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Original article

The association between the dietary inflammatory index and glioma: A case-control study

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SUMMARY

Background & aims: Dietary inflammatory potential has been associated with several cancers. However, the relationship between the dietary inflammatory index (DII®) and glioma is not clear. The aim of this study was to examine DII in relation to glioma.

Methods: In a hospital-based case-control study, we selected 128 newly-diagnosed cases of glioma and 256 controls. Cases were medically confirmed glioma patients, with no history of other cancers. A validated food frequency questionnaire was used to assess diet. DII scores were calculated based on the quantity of dietary components with inflammatory or anti-inflammatory potential. We used conditional logistic regression models to examine the association between the DII and glioma.

Result: Study participants were on average 43 years old and predominantly male (58%). After controlling for age, sex and energy intake, individuals in the highest quartile of DII had 87% (95% CI: 1.00–3.47) increased risk of glioma compared to those in the lowest quartile. Additional adjustment for environmental confounders strengthened the relationship; participants with the greatest DII scores had approximately 2.1 times (95% CI: 1.06, 3.83) increased odds of glioma than those with the lowest intake scores. The association was not substantially altered by further adjustment for BMI (2.76; 1.15–6.60).

Conclusion: In conclusion, diets with high anti-inflammatory and low inflammatory nutrient contents are recommended to prevent glioma.

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1. Introduction

Glioma is the most prevalent type of brain tumor [1]. Although brain tumors have the highest incidence in developed industrial countries [2,3], their incidence may also be artificially underestimated in developing countries [4]. In Iran, there are about

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0.6–2.4 and 1.5–2.8 new cases of men and women with brain tumors per 100,000 person years, respectively [5]. Despite the low incidence, brain tumors are associated with high mortality and morbidity rates [6]. More than 97% of people with glioblastoma die within five years of diagnosis [7]. Therefore, identification of contributing factors to this type of cancer is important.

Limited data exists regarding risk factors for gliomas; however, some risk factors have been identified including type of job, external carcinogens, allergies or atopic disease [5,6]. Several foods and nutrients, like fruits and vegetables [8], antioxidants and phytoestrogens [9,10], n-3 polyunsaturated fatty acids [11], nitrate or nitrite [12,13] and consumption of processed meats [14] have been identified as risk or protective factors. Further, inflammation contributes to the development of some cancers, including gliomas [15,16]. Among dietary factors, anti-inflammatory agents such as curcumin [17], retinoids [18], and certain polyunsaturated fatty acids [19] exert antineoplastic activity to protect from gliomas.

The Dietary Inflammatory Index (DII) is a novel population-based scale that evaluates the inflammatory potential of the overall diet [20]. The DII has been validated in relation to several inflammatory biomarkers [21,22] and has been widely used to reflect dietary inflammatory characteristics. It has been linked to risk of several chronic conditions including cancers [e.g. breast [23,24], prostate [25,26], bladder [27], colorectal [28,29] and gastric [30]]. Nonetheless, the association between DII and brain tumors, such as glioma, has not been explored.

Most prior studies on diet and cancer have been conducted in non-Asian countries [25,29,31–33]. Further, few studies have been conducted in the Middle East [34,35], a region with distinct dietary habits [36]. Regional dietary components, including high intakes of refined grains and saturated and trans fats, have high inflammatory potential, which might contribute to many common chronic diseases in the region. Of note, earlier research has not controlled for several confounders, especially environmental factors [37,38]. Control for such confounders is necessary to estimate independent associations between diet and cancers. Given the dearth of prior studies on the association between DII and glioma and the limitations of these studies, we evaluated the association between DII and risk of glioma in a case-control study in Iran.

2. Methods

2.1. Study design & subjects

We carried out a case-control study on glioma between November 2009 and September 2011. A convenience-sample of 128 cases and 256 age- (±5) and sex-matched controls were selected from the hospitals affiliated to Shahid Beheshti University of Medical Sciences in Tehran, Iran. Cases were 20–75 year-old patients with laboratory-diagnosed glioma (ICD-O-2 morphology codes 9380–9481) selected in the first month following diagnosis. Controls were enrolled from orthopedic or surgical wards. We did not include patients with a history of any other cancer, chemotherapy or radiotherapy. Before data collection, all participants completed written informed consent form.

