (g/day)	46 ± 1.8	43 ± 1.7	43 ± 1.8	0.34
Sugar-sweetened beverage (g/day)	89 ± 6	87 ± 6	69 ± 6	0.06

Note: Data are presented as mean ± standard deviations (SDs) or percentages for general characteristics. Data for dietary intakes are mean ± standard errors (SEs).
[a] Farmers were considered as having a high-risk occupation.
[b] Persons who lived in places nearby electromagnetic fields and cell phone and broadcast antennas in the last 10 years were considered as living in high-risk areas
[c] Persons who consumed fried food at least twice per week were considered as frequent fried food users
[d]Persons who used barbecue, microwave and canned foods at least twice per week were considered as frequent users
* Obtained from ANOVA or Chi-square test. *P*-value for dietary intakes were adjusted for age, sex and energy using ANCOVA.

history of exposure to chemicals, high-risk jobs, history of head trauma, history of exposure to the radiographic X-ray and be frequent fried food consumer, and to live in the high-risk areas. They were less likely to have an academic education, history of dental photography, be current smokers, frequent microwave user and to use personal hair color, and take supplements. The mean duration of cell phone use was shorter among cases than controls. Compared with controls, patients with glioma had a higher consumption of carbohydrates, refined and whole grains, red and processed meats, vitamin B12 and lower intakes of total fats, SFA, Vitamin B6, vegetables, fruits, dairy products, nuts and legumes.

General characteristics and dietary intakes of study participants across tertiles of refined grains consumption

are shown in Table 2. Comparing across tertiles of refined grain consumption, we found that those with the highest intake were more likely to be male, younger and to live in high-risk residential area than those with the lowest intake. In addition, fried food consumption, barbecue use, drug use and family history of glioma were more common among them than those in the lowest tertile. High intake of refined grains was associated with a low probability of university graduation and low prevalence of history of dental photography, history of allergy, personal hair color, and taking supplements. Also, High intake of refined grains was associated with greater intakes of energy, carbohydrate, dietary fiber, vitamin B1, B3 and B5, and lower intakes of total fats, SFA, whole grains, vegetables, dairy, and sugar-sweetened beverage.

Multivariable-adjusted ORs and 95% CIs for glioma across tertiles of refined grains consumption are shown in Table 3. A significant positive association was observed between refined grains consumption and glioma (OR: 3.51, 95% CI: 1.97–6.26, $P_{trend} < 0.001$). This association remained significant after adjustment for energy intake (OR: 4.30, 95% CI: 2.27–8.15, $P_{trend} < 0.001$). Further controlling for other potential confounders did not alter the association; such that subjects in the highest tertile of refined grains consumption were 2.92 times more likely to have glioma than those in the lowest tertile (OR: 2.92, 95% CI: 1.38–6.17, $P_{trend} = 0.007$). Even taking dietary intakes into account did not influence the association (OR: 2.54, 95% CI: 1.15–5.63, $P_{trend} = 0.02$). After additional adjustment for BMI, we also found a positive significant association between refined grains consumption and glioma (OR: 2.49, 95% CI: 1.12–5.53, $P_{trend} = 0.03$).

Table 3. Odds ratios (ORs) and 95% confidence intervals (95% CIs) of glioma according to tertiles of refined grains consumption

	Tertiles of refined grains consumption			
	T1	T2	T3	P_{trend}*
Crude	1.00	3.29 (1.84-5.88)	3.51 (1.97-6.26)	<0.001
Model 1	1.00	3.56 (1.97-6.43)	4.30 (2.27-8.15)	<0.001
Model 2	1.00	3.39 (1.71-6.71)	2.92 (1.38-6.17)	0.007
Model 3	1.00	3.53 (1.73-7.19)	2.54 (1.15-5.63)	0.02
Model 4	1.00	3.46 (1.69-7.05)	2.49 (1.12-5.53)	0.03

*Binary logistic regression was used to obtain OR and 95% CI. The overall trend of OR across increasing tertiles was examined by considering the median score in each category as a continuous variable.

Model 1: adjusted for energy intake.

