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Is Dietary Pattern Associated with Gastric Cancer Risk? A Case-control Study in Iran

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ABSTRACT

Background: Diet is considered as an important contributor to the development of the cancers. In the present study, the association of dietary patterns with gastric cancer risk was studied.
Methods: In the present case-control study, 192 newly diagnosed gastric cancer patients and 365 subjects as control group were included. The participants in each group underwent face-to-face interview. For food pattern determination, a 100-item qualitative food frequency questionnaire (FFQ) and exploratory factor analysis method were used. Logistic regression was used for determination of association between derived dietary patterns and gastric cancer risk.
Results: Four major dietary patterns with 55.48% prediction rate, namely "tubers and spices", "cereals and dairies", "healthy" and "Western-style", were identified. Tubers and spices [in males: 11.42 (4.17, 26.75); in females: 6.94 (2.24, 21.56)] and "Western-style" dietary patterns [in males: 1.16 (1.00-4.35); in females: 2.25 (1.10, 6.49] significantly increased the odds of gastric cancer risk in both sex. However, "healthy" dietary pattern and "cereals and dairies" dietary pattern were not associated with gastric cancer risk (P>0.05).
Conclusion: In Iranian population, consumption of diets high in tubers, spices and salts (labelled tubers and spices), processed meat, high energy drinks, snacks and desserts (labelled western-style) tended to increase the risk of gastric cancer. More longitudinal studies with large sample size and accurate estimate of dietary intake is suggested until more precise conclusion could be achieved.

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Introduction

Gastric cancer (GC) is one of the most important causes of death worldwide. It affects the patient's quality of life and health.[1] Considering the high mortality rate of gastric cancer, primary prevention is an important approach for improvement of gastric cancer prognosis.[2] Many factors including genetic predisposition, lifestyle and environmental factors are considered as risk factors of gastric cancer.[3] Diet is also considered as one of the important contributors to cancers[4] and many attempts have been made to identify the important food and nutrients associated with gastric cancer. However, nutrients or foods are not consumed isolated and the aetiology of cancers could not be explained only by assessment of a single nutrient or food.[5] One of the approaches for assessment of the combined effect of nutrients and food is the dietary pattern approach.[6, 7] Using this approach, the complete picture of food and nutrient interactions and their synergic effects could be achieved and the link between diet and chronic disease could be evaluated.[8]

Previously, the association between dietary pattern and gastric cancer risk have been investigated in some studies providing controversial results in different populations. In Uruguay, De Stefani et al, showed that starchy food

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pattern was significantly associated with increased risk of gastric cancer and healthy dietary pattern was associated with decreased risk of gastric cancer risk.[9] In another case-control study in Canada, it was indicated that western dietary pattern was associated with increased risk of stomach cancer; whereas healthy dietary patterns were associated with decreased risk.[10] Studies from Japan have shown that traditional japanese diet was associated with increased risk of gastric cancer; while, the western dietary pattern did not show any adverse effect.[11] The results of a meta-analysis including the results of the studies conducted in European countries, united states and japan showed a 2-fold difference in gastric cancer risk between a "healthy" and "western" dietary pattern.[12]

The association of different food items and dietary patterns and risk of gastric cancer has been studied in Iranian populations.[13] The prevalence of gastric cancer in the northwest of Iran is high and Iran recently faced with nutrition transition namely the adoption of a western diet, and its combination with traditional dietary pattern provides a particular occasion for further studies in the field of dietary pattern.[14]

In current study, the association of dietary patterns identified by factor analysis with gastric cancer risk was studied.

Materials and Methods

A hospital-based case-control study was carried out on subjects referring to four hospitals located in Tabriz, Iran between May 2009 and May 2011. The Ethics Committee of Tabriz University of Medical Sciences approved the study. The written informed consent was obtained from all participants.