2.2. Research instruments

2.2.1. Dietary assessment

We used a validated 126-item semi-quantitative FFQ in the Willett format to assess each participant's dietary intake [39]. Trained interviewers administered all FFQ questionnaires. All participants reported their individual average daily, weekly or monthly intakes of each dietary item during the last year. We estimated daily nutrients and energy intakes using Nutritionist IV software based on the US Department of Agriculture database [40] modified for Iranian foods.

A validation study indicates that this FFQ provides reasonable estimates of long-term dietary intakes [39], given its good correlation with 24-h dietary recalls (two 24-h recalls per month) that can be considered a gold standard. Estimated correlation coefficients with two 24-h recalls for vitamin E, β-carotene and vitamin C were 0.78, 0.84 and 0.83, respectively [39].

2.2.2. Dietary inflammatory score

For each individual, we used FFQ-derived dietary data to compute energy-adjusted Dietary Inflammatory Index (DII) scores. To do this, we applied Shivappa et al.'s method [20]. Since some items were uncommon in Iranian diets, DII score was computed using 29 food parameters. Items included: energy, carbohydrate, fat, protein, fiber, cholesterol, mono-unsaturated fatty acids (MUFAs), poly unsaturated fatty acids (PUFAs), saturated fats (SFAs), cobalamin, pyridoxine, folic acid, niacin, riboflavin, thiamin, vitamin A, C, D, E, β-carotene, zinc, selenium, magnesium, iron, caffeine, pepper, onion, garlic and green/black tea. We first calculated energy-adjusted quantities for all 29 nutrients using residual methods [41]. Then, for each participant, a *z*-score for all 29 food items was computed. To do this, we subtracted the "standard global mean" from the quantity of food items consumed by each subject and divided it by the "global standard deviation." Global means and SDs were obtained from Shivappa et al. [20]. In order to reduce skewness, we transformed this value to a centered percentile score. Then, we multiplied this score by the effect score for each of the food items obtained from Shivappa et al. [20]. Finally, we summed DII scores obtained from all the foods to calculate an overall DII score. A greater DII score (more positive value) represented higher inflammatory dietary potential.

2.2.3. Assessment of other variables

Trained interviewers administered questionnaires to all participants at the hospital to collect information on age, sex, marital status, place of residence, education, occupation, smoking status, use of vitamin supplements, family history of cancer and glioma, history of allergy and head trauma, history of hypertension, exposure to chemicals in the past 10 years, cooking methods, drug use, personal hair dye use, duration of cell phone use and history of x-ray exposure. The short form of the International Physical Activity Questionnaire (IPAQ) was used to assess physical activity during the last week. IPAQ is a validated self-reported seven-item measure of physical activity over the past seven days [42]. Vigorous- and moderate-intensity activities and walking (for at least 10 min) were measured separately in hours, minutes, and days. Then MET scores for vigorous-intensity, moderate-intensity and walking activities were extracted. These MET scores were multiplied by the amount of time each participant spent on that activity, while taking into consideration the frequency of engagement during the past week. Then, the sums of scores for different activities were computed as total MET-mins/week. A dietitian trained in anthropometry carried out the anthropometric measurements to quantify weight and height. We used a digital scale to measure weight to the nearest 500 g. A stadiometer was also used to measure height to the nearest 0.5 cm. Participants were asked to stand with their shoes off and their shoulders touching the wall, while looking straight ahead. Weight (kg) divided by height squared (m^2) was used to calculate body mass index (BMI).

Some risk factors for glioma have been identified in previous studies. For example, farmers who did not wash themselves immediately or did not change clothes after using pesticides were at approximately a three-fold increased risk of glioma [43]. Other

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research shows that individuals who used cell phones for ten years or more had eight times higher risk of brain tumors compared to others [44]. We categorized farming as a high-risk occupation for glioma. High risk areas were defined as living near electromagnetic fields as well as cell phone and broadcast antennas in the last 10 years. Frequent fried food consumption, barbecue use, microwave use and frequent canned food intake was considered to be at least twice a week.

2.3. Ethical approval

The study protocol was approved by the Food Security Research Center at the Isfahan University of Medical Sciences, Isfahan, Iran.