Model 2: additionally, adjusted for family history of glioma, marital status, high-risk occupation, high-risk residential area, supplement use, history of exposure to the radiographic X-ray, smoking status, exposure to chemicals, drug use, personal hair dye, frequent fried food intake, canned foods and microwave.

Model 3: further controlling was made for DASH diet (categorical) and tea and coffee consumption (categorical).

Model 4: Additional adjustment was done for BMI.

Discussion

To the best of our knowledge, this is the first study that examined the association of refined grains consumption, as the main exposure variable, with the risk of glioma in a sample of Iranian adults. We found that higher consumption of refined grains was directly associated with odds of glioma. This positive relation persisted even after adjusting for potential confounders including energy intake, several environmental risk factors, dietary intakes, and BMI.

Glioma is the most common type of tumor in the central nervous system, which is derived from glial cells [37]. Although comparatively rare, it causes considerable mortality and morbidity [38]. It has been shown that patterns of diet or specified dietary components are the major parts in the prevention and management of cancers including glioma [39,40]. For instance, previous observational studies have shown a direct association between processed meat intake and fried foods with glioma [41,42]. Conversely, higher intakes of several dietary components including vegetables, fruits, fish and poultry are associated with a lower risk [34,43]. Grains, which supply most of the energy in the diet, are the main staple foodstuffs in the majority parts of the world [44]. In developing nations, these foods may provide about 60-80% of the total daily energy intake, most of which are based on refined grains [45]. Although extensive research assessed the contribution of dietary factors to this cancer [46,47], no publication is currently available that investigated the association between refined grains consumption and glioma risk. Terry et al. in an international case–control study, carried out on 1548 cases and 2486 control in 6 countries, showed that higher grains consumption was associated with a 40% increased risk of glioma (OR = 1.4; 95% CI, 1.1–1.8). In this study, grains intake was not evaluated separately and the total consumption of grains was evaluated. Also, in another case–control study performed on 94 women with intracranial gliomas and 94 individually matched controls, higher consumption of potato and grains was linked to a higher risk of developing glioma [9]. Although records on the association of refined grains with glioma are scarce, other dietary measures, including dietary glycemic index (GI), have been studied in relation to brain tumors in earlier publications [48]. Furthermore, several investigations also showed a positive association between refined grains and high-GI foods with other types of cancers [49–51]. However, several studies did not find a significant association between refined grains consumption and risk of cancers [52–54]. Conflicting findings of these studies may be explained by different study designs, different sample

sizes, different types of cancers and different dietary assessment tools.

There are several possible biological mechanisms whereby refined grains consumption might increase the risk of glioma. Refined grains are digested quickly than whole grains, and have a high glycemic index. This means that they lead to increased plasma insulin concentrations and insulin-like growth factor I (IGF-1) levels [55]. The IGF-1 signaling system is an important controller of growth, energy metabolism, and a key mitogenic stimulus for tumor cell growth which stimulates cancer progress by preventing apoptosis and stimulating cell proliferation [56]. Long-term consumption of refined grains or high-GI foods leads to an increased risk of inflammation, cardiovascular disease, obesity, oxidative stress, and diminished antioxidant defense mechanisms [57–59]; these disorders are identified as risk factors for glioma [60,61]. Furthermore, another explanation is that a high intake of highly refined carbohydrates reduces the consumption of low-GI carbohydrate foods and, thus decreases the consumption of polyphenols and other antioxidants that may protect against cancer [62]. However, it was interesting for us to see that individuals in the highest tertile of refined grains consumption had also higher intakes of fiber. The difference in dietary fiber intake between those in the highest and lowest tertiles was 7 g/d. This is particularly interesting when we found that there was not a significant difference between these two tertiles in terms of other dietary sources of fiber. It seems that grains are the main source of dietary fiber in these individuals [63]. It must be kept in mind that refined grains consumption among those in the highest tertile was almost three times higher than those in the lowest tertile. Considering that even refined grains contain a small amount of fiber (for instance white rice contains 1–2 g fiber per 100 g weight [64]), such a 7 g/d difference in dietary fiber intake between individuals in the highest and lowest tertiles can be explained.

