

Case-Control Study of Dietary Pattern and Other Risk Factors for Gastric Cancer

Ali Nemati^{1,2}, *Reza Mahdavi³, Abbas Naghizadeh Baghi²

^{1.a.} Student Research Committee; ^{b.} Department of Biochemistry & Diet therapy, Faculty of Health and Nutrition, Tabriz University of Medical Sciences, Tabriz, Iran

^{2.} Department of Basic Sciences, Ardabil University of Medical Sciences, Ardabil, Iran

^{3.a.} Nutritional Research Center; ^{b.} Faculty of Health and Nutrition, Tabriz University of Medical Sciences, Tabriz, Iran

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ABSTRACT

Background: The rates of gastric cancer reported from Ardabil Province of Iran, are among the highest in the world. The aim of this study was to investigate the risk factors for gastric cancer in Ardabil Province.

Methods: This case-control study was conducted on 128 adults with mean age of 56.5 ± 12.8 yr old in Ardebil City, Iran in 2010 – 2011. Forty-two people with gastric cancer and 86 healthy people were recruited. Participants were interviewed using a structured questionnaire. Fasting blood samples were taken for measurement of IgG and IgA indices against *Helicobacter pylori* infection. Data were analyzed using the Chi-square and Independent sample *t*-test.

Results: Diet and *H. pylori* infection indices had the significant relationship with gastric cancer ($P < 0.05$). Among dietary patterns, drinking hot tea, low intake of fresh vegetables and fruits, and unsaturated fat were the most significant risk factors ($P < 0.05$). In gastric cancer patients, the levels of serum IgG and IgA as indicator of *H. pylori* infection were significantly ($P < 0.05$) higher than the healthy subjects (IgG 37.7 ± 29.3 vs. 16.9 ± 11.1 U/ml and IgA 50.5 ± 44.7 vs. 22.9 ± 15.8 U/ml). No significant relationship was observed between tobacco smoking and alcohol consumption with gastric cancer.

Conclusion: Dietary pattern especially drinking hot tea and low consumption of unsaturated fat, fresh vegetables, and fruits, as well as *H. pylori* infection were the most important risk factors in gastric cancer patients.

Key words: gastric cancer, *H. pylori*, dietary pattern, Iran

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Introduction

Gastric cancer is the second leading cause of cancer-related death, with 738,000 deaths annually all over the world [1]. In Iran, while the northern and northwestern areas are high-risk areas for gastric cancer, there are several intermediate and low risk

populations in other geographical regions [2]. Northwestern province of Ardabil has been reported to have the highest incidence rate in the country with age standardized incidence rates of 49.1 and 25.4 per 100,000 in men and women, respectively [3]. These

rates are almost 7 times the rate reported from the Southern Iran [4] and twice the national rate [5]. Gastric cancer constituted approximately one-third of all cancer related deaths each year in Ardabil [6]. Gastric cancer is a multi-factorial disease. Family history has been shown to be associated with its occurrence, suggesting a genetic basis [7, 8], but some classic immigrant studies [9, 10] showed that the incidence of the disease could change quickly across generation, implicating environmental, and analytical studies have shown strong links with diet [2, 11, 12], *H. pylori* infection [13], reactive oxygen species [14], and smoking [15, 16]. Several food items and dietary habits increase the risk of gastric cancer in this high-risk population [12, 17]. Regular consumption of red meat and dairy products were associated with more than doubled risk of gastric cancer [6, 18]. People who preferred higher salt intake and drinking of strong and hot tea were at higher risk than those who did not [6].

Despite importance of gastric cancer in Ardabil, no risk factor study has ever been conducted; therefore, a case-control study was carried out to explain potential risk factor in Ardabil that has the highest incidence of gastric cancer.

Material and Methods

Definition and selection of cases and control

This study was conducted in Nutrition Research Center of Tabriz University of Medical Sciences, in Iran in 2010 - 2011. The study was approved by Medical Ethical Committee of the Tabriz University of Medical. About 42 adult patients with gastric cancer in Imam and Fatemi Hospitals of Ardabil city were randomly selected. Cases were identified via the Ardabil Cancer Registry, which gastric cancer was diagnosed based on pathology, CT scan, and sonography. The mean age of all subjects in cases and control groups was 56.5 ± 12.8 yr.

To recruit controls, 100 households were visited and 86 eligible controls (86% of eligible controls) agreed to participate in the study. Control group was sought for each case, frequency matched to the case group based on age and gender. Control group was selected randomly from households of the same region depending of being visited by health professionals. The interviews took place mostly in subjects' home. The aims and study protocol were explained to the both groups and a written consent was taken prior to filling a questionnaire.

Questionnaire structure and Dietary method

A structured questionnaire administered to cases and controls sought information on demographic characteristics, smoking history, alcohol consumption, family history cancer, and eating habits. The prevalence of food frequency between both groups was evaluated using specific questionnaire. The participants were asked to indicate consumption of specified food in daily, weekly, monthly, and yearly bases. The selected frequency choice, given by the subjects for each food item from the food groups, was then converted to a weekly intake.