2.4. Statistical analysis

We first defined quartile cut-off points for the DII score in the control group. Then we classified all study participants according to these cut-offs. Quartiles of DII were defined as q_1 < -1.22; q_2 (−1.22)–(−0.22); q_3 (−0.22)–(1.02); and q_4 1.02<. We applied independent samples Student's t-tests to compare the means of continuous variables and χ^2 tests to investigate the distribution of categorical variables between cases and controls. Comparisons across quartiles of DII were conducted using one-way ANOVA and χ^2 tests, where appropriate. We computed age- and gender-adjusted food and nutrient intakes by quartiles of the DII using ANCOVA. Binary logistic regression was used to evaluate associations between the DII and glioma. We used three regression models in our analyses. First, we adjusted for age (continuous), sex (male/female) and energy intake (kcal/d). In a second model, we additionally controlled for physical activity (MET-h/wk, continues) and other potential environmental risk factors for glioma. In the final model, we additionally adjusted for BMI to observe the relationship when independent of obesity. All confounders, including food intake, were selected based on recent research [5,43,44]. The first quartile of DII was defined as the reference category and we calculated odds ratios and 95% CIs for the other quartiles. The overall trend of ORs along quartiles of DII was evaluated by defining quartiles of DII as an ordinal variable. SPSS (SPSS Inc., version 18) was used for the analysis. P values < 0·05 were defined as statistically significant.

3. Results

Compared to controls, cases were more likely to have high-risk occupations, history of exposure to radiographic x-ray, history of head trauma and family history of glioma and residence in high-risk areas. Exposure to chemicals, frequent microwave use and fried food intake were more prevalent among cases than controls. The prevalence of smoking and personal hair dye use was lower among cases than controls. A lower percentage of cases had a history of dental photography than controls. Cases and controls were not significantly different in terms of mean age, BMI and physical activity. Higher DII score was associated with younger age, more high-risk jobs, history of dental photography, family history of cancer, frequent barbecue use, frequent canned food intake, and multivitamin supplement use. A lower percentage of individuals in the highest category of DII were married than those in the lowest category. Smokers were more common in the third quartile of DII than in the first quartile. Participants showed no significant differences in mean BMI, duration of cell phone use and physical activity across categories

Table 1
Overall study participant characteristics.

	Cases (n = 128)	Controls (n = 259)	P-value[a]	Energy-adjusted dietary inflammatory index quartiles[b]				*P*-value[a]
				1 (n = 83) <−1.22	2 (n = 89) (−1.22)–(−0.22)	3 (n = 91) (−0.22)–(1.02)	4 (n = 103) 1.02<	
Age (years)	43.4 ± 14.6	42.7 ± 13.3	0.65	46.2 ± 13.3	46.9 ± 13.6	41.9 ± 12.06	37.6 ± 14.09	<0.001
BMI (kg/m^2)	26.2 ± 4.2	26.1 ± 3.8	0.75	26.1 ± 3.6	26.5 ± 4.1	25.8 ± 3.7	25.6 ± 4.2	0.38
Duration of cell phone use (year)	2.8 ± 2.8	3.7 ± 2.5	0.003	3.5 ± 3.06	3.7 ± 2.8	3.1 ± 2.6	3.3 ± 2.2	0.51
Physical activity (MET-h/week)	34.7 ± 6.3	33.8 ± 5.5	0.12	32.7 ± 5.1	35.4 ± 5.69	34.33 ± 5.5	34.00 ± 6.3	0.02
Males (%)	58	58	0.94	23	22	24	31	0.34
Married (%)	79	80	0.66	25	25.5	27	23	<0.001
University graduate (%)	12	17	0.22	32	16	18	34	0.08
High-risk jobs[c] (%)	10	3	0.003	0	25	25	50	0.03
High-risk residential area[d] (%)	30	21	0.05	23	28	25	25	0.75
History of dental photography (%)	46	59	0.02	23	26	29	23	0.04
History of x-ray exposure (%)	16	7	0.01	34	21	16	29	0.25
History of head trauma (%)	44	29	0.004	27	24	25	25	0.46
History of allergy (%)	25	29	0.37	20	30	25	24	0.37
History of hypertension (%)	2	5	0.20	19	37.5	25	19	0.60
Exposure to chemicals (%)	20	11	0.01	12	34	26	28	0.15
Family history of glioma (%)	19	5	<0.001	10.5	32	21	37	0.16
Family history of cancer (%)	33	34	0.90	24	30	16	30	0.03
Frequent use of barbecue[e] (%)	16	12	0.34	12	14	33	41	0.02
Frequent microwave use[e] (%)	8	19	0.002	35	25	23	17.5	0.06
Frequent canned food intake[e] (%)	6	6	0.87	50	25	0	25	0.006
Frequent fried food intake[f] (%)	91	78	0.001	20	25	25	30	0.12
Current smoker (%)	25	16	0.03	7	22.5	31	26	0.001
Drug use (%)	8	5	0.36	18	14	41	27	0.29
Personal hair dye use (%)	22	41	<0.001	22	30	27	21	0.10
Multivitamin supplement use (%)	8	16	0.36	20	25.5	25	30	0.01

