

ORIGINAL ARTICLE

The effects of environmental and dietary factors on the development of gastric cancer

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Summary

Purpose: Gastric cancer is the most frequent digestive system cancer in Turkey. The purpose of this study was to investigate the effect of sociodemographic, environmental, dietary and reproductive factors on the development of this malignancy.

Methods: 150 patients diagnosed with gastric cancer and 300 healthy controls were included in the present study. Sociodemographic, environmental, dietary and reproductive factors that might affect the risk of gastric cancer were retrospectively investigated.

Results: Examination of the dietary menus revealed that consumption of animal fats, pickled and salted foods were considerably higher ($p<0.001$) in gastric cancer compared to controls. Consumption of meat and eggs were significantly different ($p=0.048$) between gastric cancer patients

and the control group. Consumption of bread and cereal products ($p<0.001$), milk and milk products ($p<0.001$), orange juice ($p=0.022$), tea and coffee ($p=0.004$ and $p=0.002$) was markedly lower in the gastric cancer patients. Consumption of pickles was an independent risk factor for development of gastric cancer. Eating too hot foods and barbecued meat was also shown to increase the risk of gastric cancer ($p<0.001$). In addition, the educational level of the patients was also lower compared to those of the control group ($p=0.033$). Women with onset of menarche at 15 years and above also possessed a higher risk for gastric cancer ($p<0.001$).

Conclusion: Environmental and dietary factors play a significant role in the development of gastric cancer.

Key words: dietary habits, environmental impact, gastric cancer

Introduction

Gastric cancer is the fourth most common cancer in the world, and ranks second in terms of cancer-related deaths [1]. In Turkey, the incidence of gastric cancer is among the higher in the Eastern world and the lower in the West [2]. Large epidemiological studies have shown a correlation between diet and gastric cancer development [3-5]. In particular, pickled foods, foods rich in nitrates, and diet poor in fruits and vegetables are reported to increase the risk of gastric cancer [4-8]. An earlier study examined 24-hour urine samples from 39 populations, sampled from 24 countries and showed a correlation between gastric cancer development and nitrate consumption and salt expulsion [9]. Similarly, several studies have

demonstrated that while a diet rich in foods fried in fat, processed meat and fish, alcohol and animal fats increases the risk of gastric cancer, consumption of fresh fruits and fish reduces that risk [4,5,10,11]. Several earlier studies also suggested a positive correlation between gastric cancer risk and nitrate-based fertilizer [4,12,13], salted products containing nitroso compounds and smoked meats [4,14]. On the other hand, due to its antioxidant capacity, black tea might have anticarcinogenic properties [15], and indeed, a recent study suggests that black tea consumption might lower the risk of cancer development [16].

Gender is shown to play a role in the occurrence of certain cancers. Gastric cancer is more frequent among males than females as a whole. The male predominance of gastric cancer is

shown to be limited to the intestinal subtype only [17]. This observation might be explained by the rise in the concentration of estrogen and progesterone during pregnancy [18-20]. These hormones are thought to protect the epithelial mucosa and inhibit carcinogenic growth, either by increasing the activity of trefoil factor family protein or by inhibiting the activity of c-Erb B2 oncogene [19]. Furthermore, there are studies in the literature showing that late onset of menarche increases the risk of gastric cancer [21,22]. Likewise, occurrence of early menopause is shown to increase the risk of developing gastric cancer and this increased risk might be attributed to a decline in the concentrations of sex hormones thought to reduce the risk of gastric cancer [23]. Other factors also play a considerable role in the development of gastric cancer, similarly as in various other cancer types. For example, factors such as low socioeconomic level, cigarette use, excessive tea drinking, eating salted foods, living on a diet poor in fruit and vegetables, living in poor hygiene conditions, consuming excessively hot foods and spring water might trigger the development of gastric cancer [24-26].

The purpose of this study was to determine environmental and dietary factors that might induce the development of gastric cancer, most frequently encountered type of gastrointestinal system cancer in the Black Sea Region of Turkey.

Methods

One hundred fifty patients diagnosed with gastric cancer and 300 controls with no history of gastric or other cancers were enrolled in the present study. Patients in the control group were randomly pooled among patients with no history of cancer. Diagnosis and dates of diagnosis were determined from the pathology reports. Patients and controls were given the same questionnaire. The questionnaire included questions concerning sociodemographic features, environmental, familial, and reproductive characteristics that might affect the risk of gastric cancer. In addition, a diet questionnaire containing 35 questions regarding average consumption of various foods and drinks over the previous year was also meant to evaluate the dietary habits of the participants. The educational level of the patients was accepted as low if they were illiterate, as moderate if graduated from the primary school, and as high if graduated from the middle school, high school, or university. The barbecue habit of the patients was expressed as frequent if they consumed barbecue ≥ 4 /week, as moderate if they consumed barbecue ≤ 3 /week-4/month, and as rare if they consumed barbecue < 4 /month.