The current study has several strengths. This was the first document that examined the association between refined grains consumption and glioma. To reach an independent association, we adjusted for a wide range of confounders that may affect the overall findings. Also, subjects who participated in this study were newly diagnosed cases of glioma who had been with this malignancy in the past one month. Therefore, the probability of changing the regular diet has decreased. It should also be noted that the study comes from the Middle-East area; where most of energy intake is taken from carbohydrates, especially refined grains, and data on diet-disease relationships is very limited.

This study also has some limitations that should be taken into account when interpreting the results. First, due to the case–control design of our study, it increases the likelihood of bias including selection and recall bias. Given such a study design in the present study, we cannot confer causality. Case–control studies are used to identify the association of diet with rare diseases that have a long incubation period, including cancers. Although case–control studies are efficient in terms of time and cost, they are highly susceptible to both selection and recall biases. Recall bias, in which glioma patients may recall their past diet differently because of the diagnosis of cancer, is problematic because dietary evaluation occurs after diagnosis. Additionally, cases in this study were chosen from hospital; thus, identifying risk factors may be unique to a single hospital. Another limitation of the study relates to use of FFQ for assessing dietary intakes, in which misclassification of participants is unavoidable. Although the effect of a wide range of confounders was controlled, the residual confounding cannot be ignored. Furthermore, as the dietary intakes of the Middle-Eastern population differ from Western countries, the generalizability of our findings to other populations must be done with caution.

In conclusion, we found that high consumption of refined grains was significantly associated with odds of glioma among adults. However, further studies, in particular, prospective cohort studies are necessary to confirm these findings.

Acknowledgements

SMM, SR, MS, MMS, GS and AE conceived the study, design, data collection, statistical analyses, data interpretation, and manuscript drafting. AE supervised the study. The final version of manuscript has been read and approved by all authors.

Disclosure statement

No potential conflict of interest was reported by the authors.

Funding

The study was financially supported by the National Institute for Medical Research Development [grant number 977421].

Notes on contributors

Seyed Mohammad Mousavi is currently a Ph.D. Student at the Department of Community Nutrition, School of Nutritional Sciences and Dietetics, Tehran University of Medical Sciences, Tehran, Iran. His research interest line is investigating the association between diet and chronic diseases.

Somaye Rigi is an M.Sc. candidate at the Department of Community Nutrition, School of Nutritional Sciences and Dietetics, Tehran University of Medical Sciences, Tehran, Iran.

Mehdi Shayanfar is a research associate at the Department of Clinical Nutrition and Dietetics, National Nutrition and Food Technology Research Institute, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

Minoo Mohammad-Shirazi is a research associate at the Department of Clinical Nutrition and Dietetics, National Nutrition and Food Technology Research Institute, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

Giuve Sharifi is a research associate at the Department of Neurosurgery, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

Ahmad Esmaillzadeh is a Professor (full) at the Department of Community Nutrition, School of Nutritional Sciences and Dietetics, Tehran University of Medical Sciences, Tehran, Iran. His research interest is to develop and validate dietary strategies that effectively protect against obesity-related chronic conditions; including metabolic syndrome, cardiovascular disease, gastrointestinal disease, psychological disorders, and different types of cancer.