MET, metabolic equivalents.
All values are mean ± SD unless indicated.
[a] P values were obtained from independent Student's t tests or χ^2 tests, where appropriate.
[b] Individuals in the first quartile of DII had DII score less than (−1.22); second quartile: between (−1.22) and (−0.22); third quartile: between (−0.22) and (1.02) and forth quartile: more than 1.02.
[c] Farming was considered a high-risk occupation.
[d] Individuals who lived in locations near electromagnetic fields or cell phone and broadcast antennas in the last 10 years were considered as living in high-risk areas.
[e] Individuals who used barbecue, microwave and canned foods at least twice per week were considered as frequent users.
[f] Eating fried food at least twice per week was considered frequent fried food consumption.

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Table 2
Dietary intakes of the study participants.

	Cases (n = 128)	Controls (n = 259)	*P*-value[a]	Energy-adjusted dietary inflammatory index quartiles[b]				*P*-value[a]
				1 (n = 83) <−1.22	2 (n = 89) (−1.22)–(−0.22)	3 (n = 91) (−0.22)–(1.02)	4 (n = 103) 1.02<	
	Mean ± SD	Mean ± SD		Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	
Energy (kcal/d)	2580 ± 560	2561 ± 722	0.79	2538 ± 755	2523 ± 636	2430 ± 530	2754 ± 724	0.053
Nutrients								
Carbohydrates (g/d)	425 ± 101	411 ± 128	0.01	405 ± 118	408 ± 112	393 ± 85.4	451 ± 148	0.03
Proteins (g/d)	92 ± 22	97 ± 30	0.70	102.1 ± 39.08	97.2 ± 24.1	92.47 ± 21.1	98.61 ± 22.20	0.03
Total fats (g/d)	62 ± 19	66 ± 22	0.05	66.51 ± 21.4	64.12 ± 18.4	60.74 ± 19.3	67.26 ± 22.62	0.07
Cholesterol (mg/d)	251 ± 143	236 ± 122	0.19	257 ± 188	233 ± 97.9	232 ± 100	243 ± 120	<0.001
SFA (g/d)	18.9 ± 7.14	20.9 ± 9.11	0.007	19.75 ± 7.2	19.36 ± 6.4	19.02 ± 7.9	22.56 ± 10.8	0.12
MUFA (g/d)	22.02 ± 7.7	19.74 ± 6.7	<0.001	22.25 ± 8.00	21.33 ± 6.8	19.83 ± 7.1	21.66 ± 7.73	0.01
PUFA (g/d)	14.23 ± 4.2	12.64 ± 3.7	<0.001	14.90 ± 4.6	14.04 ± 4.4	12.78 ± 4.0	13.24 ± 3.43	<0.001
Fe (mg/d)	16.8 ± 5.13	18.1 ± 13.9	0.30	21.11 ± 22.6	17.49 ± 5.52	15.73 ± 3.91	17.01 ± 5.54	0.003
Mg (mg/d)	519 ± 153	523v ± 133	0.76	597 ± 183	530 ± 141	484 ± 107	483 ± 125	<0.001
Zn (mg/d)	12.07 ± 3.7	12.40 ± 3.31	0.25	13.13 ± 4.58	12.19 ± 3.52	11.70 ± 2.80	11.82 ± 3.25	0.002
Se (mg/d)	0.06 ± 0.03	0.07 ± 0.04	0.02	0.08 ± 0.05	0.07 ± 0.04	0.06 ± 0.02	0.05 ± 0.01	<0.001
Thiamine (mg/d)	2.40 ± 1.23	2.49 ± 0.65	0.39	2.52 ± 1.85	2.35 ± 0.78	2.26 ± 0.61	2.58 ± 0.66	0.26
