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The Association Between Index of Nutritional Quality (INQ) and Gastric Cancer and Evaluation of Nutrient Intakes of Gastric Cancer Patients: A Case-Control Study

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Abstract

Background: Gastric cancer (GC) is the fourth major malignancy and the second leading cause of cancer-related deaths worldwide. Northern and northwestern areas of Iran are among the high risk areas for GC. Studies have shown that dietary components are implicated in the etiology of GC. The index of nutritional quality (INQ) is a method of quantitative and qualitative analysis of single foods, meals, and diets. We aimed to assess the association of INQ with GC, and to evaluate the nutrient intake of GC patients.
Methods: The present case-control study included 82 cases and 95 healthy controls attending specialized centers in Tabriz, Iran, from December 2014 to May 2016. INQ scores were computed based on dietary intake assessed using a validated 168-item food frequency questionnaire (FFQ). Logistic regression models were used to estimate multivariable ORs adjusted age, gender, Body Mass Index (BMI), smoking, residency, education, and regular physical activity.
Results: After controlling for several covariates, inverse associations were observed between GC risk and INQs of vitamins A, B6, and D (ORvitA = 0.25 (0.06 - 0.98); ORvitB6 = 0.10 (0.04 - 0.28); and ORvitD = 0.14 (0.02 - 0.84)). Cases had higher intake of total fat, saturated fatty acids, beef, lamb meat, salt, and paprika compared to controls. On the other hand, controls had higher intake of vitamin A, vitamin, vitamin B6, copper, poultry, low fat milk, tea, coffee, turmeric, and saffron compared to cases.
Conclusions: Subjects who follow a more healthy and nutrient-rich diet, especially in terms of vitamins A, B6, and D, are at lower risk of having GC, compared to those who consume a more unhealthy, nutrient-poor diet.

Keywords: Gastric Cancer, Index of Nutritional Quality (INQ), Nutritional Assessment, Vitamin A, Vitamin B6, Vitamin D

1. Background

Gastric cancer (GC) is the fourth major malignancy and the second leading cause of cancer-related deaths worldwide (1, 2). According to estimates, each year more than 930 thousand new GC cases are being diagnosed, of which at least 700 thousands lose their lives due to this debilitating disease (3). In the Iranian population, GC is the most common cancer in men and the third most common cancer in women (4). Northern and northwestern areas of Iran are among the high risk areas for GC. Ardabil province in the North West has the highest incidence of GC with age standardized rate (ASR) = 49.1 for men and 25.4 for women (5, 6). East Azarbaijan, Golestan, and Semnan provinces are among the areas with high rates of GC (7). GC is one of the most common malignancies in the world with a multifactorial etiology including infection with *H. pylori*, smoking, alcohol consumption, unhealthy eating habits, and genetic predisposition (8, 9). On the other hand, there is broad consensus that the vast majority of cancers are preventable (10, 11).

Uneven geographical distribution of GC (12, 13) and the effect of immigration on this disease process (3, 14) represent a significant effect of environmental factors, especially nutritional factors such as quality of diet, in the development of this cancer (15, 16). In addition, geographic and ethnic differences in the incidence of GC and changes in the observed patterns of immigrants show that GC is closely associated with modifiable risk factors like diet (17).

Recently, there has been a growing interest to assess

the nutritional quality of the diet and its relationship with chronic diseases (18). Since in developing countries such as Iran, energy intake is the most important indicator of food security, dietary quality assessment procedures should be simple and practical (19). One of these simple methods is the index of nutritional quality or INQ that has important applications in clinical assessment of nutritional problems or situations (20, 21). The INQ is a method of quantitative and qualitative analysis of single foods, meals, and diets. It is a ratio of the nutrient-to-calorie content of foods which may be displayed as bar graphs and tabular data (17).

In the current study, we examined the relationship between INQ scores and the risk of GC. We also evaluated nutrient intakes of GC patients in an Iranian case-control study. Our hypothesis is that a poor diet and unbalanced dietary intakes increase the risk of GC incidence.