Table 1. Age and gender of patients and controls

	Patients N= 150		Controls N= 300		p value
	Male	Female	Male	Female	
Gender	47	103	96	204	0.886
Age, years (mean $\pm$ SD)	9 $\pm$ 12.95		58.44 $\pm$ 12.90		0.669

Statistics

Compatibility with normal distribution of data in both groups was analyzed using the Kolmogorov-Smirnov test. Normally distributed variables were compared between the gastric cancer patients and the control group using Student's t-test. The Mann-Whitney U test was used to analyze abnormally distributed variables. Analysis of the data obtained by counting was performed using the chi square test. A $p < 0.05$ was considered as statistically significant. Cox logistic regression analysis was performed to investigate independent risk factors affecting the risk of gastric cancer development. Results are presented as odds ratio (OR) and 95% confidence interval (CI).

Results

In the cancer group 62.8% of the patients had intestinal type and 37.2% diffuse type cancer. Assessment of the tumor location showed that 67.2% of the gastric cancer patients had tumors located in the antrum. There was no meaningful difference in terms of gender and age between the two groups ($p = 0.886$ vs $p = 0.669$, respectively). Male patients predominated (68.7%) and their body mass index recorded at the time of diagnosis was lower compared to controls ($p < 0.001$). Analyses of the questionnaires indicated that the educational levels of the patients were lower compared to the control group, and this difference was statistically significant ($p = 0.03$).

Cox multivariate logistic regression analysis revealed that the risk of getting gastric cancer was 9.63-fold higher in patients with lower levels of education than those with higher levels of education (OR=9.63 CI=3.07-30.18). The average age of the patients with gastric cancer was 58.99 $\pm$ 12.949 years (Table 1). Moreover, the patients had a lower monthly income compared to the control group ($p < 0.001$). In addition cigarette consumption was significantly higher in the gastric cancer patients compared to controls ($p < 0.001$). However, there was no marked difference in the use of alcohol between the groups ($p = 0.98$). Anamnesis on cancer history of the first degree relatives of the gastric cancer patients showed that the percentage of

the relatives with cancer history was 46.7% and 35.7% for the control group ($p<0.001$).

Women with gastric cancer had a later onset of menarche compared to controls ($p<0.001$). Evaluation of the age at the first pregnancy showed no marked difference between the women in the gastric cancer group and in the control group ($p=0.55$). The mean age at menopause in the gastric cancer patients and the control individuals was 44.90 ± 1.70 years and 48.69 ± 6.13 , respectively, showing that patients with gastric cancer entered menopause at an earlier age compared to females in the control group ($p<0.001$). No difference was noted between the mean number of pregnancies, number of children, and lactation time between the two groups ($p=0.395$ vs $p=0.490$, respectively).

Dietary habits were also different between patients and controls. Consumption of pickled ($p<0.001$) and salted foods ($p<0.001$), meat and eggs ($p=0.048$), and animal fat ($p<0.001$) was significantly higher in the gastric cancer patients when compared to the control group. By contrast, eating bread and cereal products ($p<0.001$),

milk and milk products ($p<0.001$), orange juice ($p=0.022$), tea and coffee ($p=0.004$ and $p=0.002$) were significantly lower in the gastric cancer patients than in the control group. In this study, pickle consumption was an independent risk factor for developing gastric cancer and the risk was 11.48-fold higher compared to those not consuming pickles. Moreover, the present study suggested that consumption of overheated food increases the risk for gastric cancer ($p<0.001$). We determined that 75.3% of gastric cancer patients and 25% of the healthy individuals in the control group ($p<0.001$) consumed overheated food. Eating overheated food was an independent risk factor for gastric cancer and the risk was 7.55-fold higher in those who were accustomed to consuming high temperature foods than in those who were not ($OR=7.55$, 95% $CI=3.67-15.51$). Likewise, consuming barbecued meat also increased the risk of gastric cancer ($p<0.001$). Assessment of the grill habits of the individuals indicated that the percentage of the participants (1) with frequent barbecues ($\geq 4/\text{week}$) was 42.7% among the gastric