Riboflavin (mg/d)	2.5 ± 0.58	2.6 ± 1.29	0.22	2.84 ± 2.02	2.52 ± 0.64	2.40 ± 0.55	2.63 ± 0.59	0.01
Niacin (mg/d)	30.8 ± 7.40	30.01 ± 10.26	0.18	31.90 ± 13.9	30.23 ± 8.09	27.98 ± 6.64	31.12 ± 7.49	0.01
Vitamin B6 (mg/d)	1.97 ± 0.76	1.86 ± 0.54	0.04	2.34 ± 1.06	1.97 ± 0.39	1.77 ± 0.43	1.72 ± 0.58	<0.001
b-carotene (mcg/d)	1064 ± 823	1007 ± 541	0.46	1448 ± 803	1106 ± 434	866 ± 353	743 ± 293	<0.001
Vitamin A (RE/d)	1352 ± 603	1397 ± 649	0.45	1845 ± 897	1452 ± 467	1185 ± 404	1111 ± 402	<0.001
Vitamin C (mg/d)	126 ± 59	143 ± 113	0.11	185 ± 188	139 ± 39	121 ± 32.6	111 ± 33.1	<0.001
Vitamin E (mg/d)	5.71 ± 2.97	5.04 ± 2.54	0.01	6.26 ± 2.5	5.77 ± 2.6	4.93 ± 2.6	4.96 ± 3.1	<0.001
Vitamin D (mcg/d)	1.69 ± 1.1	1.32 ± 1.05	0.003	1.84 ± 1.17	1.47 ± 0.99	1.39 ± 1.01	1.59 ± 1.25	0.01
Vitamin B12 (mcg/d)	5.92 ± 4.57	9.65 ± 16.27	0.001	6.28 ± 5.2	6.44 ± 5.6	6.37 ± 5.2	9.25 ± 17.2	0.32
Folate (mcg/d)	348 ± 90	381 ± 301	0.23	475 ± 497	367 ± 87.03	328 ± 62.6	327 ± 71.8	<0.001
Dietary fiber (g/d)	23.02 ± 14.1	23.35 ± 11.21	0.83	32.59 ± 21.1	24.33 ± 10.2	19.98 ± 6.51	17.26 ± 4.98	<0.001
Food groups								
Refined grains (g/d)	501 ± 175	421 ± 182	<0.001	409 ± 180	443 ± 185	424 ± 158	503 ± 176	0.01
Whole-grains (g/d	150 ± 134	177 ± 108	0.03	159 ± 122	155 ± 105	158 ± 117	165 ± 131	0.95
White meats (g/d)	30 ± 13	33 ± 22	0.23	37.22 ± 34.6	32.70 ± 11.1	28.47 ± 12.4	29.73 ± 14.2	0.009
Red and processed meats (g/d)	41.3 ± 27.8	35.9 ± 19.7	0.01	39.22 ± 27.0	36.11 ± 17.9	36.06 ± 16.01	40.11 ± 26.7	0.60
Fish (g/d)	9.09 ± 12	9.2 ± 9	0.86	13.63 ± 14.07	9.08 ± 8.68	6.90 ± 6.98	6.62 ± 7.54	<0.001
Fruits (g/d)	325 ± 99	391 ± 124	0.005	394 ± 130	371 ± 102	327 ± 110	304 ± 97.4	<0.001
Vegetables (g/d)	258 ± 83	274 ± 86	0.07	323 ± 98.1	276 ± 74.1	251 ± 65.9	224 ± 63.04	<0.001
Dairy products (g/d)	309 ± 117	355 ± 131	0.0001	374 ± 122	336 ± 128	325 ± 115	329 ± 128	0.01
Legumes and nuts (g/d)	40.5 ± 22.7	45.9 ± 19.9	0.008	51.29 ± 22.7	47.20 ± 21.1	38.39 ± 18.9	40.76 ± 19.8	<0.001
Green/black tea and coffee (g/d)	736 ± 387	618 ± 299	0.002	700 ± 302	688 ± 363	749 ± 348	649 ± 383	0.21

[a] All values were adjusted for age, sex and energy, except for dietary energy intake, which was only adjusted for age and sex using ANCOVA.
[b] Individuals in the first quartile of DII had DII score less than (−1.22); second quartile: between (−1.22) and (−0.22); third quartile: between (−0.22) and (1.02) and forth quartile: more than 1.02.

of the DII. There were no other significant differences across categories of the DII (Table 1).