2. Methods

2.1. Participants

This hospital based case-control study was conducted at specialized centers in Northwest of Iran from December 2014 to May 2016. The study included 82 patients with GC and 95 healthy controls. The cases were patients with GC who were diagnosed by a gastroenterologist within the previous month. These patients were selected with the random sampling procedure. Controls were randomly selected from other patients' caregivers attending the same clinics. Controls were frequency matched by age ($\pm$ 5 year) and sex. Data on cases and controls were collected at the same time and setting. After providing written and verbal explanations about the methodology of the study, informed consent was received from each participant. The study protocol was approved by the local ethics review committee at Shahid Beheshti University of Medical Sciences, Tehran, Iran.

2.2. Inclusion and Exclusion Criteria

Inclusion criteria included the following: a, the absence of any malignancy (except for GC in cases); b, not following special diets such as vegetarian, or the diets resulting in weight changes during the year prior to the interview; c, the absence of conditions such as pregnancy, lactation, or a history of neurological, gastrointestinal, hepatic, endocrine, immunological, renal, or cardiovascular disorders and diseases; d, the age range of 20 - 80 years; and e, willingness to cooperate in the study.

Exclusion criteria included the following: a, not sticking to the study protocol; b, major dietary changes during the study; c, reported energy intake of outside the range of 800 - 5500 kcal.

2.3. Assessment of Dietary Intake

In this study, past year dietary intakes of the subjects were evaluated by a semi-quantitative, valid and reliable food frequency questionnaire (FFQ) (22). This FFQ asks about the average consumption frequency of 168 food items. Participants were asked to report the frequency of consumption of each food item in the last year according to the standard serving size in the questionnaire. Depending on the type of food, subjects indicated their intake of the food items per day, week, month or year, or as never. Then, the information obtained from the questionnaires was analyzed using Nutritionist V software (First Databank, Hearst Corp., SanBruno, CA, USA) to calculate the average daily intake of energy and nutrients. The INQ was calculated according to the daily intake of food items.

2.4. Assessment of INQ

The INQ is a method of quantitative and qualitative analysis of single foods, meals, and diets which has special significance in assessing clinical nutritional problems. The INQ is a ratio of the nutrient-to-calorie content of foods. The number of nutrients and the nutrient standards used for analysis are flexible parameters which may be varied for each clinical situation. Illustrative examples include INQ analysis of simple foods, an institutional house diet, the diabetic exchange list, and the diagnostic evaluation of the dietary intake of a hospitalized patient (17).

We calculated the INQ of each nutrient, for which there was a defined recommended dietary allowance (RDA) or adequate intake (AI) in dietary reference intake (DRI) tables, using the following formulae: INQ = consumed amount of a nutrient per 1,000 kcal/RDA or AI of that nutrient per 1,000 kcal (17).

FFQ-derived dietary data were used to calculate INQ scores for all participants. Major food items that were used in the calculation of INQ were as follows: protein, sodium, potassium, vitamin A, vitamin C, iron, vitamin D, vitamin E, thiamin, riboflavin, niacin, vitamin B6, folate, vitamin B12, biotin, pantothenic acid, vitamin K, magnesium, zinc, manganese, selenium, and fiber.

2.5. Assessment of Other Variables

For all participants the required information about age (year), gender (male, female), education ($\leq$ high school diploma, $>$ high school diploma), smoking (yes, no), *H. pylori* infection (positive, negative), residency (urban, rural), regular physical activity (yes, no), family history of cancer (yes, no), and alcohol consumption were collected through general information questionnaire during the interviews.

The weight of each participant was measured with light clothing using a SECA digital scale with a100-gram accuracy. The height was measured without shoes in standing position, leaning against the wall and shoulder blades under normal circumstances with an accuracy of 0.5 cm by a tape measure mounted on the wall. Body Mass Index (BMI) was calculated by dividing weight (in kilograms) by the square of height (in square meters).

During several training sessions, the main investigators trained a nutritionist, who was not aware of the study objectives, about how to complete the general information questionnaire and FFQ, and to do the anthropometric measurements.