Measuring of antibody concentration

Fasting venous blood samples were taken for measurement of immunoglobulin A (IgA) and immunoglobulin G (IgG) as indices of *H. pylori* infection. IgA and IgG were measured using appropriate enzyme linked immunosorbent assay (ELISA) kits was purchased from Pishtazteb (Tehran, Iran), according to the manufacturer instructions. For the accuracy of assessment, duplicate assay were performed. Quantification of immunoreactive IgA and IgG was carried out on 96-well microtiter ELISA plates using standard protocols. The color formation was measured at 450 nm and 630 nm (Anhos 2000 microplate reader) and the sample concentration of IgA and IgG was estimated using Multicalc program (Wallac, Turku, Finland). Titers of sera IgG and IgA anti-

body were determined more than 10 U/ml and 20 U/ml as positive for *H. pylori* infection, respectively.

Statistical analysis

Data were analyzed by descriptive and analytical statistical methods using SPSS software version 16 for windows. Chi-square and Independent sample *t*-test were used for data analysis. Statistically significant level for all tests was considered as $P < 0.05$.

Results

As indicated in Table 1, of 42 cases, 29 (69%) were male and 13 were (31%) female. There was no significant relationship among sex, family history, and residence with gastric cancer. Using Chi-square showed no significant relationship between tobacco smoking and alcohol consumption between both groups. As indicated in Table 2, high intake of fresh vegetables and fruits, especially citrus fruit and unsaturated fat were the most protective factor ($P < 0.05$). There

was no significant relationship among red meat, roasted meat, sausage, milk, salty foods, pickles, fresh and smoked fish with gastric cancer. Surprisingly drinking hot tea had significant with incidence of gastric cancer ($P < 0.05$). An increasing risk was observed among those who drunk hot tea. About 71.4% of patients with gastric cancer were accustomed to drinking hot tea. The results of *H. pylori* infection indices are presented in Fig. 1. The results showed that 54.8% of patients had serum IgG level more than 10 U/ml, while in control group only 32.6% subjects had serum IgG level more than 10 U/ml ($P < 0.01$). About 42.82% of patients with gastric cancer had high serum concentration of *H. pylori* IgA antibody, whereas only 18.6% of healthy subjects showed an optical density value greater than 20 U/ml ($P < 0.01$). In gastric cancer patients the levels of serum IgG and IgA were significantly ($P < 0.05$) higher than the healthy subjects (IgG 37.7 ± 29.3 vs. 16.9 ± 11.1 U/ml and IgA 50.5 ± 44.7 vs. 22.9 ± 15.8 U/ml).

Table1: General characteristics of subjects

	Groups		P value
	Case(N=42)	Control(N=86)	
Sex			
Male	29	57	0.45
Female	13	29	
Family history			0.23
Yes	11	14	
No	31	72	
Residence			0.32
Urban	31	68	
Rural	11	18	
Tobacco smoking			0.39
Yes	10	24	
No	32	62	
Alcohol consumption			0.58
Yes	5	10	
No	37	76	

Table2: Dietary pattern and food frequency per week of case and control groups

Food frequency per week	Groups		P value
	Case	Control	
	M ± SD	M ± SD	
Bread and rice	18.6 ± 2.7	16.6 ± 6.7	0.08
Vegetables	2.2 ± 2	3.15 ± 3.12	0.03*
Fresh fruits	2.6 ± 1.8	6.4 ± 4.6	0.00*
Citrus fruit	3.1 ± 1.7	4.3 ± 3.8	0.00*
Garlic, onion and shallot	4.5 ± 4.2	4.6 ± 4.2	0.95
Red meat	5.1 ± 3.7	4.1 ± 3	0.11
Roast meat	1 ± 0.9	1.25 ± 1	0.58
Sausage	0.54 ± .007	0.64 ± 0.37	0.07
Pickles	3.6 ± 0.84	3.3 ± 2.9	0.11
Saturated fat	7.3 ± 5.4	7.2 ± 5.7	0.93
Unsaturated fat	2.4 ± 1.4	4.7 ± 4.2	0.00*
Milk	4.3 ± 3.5	3.5 ± 3	0.18
Yoghurt	4.3 ± 2.4	3.7 ± 3.2	0.30
Fresh fish meat	1 ± 0.7	1.3 ± 1.1	0.14
Smoked fish	0.26 ± 0.11	0.17 ± 0.07	0.34
Dietary pattern	Case(N=42)	Control(N=86)	
Temperature of tea			0.00[■]
Hot	30	23	
Moderate warm	3	14	
After cold	9	49	
Salty food intake			0.84
Salty food	9	22	
Moderate salty food	8	14	
Low salty food	25	40	