ORCID

Ahmad Esmaillzadeh http://orcid.org/0000-0002-8735-6047

References

[1] Chicago. American brain tumor association (2014) Brain tumor dictionary.
[2] Sant M, Minicozzi P, Lagorio S, Børge Johannesen T, Marcos-Gragera R, Francisci S, et al. Survival of European patients with central nervous system tumors. Int J Cancer. 2012;131(1):173–85.
[3] Winter SF, Loebel F, Dietrich J. Role of ketogenic metabolic therapy in malignant glioma: a systematic review. Crit Rev Oncol Hematol. 2017/04/01/;112:41–58.
[4] Jazayeri SB, Rahimi-Movaghar V, Shokraneh F, Saadat S, Ramezani R. Epidemiology of primary CNS tumors in Iran: a systematic review. Asian Pac J Cancer Prev. 2013;14(6):3979–85.
[5] Verhaak R. Cancer Genome Atlas Research Network: integrated genomic analysis identifies clinically relevant subtypes of glioblastoma characterized by abnormalities in PDGFRA, IDH1, EGFR, and NF1. Cancer Cell. 2010;17:98–110.
[6] Sandrone SS, Repossi G, Candolfi M, Eynard AR. Polyunsaturated fatty acids and gliomas: a critical review of experimental, clinical, and epidemiologic data. Nutrition. 2014;30(10):1104–9.
[7] Kyritsis AP, Bondy ML, Rao JS, Sioka C. Inherited predisposition to glioma. Neuro Oncol. 2009;12(1):104–13.
[8] Chen H, Ward MH, Tucker KL, Graubard BI, McComb RD, Potischman NA, et al. Diet and risk of adult glioma in eastern Nebraska, United States. Cancer Causes Control. 2002;13(7):647–55.
[9] Blowers L, Mack W, Preston-Martin S. Dietary and other lifestyle factors of women with brain gliomas in Los Angeles County (California, USA). Cancer Causes Control. 1997;8(1):5–12.
[10] Lee M, Wrensch M, Miike R. Dietary and tobacco risk factors for adult onset glioma in the San Francisco Bay area (California. USA). Cancer Causes Control. 1997;8(1):13–24.
[11] Hu J, La Vecchia C, Negri E, Chatenoud L, Bosetti C, Jia X, et al. Diet and brain cancer in adults: a case-control study in Northeast China. Int J Cancer. 1999;81(1):20–3.
[12] Kaplan S, Novikov l, Modan B. Nutritional factors in the etiology of brain tumors potential role of nitrosamines, fat, and cholesterol. Am J Epidemiol. 1997;146(10):832–41.
[13] Hu J, Johnson KC, Mao Y, Guo L, Zhao X, Jia X, et al. Risk factors for glioma in adults: a case-control study in northeast China. Cancer Detect Prev. 1998;22(2):100–8.
[14] Schwartzbaum JA, Fisher J, Goodman J, Cornwell D. Hypotheses concerning roles of dietary energy, cured meat, and serum tocopherols in adult glioma development. Neuroepidemiology. 1999;18(3):156–66.
[15] Boeing H, Schlehofer B, Blettner M, Wahrendorf J. Dietary carcinogens and the risk for glioma and meningioma in Germany. Int J Cancer. 1993;53(4):561–5.
[16] Food U, Administration D. FDA provides guidance on 'Whole Grain' for manufacturers. Available from: www fda gov/NewsEvents/Newsroom/Press Announcements/2006/ucm108598 htm FDA, Silver Spring, MD. 2006.
[17] Kjærheim K, Gaard M, Andersen A. The role of alcohol, tobacco, and dietary factors in upper aerogastric tract cancers: a prospective study of 10,900 Norwegian men. Cancer Causes Control. 1998;9(1):99–108.
[18] Levi F, La Vecchia C, Franceschi S, Negri E. Dietary factors and the risk of endometrial cancer. Cancer. 1993;71(11):3575–81.
[19] Modan B, Lubin F, Barell V, Greenberg RA, Modan M, Graham S. The role of starches in the etiology of gastric cancer. Cancer. 1974;34(6):2087–92.
[20] Tuyns AJ, Kaaks R, Haelterman M. Colorectal cancer and the consumption of foods: a case-control study in Belgium. 1988.
[21] Benito E, Obrador A, Stiggelbout A, Bosch F, Mulet M, Munoz N, et al. A population-based case-control study of colorectal cancer in Majorca. I. dietary factors. Int J Cancer. 1990;45(1):69–76.
[22] Potter JD. Nutrition and colorectal cancer. Cancer Causes Control. 1996;7(1):127–46.
[23] Slattery ML, Berry TD, Potter J, Caan B. Diet diversity, diet composition, and risk of colon cancer (United States). Cancer Causes Control. 1997;8(6):872–82.
[24] Trichopoulou A, Katsouyanni K, Stuver S, Tzala L, Gnardellis C, Rimm E. Consumption of olive oil and specific food groups in relation to breast cancer risk in Greece. J Natl Cancer Inst. 1995;87(2):110–6.
[25] Brand-Miller JC, Stockmann K, Atkinson F, Petocz P, Denyer G. Glycemic index, postprandial glycemia, and the shape of the curve in healthy subjects: analysis of a database of more than 1000 foods. Am J Clin Nutr. 2009;89(1):97–105.
[26] Ullrich A, Gray A, Tam AW, Yang-Feng T, Tsubokawa M, Collins C, et al. Insulin-like growth factor I receptor