2.6. Statistical Analyses

In this study we used IBM SPSS software (version 21) for statistical analysis of the data. Chi-square or Fisher's exact test was used for comparison of categorical variables between groups. In the case of quantitative variables before choosing a statistical test was investigated normality of their distribution using the Kolmogorov-Smirnov test. Then, the independent samples T-test or Mann-Whitney U tests were used for comparison of continuous variables with normal and non-normal distribution between groups, respectively. Crude and multivariable adjusted logistic regression models were used to estimate ORs and 95% CIs of having GC in relation to each nutrient's INQ. Adjustments were done for age, BMI, gender, education, smoking, residency, and regular physical activity in the adjusted models.

3. Results

Table 1 shows the distribution of socio-demographic, anthropometric, and life-style related characteristics across cases and controls. Cases had higher BMI and *H. pylori* infection compared to controls. The average BMI was 26.3 in the cases and 24.9 in the controls (P = 0.02). In addition, 74.4% of cases and 51.6% of controls had *H. pylori* infection (P < 0.01). On the other hand, controls were more active compared to cases. Table 2 shows the distribution of daily dietary intakes across cases and controls. According to Table 3 cases had higher intake of total fat (119.7 ± 42.9 vs. 106.6 ± 32.6), SFA (53.1 ± 38.2 vs. 40.1 ± 26.7), beef (17.7 ± 25.4 vs. 10.3 ± 13.7), lamb meat (17.7 ± 19.0 vs. 12.2 ± 16.0), sunflower seeds (7.1 ± 8.9 vs. 4.1 ± 8.2), salt (2.5 ± 0.8 vs. 1.8 ± 0.6), and paprika (3.2 ± 3.6 vs. 1.1 ± 2.0) compared to controls. On the other hand, controls had higher intake of vitamin A (696.4 ± 377.2 vs. 585.5 ± 203.3), vitamin D (2.4 ± 1.6 vs. 1.9 ± 1.5), vitamin B6 (2.7 ± 1.0 vs. 2.0 ± 0.5), copper (2.8 ± 1.1 vs. 2.4 ± 1.3), poultry (39.4 ± 28.7 vs. 27.4 ± 24.8), low fat milk (76.6 ± 92.2 vs. 52.5 ± 69.8), tea (740.9 ± 662.4 vs. 495.9 ± 499.3), coffee (8.6 ± 19.7 vs. 4.5 ± 6.5), turmeric (1.0 ± 1.0 vs. 0.5 ± 0.8) and saffron (0.4 ± 1.0 vs. 0.2 ± 0.5) compared to cases. There was no significant difference between groups in terms of energy, protein, carbohydrate, MUFA, PUFA, vitamin C, vitamin E, thiamin, riboflavin, folate, vitamin B12, magnesium, zinc, selenium, sugar, and spice intake. Table 3 shows comparison of the INQ of the subjects. Table 3 shows that only the INQ of vitamin A (0.52 ± 0.2 vs. 0.45 ± 0.1) and vitamin B6 (1.4 ± 0.05 vs. 1.0 ± 0.3) are higher in controls compared to cases. To avoid presenting so many statistically insignificant results, only the ORs and 95% CIs for GC risk in relation to INQ of vitamins A, B6, and D are presented in Table 4. After controlling for several covariates, inverse associations were observed between GC risk and INQs of vitamins A, B6, and D (OR_{vitA} = 0.25 (0.06 - 0.98); OR_{vitB6} = 0.10 (0.04 - 0.28); and OR_{vitD} = 0.14 (0.02 - 0.84)).

4. Discussion

The present study is the first one to investigate the relationship between INQs and GC risk in Iran. In this study, we observed inverse associations between GC risk and INQs of vitamins A, B6, and these results supported our hypothesis that following a healthier and nutrient-rich diet is associated with a reduced risk of GC. Also, in this study we observed that GC patients' intake of total fat, SFA, beef, lamb meat and salt were significantly higher compared to controls. In line with our study, several studies (17), including meta-analysis studies (23, 24), have shown that high intake of total fat and SFA are associated with increased risk of GC. However, it should be noted that some studies (25) have not observed a significant association between total fat and SFA intake and GC risk. Furthermore, consistent with our findings, several studies (26) have observed significant positive association between the consumption of beef, lamb meat, and salt and GC.