Compared with controls, cases had higher consumption of carbohydrates, PUFA, MUFA, vitamin B6, E and D, refined grains, red and processed meats, green/black tea and coffee. Cases had lower intakes of total fats, SFA, vitamin B12, whole-grains, fruits, dairy products and legumes and nuts. Higher DII score was related to lower intakes of selenium, magnesium, vitamin B6, b-carotene, vitamin A, vitamin C, folate, dietary fiber, fish, fruits, vegetables as well as higher intakes of carbohydrates and refined grains. Also,

Table 3
Odds ratios (ORs) and 95% confidence intervals (95% CIs) for glioma according to quartiles of energy-adjusted dietary inflammatory index quartiles.

	Energy-adjusted dietary inflammatory index quartiles[a]				*P*[b]
	1 (n = 83) <−1.22	2 (n = 89) (−1.22)–(−0.22)	3 (n = 91) (−0.22)–(1.02)	4 (n = 103) 1.02<	
	OR	OR (95% CI)	OR (95% CI)	OR (95% CI)	
Crude	1.00	1.19 (0.62–2.30)	1.22 (0.63–2.34)	1.87 (1.006–3.47)	0.04
Model 1	1.00	1.19 (0.61–2.30)	1.26 (0.65–2.45)	2.02 (1.06–3.83)	0.03
Model 2	1.00	1.61 (0.70–3.71)	2.31 (0.96–5.53)	2.76 (1.159–6.60)	0.01
Model 3	1.00	1.61 (0.70–3.71)	2.31 (0.96–5.53)	2.76 (1.15–6.60)	0.01

Model 1: Adjusted for age (continuous), sex (male/female) and energy intake (kJ/d or kcal/d).
Model 2: Further adjustments were made for physical activity (continues), family history of cancer (yes/no), family history of glioma (yes/no), marital status (married/single/divorced), education (university graduate/no university education), high-risk occupation (farmer/non-farmer), high-risk residential area (yes/no), duration of cell phone use (continuous), supplement use (yes/no), history of exposure to x-ray (yes/no), history of head trauma (yes/no), history of allergy (yes/no), history of hypertension (yes/no), smoking status (smoker/non-smoker), exposure to chemicals (yes/no), drug use (yes/no), personal hair dye use, frequent fried food intake (yes/no), frequent use of barbecue, canned foods or microwave ovens (yes/no).
Model 3: This model was additionally adjusted for BMI (continuous).
[a] Individuals in the first quartile of DII had DII score less than (−1.22); second quartile: between (−1.22) and (−0.22); third quartile: between (−0.22) and (1.02) and forth quartile: more than 1.02.
[b] Binary logistic regression models were used to obtain odds ratios (ORs) and 95% CIs. The overall trend of ORs across increasing tertiles was examined by considering the median score in each category as a continuous variable.

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individuals in the third quartile of DII had the lowest intake of proteins, cholesterol, MUFA, PUFA, Fe, Zn, riboflavin, vitamin E, vitamin D, white meat, dairy products as well as legumes and nuts (Table 2).

Multivariable-adjusted ORs and 95% CIs for glioma by quartiles of DII are displayed in Table 3. After adjustment for age, sex and energy intake, participants in the highest quartile of DII had 87% (95% CI: 1.006–3.47) increased risk of glioma compared with those in the lowest quartile. Additional adjustment for other environmental confounders strengthened the relationship; participants with the greatest DII scores had approximately 2.1 times (95% CI: 1.06, 3.83) increased odds of glioma than those with the lowest adherence. The association was not altered substantially by further adjustment for BMI.

4. Discussion

Our findings revealed a positive relationship between DII score and odds of glioma. These findings support the current recommendations of high intake of anti-inflammatory nutrients and low intake of foods with pro-inflammatory potential. The association was independent of potential confounders including age, sex, BMI and various environmental risk factors. To our knowledge, this is the first study examining the relationship between DII and risk of glioma.