Table 2. Frequency of consumption of various foods in patient and control groups

Frequency of consumption	Patients		Controls		<i>p value</i>
	<i>N</i>	%	<i>N</i>	%	
Milk and milk products					<0.001
Never	75	50.0	144	48.0	
≤ 3 times a week	48	32.0	141	47.0	
≥ 4 times a week	27	18.0	15	5.0	
Fruits and vegetables					0.174
Never	70	47.3	115	38.6	
≤ 3 times a week	49	33.1	107	35.9	
≥ 4 times a week	29	19.6	76	25.5	
Bread and cereal					<0.001
Never	57	38.0	4	1.3	
≤ 3 times a week	75	50.0	53	17.7	
≥ 4 times a week	18	12.0	242	80.9	
Meat and egg					0.048
Never	64	42.7	118	39.3	
≤ 3 times a week	69	46.0	165	55.0	
≥ 4 times a week	17	11.3	17	5.7	
Consumption of pickles					<0.001
Never	6	4.0	41	13.7	
≤ 3 times a week	28	18.7	176	58.7	
≥ 4 times a week	116	77.3	83	27.7	
Consumption of salted foods					<0.001
Never	33	22.0	134	44.7	
≤ 3 times a week	82	54.7	164	54.7	
≥ 4 times a week	35	23.3	2	0.7	

Table 3. Distribution of barbecue, tea and coffee consumption in patients and controls

	Patients		Controls		<i>p</i> value
	N	%	N	%	
Barbecue					<0.001
Never	36	24.0	253	84.3	
≤3 times a week	50	33.3	19	6.3	
≥4 times a week	64	42.7	28	9.3	
Tea consumption					0.004
Never	5	3.3	0	0	
≤3 times a week	145	96.7	300	100.0	
≥4 times a week	150	100.0	300	100.0	
Coffee consumption					0.002
Never	63	42.0	87	29.0	
≤3 times a week	68	45.3	136	45.3	
≥4 times a week	19	12.7	77	25.7	

Table 4. Multivariate logistic regression analysis of risk factors for gastric cancer

Independent variables	Odds ratio	95% CI		<i>p</i> value
		Lower	Upper	
Education				<0.001
Not educated	9.63	3.07	30.18	
Educated	1			
Consumption of pickles				<0.001
Never	1			
≤3 times a week	1			
≥4 times a week	11.48	3.42	38.49	
High temperature food				<0.001
No	1			
Yes	7.55	3.67	15.51	
Barbecue				<0.001
No	1			
Yes	33.02	13.82	78.87	

cancer patients and 9.3% among the control group ($p<0.001$); (2) with moderate barbecues it was 33.3% among the gastric cancer patients and 6.3% among the control group ($p<0.001$). Akin to eating overheated food, consuming barbecued meat was an independent risk factor for gastric cancer and the risk was 33.02-fold higher in the patients than in the controls (OR=33.02 95% CI=13.82-78.87) (Tables 2-4).

Discussion

In this study we investigated the sociodemographic, environmental, familial and reproductive factors that might affect the risk of getting gastric cancer. Excessive consumption of red meat

and meat products is thought to be a factor increasing the risk of gastric cancer. Nitrosamines are shown to be responsible for increased risk of gastric cancer incidence [5,8,27,28]. Meat products cooked for a long time at high temperatures contain mutagenic and heterocyclic amines [29]. We determined that gastric cancer patients consumed more animal products consisting of meat, eggs and fish compared to the control group ($p=0.048$). Salted foods and barbecued meats have been shown to increase the risk of gastric cancer [4,5,7,8,14,25,30,31].

The correlation between salted foods and gastric cancer is thought to be associated with the salt directly injuring the gastric mucosa and achlorhydria provoked by the nitrosamines contained

therein, preparing thus the way for bacterial colonization [30]. The results of the present study on the grill habits of the individuals indicated that the percentage of the participants with frequent barbecues (≥ 4 /week) was 42.7% among the stomach cancer patients, and 9.3% among the control group ($p < 0.001$), indicating a relationship between gastric cancer incidence with the frequency of consuming barbecued food. The consumption of barbecued meat was higher in the patient than in the control group in the present study. Use of barbecued meat was determined as an independent risk factor and gastric cancer incidence was 33.02-fold higher in people who were accustomed to consuming barbecues compared to those not eating barbecued meat so often ($OR = 33.02$, $p < 0.001$). These results are consistent with the literature.

Moreover, consumption of high-temperature foods and beverages is stated to augment the risk of gastric cancer. Accordingly, the majority of our gastric cancer patients claimed to eat excessively high-temperature foods. Likewise, in the current study we noticed that the percentage of the patients consuming high-temperature foods was 75.3% in the gastric cancer group and 25% in the control group. The difference was highly significant ($p < 0.001$). The present results pointed out that being accustomed to consuming high-temperature foods was an independent risk factor and gastric cancer risk was 7.55-fold higher in those who were used to eating high-temperature foods than in those who were not.