In the present study, it was observed that the controls had higher intakes of vitamin A, vitamin D, vitamin B6, poultry, low fat milk, turmeric, and saffron compared to cases. Similar previous studies have shown that there is inverse association between GC risk and intakes of vitamin A (24, 27, 28) D (27, 29, 30) and B6 (31, 32) a finding which is in line with our results. Moreover, studies investigating the association of GC risk and intakes of turmeric (curcumin) (33, 34) and saffron (35, 36) have reported similar inverse relationships. However, regarding the relationship between GC risk and intakes of white meat (37, 38) and low-fat milk (28, 39) the finding of previous studies are conflict-

Table 1. Distribution of Socio-Demographic, Anthropometric, and Life-Style Related Characteristics Across Cases and Controls[a,b]

Characteristics	Cases (N = 82)	Controls (N = 95)	P Value
Age, y	51.3 ± 11.8	48.3 ± 10.7	0.07
Body mass index (BMI)	26.3 ± 5.1	24.9 ± 2.7	0.02
Gender			0.98
Females	52 (54.74)	45 (54.88)	
Males	43 (45.26)	37 (45.12)	
Education			0.24
≤ High school diploma	51 (62.2)	67 (70.5)	
> High school diploma	31 (37.8)	28 (29.5)	
Smoking			0.81
Yes	14 (17.1)	15 (15.8)	
No	68 (82.9)	80 (84.2)	
H. pylori			0.00
Positive	61 (74.4)	49 (51.6)	
Negative	21 (25.6)	46 (48.4)	
Residency			0.28
Urban	60 (73.2)	76 (80.0)	
Rural	22 (26.8)	19 (20.0)	
Physical activity			0.02
Yes	14 (17.1)	30 (31.6)	
No	68 (82.9)	65 (68.4)	
Family history of cancer			0.40
Yes	13 (15.9)	11 (11.6)	
No	69 (84.1)	84 (88.4)	
Alcohol consumption			0.40
Yes	11 (13.4)	9 (9.5)	
No	71 (86.6)	86 (90.5)	

[a] Independent samples T-test or Mann-Whitney U tests and Chi-square or Fisher's Exact tests were used for comparison of continuous and categorical variables between groups, respectively.
[b] Values are expressed as mean ± SD or No. (%).

ing, which could be due to a host of different reasons such as difference in methodology, and residual confounding.

We observed fewer differences in dietary intakes between groups when using INQs instead of absolute intakes. This indicates that the application of standard tools and indexes such as INQ might result in more precise and functional comparisons when assessing the association of dietary exposures with different health outcomes, compared to the traditional evaluation of absolute dietary intakes.

In a similar study by Lim et al. in Korea (17), as in our study, a higher INQ of vitamin A was observed in GC patients compared to the controls. In contrast, the opposite was observed in case of vitamin B6 (17). Despite these differences, our findings regarding the inverse association of GC risk and INQs of vitamins A, B6, and D is generally supported by those obtained from previous studies (17) in which a protective role for each of these vitamins has been postulated against GC.

The inverse association between INQs of some nutrients and GC risk in this study is very encouraging. Although the exact mechanisms of the potential protective effects of vitamins A, B6, and D against GC have not yet been clarified, a few mechanisms have been proposed.

One of the proposed mechanisms is the crucial role of vitamin A and D in combating the chronic inflammation, an important contributor in developing GC, via their

Table 2. Distribution of Daily Dietary Intakes Across Cases and Controls[a,b]