The cases were newly diagnosed patients with histologically confirmed gastric cancer living in East Azerbaijan province for more than twenty years who aged between 20-85 years. They were recruited from two hospitals in Tabriz, Iran. A total of 192 cases were identified. In the present study, 90.56% of the invited patients accepted the invitation to participate in the study. There was no significant difference in age, sex, marital status, educational level and BMI between study participants and non-participants. For each case, two subjects as control were assigned from apparently healthy people referring to other departments such as orthopaedic and ophthalmic departments of two other hospitals. The control subjects were excluded if they reported any history of cancer or any other disease that could affect dietary patterns such as diabetes or cardiovascular disease, family history of cancers and gastrointestinal disorders. Totally, 365 individuals were selected as a control group. There was no significant difference in age, sex, marital status, educational level and BMI between study participants and non-participants.

Covariates for multivariate regression analysis included sex, age, BMI, education, marital status, smoking status (over the past year), alcohol consumption (over the past year), history of helicobacter pylori infection, number of meals/day, the habit of drinking or eating hot tea and foods. The trained nurses in each hospital gathered all the dietary and demographic data through a questionnaire.

For determination of food pattern, a 100-item qualitative food frequency questionnaire (FFQ), asking about the consumption of food and beverages over the past year in case and control group was used. This questionnaire was completed by face-to-face personal interviews. Each food item was assigned to one of the defined food groups according to their nutrient content (Table 1).

For statistical analyses, SPSS V18 was used. Factor analysis with principal component extraction method and Varimax rotation was used. We also checked the variable communalities (proportion of each variable's variance that can be explained by the factors) and food groups that had communalities >0.20 were retained in the factor analysis. The derived dietary patterns were labelled considering the food group that had high positive loading. The factor score was calculated for each dietary pattern. This score is a numerical value that indicates a person's relative standing on a factor. Participants were categorized according to tertiles of dietary pattern scores. Comparisons between the groups for continuous and categorical variables were determined using independent sample t-test and chi-square test, respectively. The stepwise forward Logistic regression was used to determine the association between dietary patterns and risk of gastric cancer (criteria for entry and retain in the

Table 1: Factor-loading matrix for major dietary patterns

Food groups	Tuber and spices	Cereals and dairies	Healthy	Western-style
Tuber	0.69	-	-	-
Spices	0.66	-	-	-
Vegetables	0.65	-	-	-
Oil	0.63	-	-	-
Salt	0.57	-	-	-
Egg	0.55	-	-	-
Legumes	0.47	-	-	-
Cereals	-	0.96	-	-
Dairy products	-	0.96	-	-
Nuts and dry fruits	-	-	0.77	-
Fruits	-	-	0.56	-
High energy drinks	-	-	-	0.76
Processed meats	-	-	-	0.58
Snacks and desserts	-	-	-	0.38

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model: P≤0.05 and P≤0.20, respectively).

Results

Using factor analysis method, four major dietary patterns were identified (Table 2). The first pattern accounted for 19.35% of the variance loaded positively for tubers, spices, vegetables, salt, oil, eggs and legumes, labelled tubers and spices. The second pattern (named cereals and dairies) accounted for 13.25% of total variance, was characterized by high intake of cereals and dairy products. Considering the positive load of nuts and dry fruits on the third dietary pattern, this pattern was labelled healthy pattern. This pattern accounted for 12.53% of total variance. Finally the last extracted pattern which was accounted for 1.33% of the variance was characterized by high consumption of high energy drinks, processed foods and

Table 2: Characteristics of participants in case and control groups

Variables	Gastric cancer patients (n=192)	Healthy controls (n=365)	P value*
Age (years)	59.87±15.24	55.13±15.24	0.001
Sex (males/females)	131/61	193/172	0.001
Education n (%)			0.04
Illiterate/reading and writing	119 (61.97)	193 (52.87)	
≤High school diploma	57 (29.68)	132 (36.16)	
≥College degree	16 (8.33)	39 (10.68)	
Marital status			0.01
Single	9 (4.68)	39 (10.68)	
Married	165 (85.93)	292 (80)	
Divorced/widow	18 (9.37)	34 (9.31)	
Weight (kg)	64.45±19.09	67.62±17.82	0.06
BMI (kg/m^2)	23.08±6.72	25.36±5.34	<0.001
Waist circumference	71.47±36.51	73.29±44.37	0.62
Current smoker n (%)	69 (35.93)	64 (17.53)	0.001
Current alcohol consumption	10 (5.20)	13 (3.56)	0.20
History of H.pylori infection (yes)	5 (2.60)	28 (7.67)	0.01
Number of meals/day			
3 meals	129	253	0.65
4 meals	49	86	
≥5 meals	14	26	
Drinking hot tea and eating hot food habit yes (%)	155	110	0.005