*P < 0.05 in Independent Sample t Test between two groups

■P < 0.05 in Chi-square between two groups

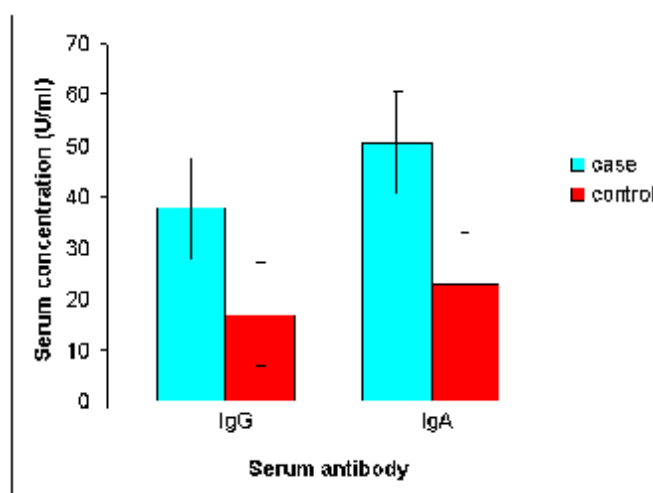


Fig.1: Comparison of mean serum concentration of IgA and IgG as an index of *H. pylori* infection in study groups

Discussion

In this study, strong association was observed between hot drinking tea, low intake of vegetables, fruits, and unsaturated fat with gastric cancer. In addition, the results showed, an inverse association between gastric cancer and high consumption of fresh fruits especially citrus fruit.

The majority of epidemiologic studies in gastric cancer during the last decade have reported a protective role for high consumption of fresh fruits and vegetables [19-21]. Fruits and vegetables are rich source of dietary fiber, vitamin and minerals and some other bioactive compounds, which may inhibit initiation or progression of cancer [22]. Although the mechanism by which fruits inhibit gastric cancer is not yet clear, antioxidant activity has been frequently cited as a possible positive mechanism. In this study, the consumption of citrus fruit was more protective than other fruits in the development of gastric cancer, which may be due to high content of ascorbic acid and β -carotene [23]. It has been suggested that ascorbic acid may acts as a scavenger of nitrite, which is thought to be carcinogenic in the form of N-nitroso, compounds [24]. A protective role for citrus fruit has been reported in several case-control and a few cohort studies too [25-28]. Although in previous studies, the protection role of allium vegetables (garlic and onion) in gastric cancer has been reported [7, 27, 29, 30]. In this study, we did not observe any significant relation. This disagreement may be due to low sample size of this study. Moreover, this study did not find any evidence to support a protective role for allium vegetables. Some results indicated an inverse association only between onion and gastric cancer [31].

In our findings, an increasing risk was observed among those who had used to drink hot tea. Causative role for drinking hot tea has been reported in the development of esophageal cancer [32] and gastric cancer [6]. A large case-control study in Mongolia on 1,263 cases and 2,526 healthy controls re-

ported almost 3 times increased risk for gastric cancer with drinking hot tea [33]. Although the mechanism by which hot tea increases the risk is not clear, cellular damage may explain this association. Some case-control studies have suggested that the hot food may play a role in development of gastric cancer by thermal irritation [29, 34].

We observed a significant inverse association between consumption of unsaturated fat and gastric cancer. It is thought that polyunsaturated fatty acid may inhibit gastric carcinogenesis. This inhibitory role was experimentally shown in mice [35]. An inverse association was reported between consumption of polyunsaturated fat and gastric cancer with a significant dose dependency [36]. Information on a potentially protective effect of vegetable oil consumption (polyunsaturated fat), or regarding specific types of polyunsaturated fatty acids and gastric cancer is very limited. In some studies, protective effect of vegetable oil consumption in gastric cancer has been reported [28, 37].

In relation to animal products, our data suggests that frequent consumption of red meat, roasted meat, sausage, and smoked fish would not increase the risk of development of gastric cancer. Although the association between high consumption red meat, sausage, and smoked fish with gastric cancer has already been shown in some case control studies [38-43], we did not observe any significant association, which may be due to low sample size of this study.

In this study, strong association was observed between *H. pylori* infection with gastric cancer. Infection with *H. pylori* is an important known risk factor for stomach cancer and has high prevalence in the developing countries [44, 45]. Crowded living conditions, poor hygiene, large families, and low socio-economic status are all associated with high rates of *H. pylori* infection [46, 47]. It has been showed that the presence of positive serum levels of antibody for IgA [48] and IgG [49] may indicate the past *H.*

pylori infection with related gastric cancer. This hypothesis is in line with results from prospective serologic studies that have shown higher incidence of noncardia gastric cancer in subjects with *H. pylori* infection, verified by specific IgG antibodies, than in no infected ones [49]. Practically, all *Helicobacter*-infected subjects have IgG antibodies, whereas IgA antibodies exist in approximately two-thirds of infected subjects [50]. Chronic infection with *H. pylori* leads to chronic gastritis, which may progress to atrophy, intestinal metaplasia and finally to noncardia gastric cancer [51].

In conclusion, our results showed that dietary patterns and *H. pylori* infection were the most important factors associated with gastric cancer. The study found that regular consumption of vegetables and fruits, especially citrus fruit, could reduce the risk of gastric cancer. In addition, consumption of unsaturated fat was found to play a protective role in development of gastric cancer. Also drinking hot tea was associated with more than doubled risk of gastric cancer. According to the findings, proper preventive nutritional education may be beneficial.

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