Variables	Cases (N = 82)	Controls (N = 95)	P Value
Energy, Kcal	3012.9 ± 625.5	2991.2 ± 549.0	0.80
Protein, gr	101.1 ± 39.2	109.4 ± 39.8	0.16
Carbohydrate, gr	308.4 ± 114.1	373.5 ± 118.1	0.69
Total Fat, gr	119.7 ± 42.9	106.6 ± 32.6	0.02
Saturated fatty acid, gr	53.1 ± 38.2	40.1 ± 26.7	< 0.01
Mono-unsaturated fatty acid, gr	29.3 ± 11.3	30.2 ± 9.6	0.60
Poly-unsaturated fatty acid, gr	28.1 ± 16.6	31.4 ± 20.5	0.24
Vitamin A, mcg	585.5 ± 203.3	696.4 ± 377.2	0.01
Vitamin C, mg	154.4 ± 75.9	160.3 ± 55.8	0.55
Vitamin D, mcg	1.9 ± 1.5	2.4 ± 1.6	0.02
Vitamin E, mg	19.2 ± 9.1	18.6 ± 6.7	0.62
Thiamin, mg	2.0 ± 0.7	2.2 ± 0.9	0.19
Riboflavin, mg	2.1 ± 0.6	2.2 ± 0.8	0.38
Vitamin B6, mg	2.0 ± 0.5	2.7 ± 1.0	0.00
Folate, mcg	663.5 ± 257.6	709 ± 216.2	0.19
Vitamin B12, mcg	5.7 ± 3.9	5.2 ± 2.5	0.32
Magnesium, mg	507.8 ± 155.4	541.7 ± 147.8	0.14
Zinc, mg	15.1 ± 4.4	15.1 ± 5.7	0.94
Copper, mcg	2.4 ± 1.3	2.8 ± 1.1	0.05
Selenium, mcg	121.6 ± 48.2	128.6 ± 42.0	0.30
Sugar, gr	138.7 ± 50.7	127.5 ± 38.0	0.09
Beef, gr	17.7 ± 25.4	10.3 ± 13.7	0.01
Lamb Meat, gr	17.7 ± 19.0	12.2 ± 16.0	0.03
Poultry, gr	27.4 ± 24.8	39.4 ± 28.7	0.00
Low Fat Milk, gr	52.5 ± 69.8	76.6 ± 92.2	0.05
Sunflower seeds, gr	7.1 ± 8.9	4.1 ± 8.2	0.02
Tea, mg	495.9 ± 499.3	740.9 ± 662.4	0.00
Coffee, mg	4.5 ± 6.5	8.6 ± 19.7	0.05
Salt, gr	2.5 ± 0.8	1.8 ± 0.6	0.00
Paprika, mg	3.2 ± 3.6	1.1 ± 2.0	0.00
Turmeric, mg	0.5 ± 0.8	1.0 ± 1.0	0.00
Spice, mg	0.6 ± 0.9	0.9 ± 1.0	0.09
Saffron, mg	0.2 ± 0.5	0.4 ± 1.0	0.04

[a] Independent samples T-test and Mann-Whitney U tests were used for comparison of continuous variables with normal and non-normal distributions between groups, respectively.
[b] Values are expressed as mean ± SD.

effects in inhibition of inflammatory markers' gene expression (17, 29). Another proposed mechanism involves the roles of these vitamins in decreasing systemic inflammation, and subsequently the GC incidence, by reducing insulin resistance (40-43). In case of Vitamin B6, as this vitamin has a crucial role in amino acid and amines metabolism, it is logical to assume an essential part for this vitamin in reducing the chronic inflammation. In fact,

Table 3. Comparison of the Index of Nutritional Quality (INQ) of the Subjects[a,b]