BMI: body mass index; *Chi-square test for comparison between categorical variables, independent test for comparison between continuous variables

Table 3: Odds ratio of gastric cancer risk by tertiles of dietary patterns.

Tubers and spices	Males		Females		Total	
	OR*	95%CI	OR*	95%CI	OR*	95%CI
T 1	1	-	1	-	1	-
T 2	3.51	1.53-7.96	1.97	0.61-6.22	3.25	1.71-6.16
T 3	11.42	4.87-26.75	6.94	2.24-21.56	9.95	5.25-18.53
P value for trend	<0.001		0.001		<0.001	
Cereals and dairy products						
T 1	1	-	1	-	1	-
T 2	0.99	0.48-2.07	0.62	0.24-1.55	0.84	0.49-1.45
T 3	1.30	0.60-2.82	0.26	0.08-1.00	0.79	0.44-1.44
P value for trend	0.29		0.1		0.91	
Healthy dietary pattern						
T 1	1	-	1	-	1	-
T 2	1.08	0.54-2.17	1.27	0.60-4.32	1.18	0.67-2.08
T 3	1.71	0.83-3.50	1.93	0.90-6.99	1.77	1.00-3.16
P value for trend	0.13		0.07		0.05	
Western-style dietary pattern						
T 1	1	-	1	-	1	-
T 2	1.60	0.73-3.29	3.87	1.70-12.52	2.36	1.25-4.15
T 3	2.06	1.00-4.23	2.85	1.10-6.49	2.63	1.39-4.49
P value for trend	0.04		0.003		<0.001	

OR: Odds ratio; 95%CI: 95% confidence interval; T: Tertile, T 1: lowest compliance to dietary pattern, T 3: highest compliance to dietary pattern; Adjusted for age, sex, education, marital status, BMI, smoking status, history of H. pylori infection, habit of drinking hot tea or eating hot food

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snacks and desserts labelled as "western-style" dietary pattern. Totally, these patterns explained 55.48% of the total variance in dietary patterns.

The demographic characteristics of the case and control group are presented in Table 3. There were significant differences between two groups in the case of sex, age, BMI, smoking status and self-reported history of helicobacter pylori infection.

The association between dietary pattern and gastric cancer is shown in Table 2. After adjusting for sex. age, education, marital status, BMI, smoking status, drinking and eating hot tea and food and history of helicobacter infection, subjects in the highest tertiles of "tubers and spices" dietary patterns were tended to have 11.42 (4.17, 26.75) and 6.94 (2.24, 21.56) fold higher odds for gastric cancer risk, respectively. In the case of "western-style" dietary pattern, the risk of gastric cancer was found to be significantly higher in individuals in the highest tertile of this dietary pattern (males: 1.16 (1.00-4.35); females: 2.25 (1.10, 6.49)). In contrast, "healthy" dietary pattern and "cereals and dairies" dietary pattern were not significantly associated with gastric cancer risk neither in males nor females (P>0.05).