Patients with glioma have short survival times and almost ninety percent die within three years after diagnosis [45]. Therefore, preventive measures are critical and diet is as an important modifiable contributing factor for glioma. The DII score, a proxy measure of an inflammatory diet [20,46], is associated with inflammatory markers such as C-reactive protein (CRP) and IL-6 [47,48]. The association between these inflammatory factors and some cancers is well established. For instance, high serum concentrations of hs-CRP or TNF-α are associated with increased risk of colorectal, breast, ovarian and renal cancers [49–51]. Although some research has examined the relationship between the DII and several cancers including gastrointestinal, breast, ovarian, prostate, and lung cancers, data on glioma are limited. Most previous studies have shown that people with greater DII scores had higher risk of cancers [24,25,28–30,52,53]. In this study, we observed that after controlling for various confounders, participants with higher DII scores had 2.7 times higher odds of glioma than those with the lowest DII scores. Although several studies have linked individual nutrients and foods to the risk of glioma, we have found no other study that used the DII. However, prior research has shown that adherence to the Dietary Approaches to Stop Hypertension (DASH) pattern, which has anti-inflammatory potential (due to high content of vegetables, fruits, low-fat dairy products and whole grains), was related to decreased risk of glioma. People in the highest tertile of the DASH diet score were 72% less likely to have glioma compared with those in the lowest tertile [54]. Individual foods or nutrients with inflammatory potential have previously been associated with greater risk of glioma. For instance, glioma risk was increased by 30% in individuals consuming high amounts of processed red meat (RR = 1.30; 95 CI, 1.08–1.58) [55]. Cured meat and other cured foods are also associated with increased risk of glioma [12,56]. In constrast, consumption of foods with anti-inflammatory potential was inversely related to glioma risk [12,56]. Our findings with respect to DII confirm earlier research on individual nutrients and foods. However, some previous studies have not found these associations [57,58]. In a study based on three large U.S. cohorts, consumption of vegetables, fruit and carotenoids was not linked with risk of adult glioma. However, consumption of specific kinds of vegetables like cabbages, cauliflower or brussel sprouts was associated with reduced glioma risk [59]. Differences between our findings and that of earlier studies might be attributable to the different study designs, lack of control for several confounders or different sample sizes. Overall, further research using the DII or other holistic approaches (that do not classify the anti-inflammatory or pro-inflammatory potential using individual foods and nutrients) could help resolve these inconsistencies.

Similar to other cancers, inflammation results in the development and aggressiveness of glioma [16]. Available documents suggest that the composition of fatty acids in human gliomas is different from non-malignant brain tissue and contains lower levels of n-3 unsaturated fatty acids with more anti-inflammatory properties [11]. Therefore, anti-inflammatory components in the diet may have a beneficial effect on glioma malignancy. Similarly, it has been shown that medicines such as non-steroid anti-inflammatory drugs (NSAID) were related to a 33% reduced glioma risk [16]. Vitamins A, C, D, E and zinc can act against cancers and may also modulate the onset and spreading of glioma [60]. In vitro studies have shown that retinoids, chemical components linked to vitamin A, forcefully inhibited the proliferation of glioblastoma cells [61]. Also ascorbic acid can enhance apoptosis of T98G glioma cells. Apoptosis may be facilitated by alteration of insulin-like growth factor-I receptor expression [62].

One strength of our study was adjustment for various environmental covariates when assessing the relationship between DII and risk of glioma. Also, we enrolled newly diagnosed cases of glioma to decrease bias that might result from altered dietary habits in these individuals. Moreover, this study extends current knowledge, given the lack of information with regard to diet and glioma, especially in the Middle-East. There are limitations to this study. Similar to other hospital-based case-control studies, the possibility of recall bias and selection bias should be considered. Controls from hospitals may make different dietary choices than the general population. Although the FFQ is commonly used for assessing food intake in epidemiologic studies, misclassification remains a possibility. To reduce this possibility, the DII was energy-adjusted in the current study. We also lacked data on some components of the DII including eugenol, ginger, n-3 and n-6 fatty acids, saffron, trans fat, turmeric, thyme/oregano, rosemary and flavonoids, which may have influenced our results.

5. Conclusion

In conclusion, diets with a high content of anti-inflammatory nutrients and a low content of inflammatory nutrients are recommended to prevent glioma.

Statement of authorship

Azadeh Aminianfar and Mehdi Shayanfar contributed to the conception of the study, design, statistical analyses, data interpretation and drafting of this manuscript. Farhad Vahid, Sayed Hossein Davoodi, Pamela J. Surkan and Zeinab Faghfoori contributed to the drafting of this manuscript. Minoo Mohammad-Shirazi contributed to the design and interpretation of the results. Farhad Vahid, Nitin Shivappa and James R. Hebert contributed to the statistical analysis and data interpretation. Giuve Sharifi and Ahmad Esmaillzadeh contributed to its conception, design, and statistical analyses. Ahmad Esmaillzadeh supervised the study. All authors approved the final manuscript prior to submission.

Conflict of interest

All authors declare no personal or financial conflicts of interest.

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