primary structure: comparison with insulin receptor suggests structural determinants that define functional specificity. EMBO J. 1986;5(10):2503–12.
[27] Yu H, Rohan T. Role of the insulin-like growth factor family in cancer development and progression. J Natl Cancer Inst. 2000;92(18):1472–89.
[28] Bahreinian M, Esmaillzadeh A. Opinion: quantity and quality of carbohydrate intake in Iran: a target for nutritional intervention. Arch Iran Med. 2012;15(10):648–9.
[29] Malekshah A, Kimiagar M, Saadatian-Elahi M, Pourshams A, Nouraie M, Goglani G, et al. Validity and reliability of a new food frequency questionnaire compared to 24 h recalls and biochemical measurements: pilot phase of Golestan cohort study of esophageal cancer. Eur J Clin Nutr. 2006;60(8):971.
[30] Haytowitz D, Lemar L, Pehrsson P, Exler J, Patterson K, Thomas R, et al. USDA national nutrient database for standard reference, release 24. Washington (DC): US Department of Agriculture; 2011.
[31] Merve A, Millner T, Marino S. Integrated phenotype-genotype approach in diagnosis and classification of common CNS tumours. Histopathology. 2019;75 (3):299–311.
[32] Ruder AM, Carreón T, Butler MA, Calvert GM, Davis-King KE, Waters MA, et al. Exposure to farm crops, livestock, and farm tasks and risk of glioma: the Upper Midwest Health Study. Am J Epidemiol. 2009;169 (12):1479–91.
[33] Morgan LL, Miller AB, Sasco A, Davis DL. Mobile phone radiation causes brain tumors and should be classified as a probable human carcinogen (2A). Int J Oncol. 2015;46(5):1865–71.
[34] Benisi-Kohansal S, Shayanfar M, Mohammad-Shirazi M, Tabibi H, Sharifi G, Saneei P, et al. Adherence to the dietary approaches to stop hypertension-style diet in relation to glioma: a case-control study. Br J Nutr. 2016;115(6):1108–16.
[35] Malmir H, Shayanfar M, Mohammad-Shirazi M, Tabibi H, Sharifi G, Esmaillzadeh A. Tea and coffee consumption in relation to glioma: a case-control study. Eur J Nutr. 2019;58(1):103–11.
[36] Ohgaki H, Kleihues P. Epidemiology and etiology of gliomas. Acta Neuropathol. 2005;109(1):93–108.
[37] Jiang H, Cui Y, Wang J, Lin S. Impact of epidemiological characteristics of supratentorial gliomas in adults brought about by the 2016 world health organization classification of tumors of the central nervous system. Oncotarget. 2017;8(12):20354.
[38] Ostrom QT, Bauchet L, Davis FG, Deltour I, Fisher JL, Langer CE, et al. The epidemiology of glioma in adults: a 'state of the science' review. Neuro Oncol. 2014;16 (7):896–913.
[39] Roomi M, Niedzwiecki A, Rath M. Scientific evaluation of dietary factors in cancer. J Nutri Med Diet Care. 2018;4:029.
[40] Grosso G, Bella F, Godos J, Sciacca S, Del Rio D, Ray S, et al. Possible role of diet in cancer: Systematic review and multiple meta-analyses of dietary patterns, lifestyle factors, and cancer risk. Nutr Rev. 2017;75(6):405–19.
[41] Wei Y, Zou D, Cao D, Xie P. Association between processed meat and red meat consumption and risk for glioma: a meta-analysis from 14 articles. Nutrition. 2015;31(1):45–50.
[42] Saneei P, Willett W, Esmaillzadeh A. Red and processed meat consumption and risk of glioma in adults: a systematic review and meta-analysis of observational studies. J Res Med Sci: Off J Isfahan Univ Med Sci. 2015;20(6):602.
[43] Li Y. Association between fruit and vegetable intake and risk for glioma: a meta-analysis. Nutrition. 2014;30(11–12):1272–8.
[44] Sturgess R, Ellis H, Ciclitira P. Cereal chemistry, molecular biology, and toxicity in coeliac disease. Gut. 1991;32 (9):1055.