Discussion

In this study, we identified four major dietary patterns (Tubers and spices, cereals and dairies, "healthy" and "Western-style" dietary patterns) using factor analysis for the first time in Iranian population with gastric cancer. The results indicated that consumption of "tubers and spices" was significantly associated with increased risk of gastric cancer. This dietary pattern was loaded positively with tubers, spices, vegetables, salt, oil, eggs and legumes. Previous studies showed a positive association between tubers and spices consumption and the risk of gastric cancer.[9] Tubers are rich in starch and nitrite that have been known as possible risks of gastric cancers. Although there is an inconsistency regarding the association of the nitrite and gastric cancer, a recent meta-analysis study showed that there is a significant positive association between high consumption of nitrite and gastric cancer.[15] Spices were the next food group that had significantly loaded on this dietary pattern. Another recent meta-analysis confirmed the significant unfavourable effect of high consumption of spices on gastric cancer.[16] Previous animal studies also showed the carcinogenetic effect of some spices such as chili extract. In addition, human studies showed that high-level consumption of capsaicin-containing foods were associated with an increased risk of cancer.[16] Another food that showed significant loading on this dietary pattern was salt. Salt has been considered as an important risk factor of gastric cancer. The effect of high consumption of salt and salty food on development of gastric cancer can be attributed to its direct effect on gastric mucusa and its synergic effect with helicobacter infection. Epidemiological studies showed a significant association between salt consumption and rate of infection with helicobacter pylori.[17] Another food group that showed high loading on this pattern was vegetables. Although some previous studies showed the protective effect of vegetables in gastric cancer, a recent meta-analysis in Eastern Asian countries did not show this protective effect.[18] Moreover, according to previous studies conducted in Iran, the nitrite content of the vegetables consumed in Iran is higher than recommended amount of WHO.[19] This may justify the observed positive association between consumption of vegetables and gastric cancer.

Although in the present study, we did not reach any significant association between "healthy" dietary pattern and gastric cancer risk, we showed a significant positive correlation between "western-style" pattern and gastric cancer. This result was consistent with the results of a recent meta-analysis in this regard. In the present study, the "western-style" pattern was characterized by high consumption of processed meat, high energy drinks, and desserts. It is postulated that these food groups had unfavourable effect on the pathway of gastric cancer through increasing overweight and obesity.[20]

There was not a significant association between "cereals and dairies" dietary pattern and gastric cancer. In the present study, this dietary pattern was characterized by high consumption of cereals and dairy products. Cereals are rich in starch. It has been shown that starchy foods increase the risk of gastric cancer.[21] On the other hand, in earlier studies, the protective effect of dairy products on gastric cancer had been demonstrated.[22] So, the absence of an association between this dietary pattern and gastric cancer could be attributed to the counteraction of these food groups on gastric cancer.

Following limitations should be considered when interpreting the results. In the present study, we used factor analysis approach. Different steps used in this method are subjective. Moreover, qualitative FFQ was used in approach to dietary patterns. Moreover, in the present study, due to using qualitative FFQ, we did not calculate the participants dietary energy intake and accordingly, we did not consider energy intake as a covariate in regression analysis.

In this study, we used a trained health professional team for the administration of FFQ instead of self-employed questionnaire which increases the validity of the data. Additionally, the hospital-based design of the study could be considered as another limitation of the study. We did not match control subjects individually with the case group, but in the regression analysis the results were controlled for a large number of potential confounders such as sex, age, dietary patterns, and anthropometric measurements.

Conclusion

Consumption of diets high in tubers, spices and salt (labelled tubers and spices), processed meat, high energy drinks and snacks and desserts (labelled as western-style) tended to increase the risk of gastric cancer. As a result, by determination of the role of unfavourable dietary patterns in development of gastric cancer, more effective and precise prevention strategies could be implemented in order to decrease the incidence of gastric cancer in Iran. From the research point of view, more longitudinal

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studies with large sample size and accurate estimate of dietary intake could be suggested for drawing more precise conclusions.

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Author Contribution
MHS & EF conceived the study, ShN collected all data, ZN contributed to partial data analysis and wrote the manuscript. MAJ contributed to data organization and further data analysis. All authors have read and approved the manuscript.

Availability of Data and Materials
The datasets used and/or analysed during the current study are available in Liver and gastrointestinal diseases research center, Tabriz University of medical sciences, Tabriz, Iran and will be available on request.

Ethical Approval
The Ethics Committee of Tabriz University of Medical Sciences approved the present study and the written informed consent was obtained from all participants.

Conflict of Interest: None declared.

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