Variables	Cases (N = 82)	Controls (N = 95)	P Value
Protein, gr	1.2 ± 0.4	1.3 ± 0.4	0.11
Sodium[c]	89.3	88.7	0.93
Potassium	0.58 ± 0.2	0.54 ± 0.2	0.18
Vitamin A	0.45 ± 0.1	0.52 ± 0.2	0.03
Vitamin C	1.2 ± 0.6	1.2 ± 0.4	0.87
Iron	1.6 ± 0.6	1.6 ± .06	0.60
Vitamin D	0.2 ± 0.1	0.2 ± 0.1	0.06
Vitamin E	0.8 ± 0.4	0.8 ± 0.3	0.67
Thiamin	1.2 ± 0.5	1.3 ± 0.6	0.43
Riboflavin	1.1 ± 0.3	1.1 ± 0.5	0.37
Niacin	1.2 ± 0.5	1.2 ± 0.5	0.72
VitaminB6	1.0 ± 0.3	1.4 ± .05	< 0.01
Folate	1.1 ± 0.5	1.2 ± 0.4	0.23
VitaminB12	1.6 ± 1.1	1.5 ± 0.8	0.27
Biotin[c]	85.1	92.3	0.35
Pantothenic acid	1.0 ± 0.4	1.0 ± 0.4	0.77
Vitamin K	1.5 ± 0.8	1.7 ± 0.8	0.18
Magnesium	0.8 ± 0.2	0.9 ± 0.2	0.15
Zinc	1.0 ± 0.3	1.0 ± 0.4	0.90
Manganese	2.7 ± 1.3	2.6 ± 1.0	0.51
Selenium	1.5 ± 0.6	1.6 ± 0.5	0.26
Fiber[c]	85.1	92.3	0.35

[a] ANOVA was used for continuous variables and Chi-square was used for categorical variables.
[b] Values are expressed as mean ± SD.
[c] Mann-Whitney U test used for the quantitative variables with non-normal distribution.

Table 4. Odds Ratios (OR) and 95% Confidence Intervals for Gastric Cancer Risk in Relation to Index of Nutritional Quality (INQ) of Vitamins A, B6, and D

INQ	ORs	Lower Bound	Upper Bound	P Value
Vitamin A[a]	0.17	0.02	1.00	0.05
Vitamin B6[a]	0.06	0.02	0.22	0.00
Vitamin D[a]	0.21	0.04	1.10	0.06
Vitamin A[b]	0.25	0.06	0.98	0.04
Vitamin B6[b]	0.10	0.04	0.28	0.00
Vitamin D[b]	0.14	0.02	0.84	0.03

[a] crud model.
[b] Adjusted model. Adjustments were done for age, body mass index, gender, education, smoking, residency, and regular physical activity.

some studies have shown a direct association between vitamin B6 deficiency and increased levels of inflammatory markers, such as C-reactive protein, interleukin 6, and tumor necrosis factor alpha, all of which have been postulated to play a role in gastric carcinogenesis (43-46). However, future comprehensive studies are necessary to investigate the exact mechanisms of protective effects of vitamin A, B6, and D against GC.

An important strength of this study is the fact that it is the first one in Iran to examine the association of INQ and GC. Since the INQ is based on standards and adjusts energy intake, it assesses the nutritional status of subjects more accurately than the usual and routine evaluation procedures. Another important strength is the use of a validated and reproducible FFQ (22), which allowed for a comprehensive assessment of major nutrient sources in diet, although some measurement errors inherent in the FFQ may be present. Also, controls were selected carefully by ensuring that none of them had any condition related to diet or other major risk factors associated with GC. However, there are a few limitations inherent in our study which needs to be considered. As with other case-control studies the probability of recall and selection biases could not be entirely ruled out.

However, administering validated FFQs by trained interviewers in a hospital setting might have, to some extent, reduced the recall bias and improved comparability of information of cases and controls. Another limitation of the study is related to the use of INQ. Since INQ is calculated based on the DRI, it cannot be calculated for nutrients or food items for which there is no defined DRI. Therefore, it is possible that the potential effects of these nutrients or food items on GC have been ignored in the present study. However, it should be noted that we did our best to compensate for this limitation by comparing the intakes of these nutrients or food items between cases and controls by using conventional methods.

In conclusion, findings of the present study suggest that subjects who follow a more healthy and nutrient-rich diet, especially in terms of vitamins A, B6, and D, are at lower risk of having GC, compared to those who consume a more unhealthy, nutrient-poor diet. Thus, encouraging higher intake of these nutrients and recommendations regarding following a more nutrient-rich diet could be a potentially effective strategy in prevention of GC. However, future studies of high methodological quality are warranted to gain a clear insight into the relationship between diet and GC, and to further deepen our understanding about the role of dietary components in gastric carcinogenesis.

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Footnotes

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