[45] Crawford D, Jeffery RW, Ball K, Brug J. Obesity epidemiology: from aetiology to public health. London: Oxford University Press; 2011.
[46] Sieri S, Agnoli C, Pala V, Grioni S, Brighenti F, Pellegrini N, et al. Dietary glycemic index, glycemic load, and cancer risk: results from the EPIC-Italy study. Sci Rep. 2017;7(1):9757.
[47] Abdelwahab MG, Fenton KE, Preul MC, Rho JM, Lynch A, Stafford P, et al. The ketogenic diet is an effective adjuvant to radiation therapy for the treatment of malignant glioma. PLoS One. 2012;7(5):e36197.
[48] Strowd RE, Cervenka MC, Henry BJ, Kossoff EH, Hartman AL, Blakeley JO. Glycemic modulation in neuro-oncology: experience and future directions using a modified Atkins diet for high-grade brain tumors. Neurooncol Pract. 2015;2(3):127–36.
[49] Xu Y, Yang J, Du L, Li K, Zhou Y. Association of whole grain, refined grain, and cereal consumption with gastric cancer risk: a meta-analysis of observational studies. Food Sci Nutr. 2019;7(1):256–65.
[50] Mullie P, Koechlin A, Boniol M, Autier P, Boyle P. Relation between breast cancer and high glycemic index or glycemic load: a meta-analysis of prospective cohort studies. Crit Rev Food Sci Nutr. 2016;56 (1):152–9.
[51] Wang T, Zhan R, Lu J, Zhong L, Peng X, Wang M, et al. Grain consumption and risk of gastric cancer: a meta-analysis. Int J Food Sci Nutr. 2019;71(2):1–12.
[52] Nicodemus KK, Jacobs D, Jr., Folsom AR. Whole and refined grain intake and risk of incident postmenopausal breast cancer (United States). Cancer Causes Control. 2001 Dec;12(10):917–25.
[53] Kasum CM, Nicodemus K, Harnack LJ, Jacobs DR, Folsom AR. Whole grain intake and incident endometrial cancer: the Iowa Women's Health Study. Nutr Cancer. 2001;39(2):180–6.
[54] Farvid MS, Cho E, Eliassen AH, Chen WY, Willett WC. Lifetime grain consumption and breast cancer risk. Breast Cancer Res Treat. 2016;159(2):335–45.
[55] Boyd DB. Insulin and cancer. Integr Cancer Ther. 2003;2 (4):315–29.
[56] Bowers LW, Rossi EL, O'Flanagan CH, deGraffenried LA, Hursting SD. The role of the insulin/IGF system in cancer: lessons learned from clinical trials and the energy balance-cancer link. Front Endocrinol (Lausanne). 2015;6(77):1–16.
[57] Masters RC, Liese AD, Haffner SM, Wagenknecht LE, Hanley AJ. Whole and refined grain intakes are related

to inflammatory protein concentrations in human plasma. J Nutr. 2010;140(3):587–94.
[58] Gaesser GA. Perspective: refined grains and health: genuine risk, or guilt by association? Adv Nutr. 2019;10 (3):361–71.
[59] Federico A, Morgillo F, Tuccillo C, Ciardiello F, Loguercio C. Chronic inflammation and oxidative stress in human carcinogenesis. Int J Cancer. 2007;121 (11):2381–6.
[60] Koene RJ, Prizment AE, Blaes A, Konety SH. Shared risk factors in cardiovascular disease and cancer. Circulation. 2016;133(11):1104–14.
[61] Nayak L, Lee EQ, Wen PY. Epidemiology of brain metastases. Curr Oncol Rep. 2012;14(1):48–54.
[62] Williams CD. Antioxidants and prevention of gastrointestinal cancers. Curr Opin Gastroenterol. 2013;29(2):195–200.
[63] Slavin JL. Whole grains, refined grains and fortified refined grains: what's the difference? Asia Pac J Clin Nutr. 2000;9(S1):S23–S7.
[64] McGuire S. US department of agriculture and US department of health and human services, dietary guidelines for Americans, 2010. Washington (DC): US government printing office; January 2011; Oxford University Press; 2011.