While a diet rich in saturated fat and cholesterol is shown to increase the risk of gastric cancer, plant foods are reported to reduce it [4,32,33]. We evaluated gastric cancer patients in terms of the type of fat they used in their meals and noticed that they consumed more animal fats compared to the controls ($p < 0.001$). Milk and milk products are shown to prevent atrophic gastritis and intestinal metaplasia [33], and our results regarding milk and milk product consumption in the two groups were compatible with those in the relevant literature ($p < 0.001$).

A relatively recent study demonstrated that fibrous foods exert a protective effect against diffuse type gastric cancer but are not protective against intestinal cancer [34]. In the present study, 62.8% of the tumors were of the intestinal type and 37.2% were of the diffuse type. Assessment of the tumors in terms of their localization demonstrated that 67.2% of the patients had antral gastric cancer.

It was also determined that our control group

consumed significantly ($p < 0.001$) more bread and cereal products when compared to the gastric cancer group. This difference may suggest that consumption of more bread and cereal products might protect gastric mucosa against acidic erosion by lowering or regulating gastric pH. Some authors claim that obesity might increase gastric cancer development by increasing gastric carcinogenesis in the antral region of the stomach [4]. The results of the present study showed that gastric cancer patients possessed low body mass index at the time of diagnosis ($p < 0.001$). The presence of low body mass index in gastric cancer patients is thought to be attributed to late diagnosis of cancer and loss of the body weight at the time of diagnosis.

Furthermore, black tea has been shown to have anticarcinogenic properties [35]. Animal studies have established that substances with polyphenol structure found in the tea increase tumor cell apoptosis by damaging DNA, RNA and protein structures of cancer cells and reducing cell proliferation [15]. Likewise, the substances found in the tea are reported to prevent also carcinogenesis and inflammation by inhibiting the secretion and activity of IL-8 and NF-KappaB. Studies have also shown that high tea consumption reduces the risk of gastric cancer [15,36]. In line with all these, we determined a significantly higher tea consumption in the control group. The difference in tea consumption between the two groups was highly significant ($p = 0.004$).

Some studies claim that cigarette smoking is an independent risk factor increasing the risk of developing gastric cancer [4,25,26]. The present results were consistent with the literature and showed that the consumption of cigarettes was markedly higher in the gastric cancer patients ($p < 0.001$). However, a recent study indicated no relation between smoking and gastric cancer development [26].

The effect of alcohol consumption on the development of gastric cancer is controversial. In the present study there was no difference in the use of alcohol between the two groups ($p = 0.98$).

When cancer history in the first degree relatives of the patients was assessed, it turned out that while 46.7% of the relatives of the gastric cancer patients had cancer history, this figure was only 35.7% among the relatives in the control group ($p < 0.001$).

Gastric cancer is generally seen after the age of 40. The average age of gastric cancer patients in our study was 58.99 ± 12.94 years and the major-

ity was in the 50 and above-year age group. This is in agreement with the studies showing that the incidence of gastric cancer increases with ageing [37,38]. In addition, some studies have reported that the risk of gastric cancer rises in people with a low socioeconomic or educational level [37-40]. Similarly, in the present study the subjects in the gastric cancer group had lower educational and socioeconomic levels compared to those in the control group ($p<0.001$ and $p<0.001$, respectively). In addition, the educational status was an independent risk factor and the risk of gastric cancer was 9.63-fold higher in the people with lower educational level with regard to those with higher educational level.

Late onset of menarche is reported to increase the risk of gastric cancer in females [21,22]. The risk of developing gastric cancer in women with an onset of menarche at the age of 12 years or younger is reported to be 50% lower than in those with an onset at the age 15 years or older [28], and the results of the present study are consistent with the literature. In the present study, while the percentage of the participants reported to have

onset of menarche at the age of 15 years or older was 76.6% in gastric cancer patients, it was 16.7% in the controls ($p<0.001$). Assessment of the age at the first pregnancy revealed no meaningful difference between gastric cancer patients and controls ($p=0.55$). The mean age at menopause in the females with gastric cancer was 44.90 ± 1.70 years, showing that females with gastric cancer entered menopause at an earlier age compared to controls ($p<0.001$). Of note, no difference was established between the mean number of pregnancies, number of children, and lactation time between the two groups ($p=0.395$ vs $p=0.490$, respectively).

In conclusion, the results of the present study indicate that dietary differences might play a considerably significant role in the development of gastric cancer. While we cannot control certain risk factors such as genetic factors, we can certainly improve our environmental conditions and readjust our dietary intake such as consuming moderately heated and unsalted or low-salted foods to reduce the risk of developing gastric cancer, a significant step toward the prevention of gastric cancer.

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