Risk of Gastric Cancer Associated with Family History of other Cancers of the Digestive System

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Background: The objective of the present study is to investigate the relationship between the familial history of digestive system cancers and development of gastric cancer.

Methods: In this case-control study conducted in 2012, 84 patients with a definite diagnosis of gastric cancer, diagnosed using endoscopy and pathological study of biopsies, were compared with 84 people with the same age and sex as the control group. The control group consisted of outpatients referring to the dermatology and ophthalmology clinics. All patients having a chronic condition were excluded from the control group. All patients filled out a questionnaire to determine whether they had any first-degree relatives with upper or lower digestive tract cancers. Data were analyzed using the Fisher's exact and logistic regression tests.

Results: The mean age of the patients was 65.4±10.7 and 64.3 percent of the patients were male. A statistically significant relationship between a background of gastric or colon cancer among first-degree relatives and the development of gastric cancer was observed An estimation of the odds ratio of the development of gastric cancer among patients with first-degree relatives who had developed gastric or colon cancers to the control group was 4.5 (95% CI=2.21-8.16) and 5.5 (95% CI=2.11-10.71), respectively. No significant relationship was found between a background of esophageal cancer among first-degree relatives and the development of gastric cancer among the participants (P_value = 0.24).

Conclusion: The presence of relationships between the development of gastric cancer and a familial background of digestive tract cancers need to be studied in further research and with larger samples.

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Introduction

Gastric cancer is the second most common cancer worldwide, with 900000 new diagnoses made each year.[1-3] The prevalence of this cancer is higher in Asia than in Western countries, which might be due to lifestyle or the genetic features of the patients.[4] Although in the previous decades, the fewer people have been diagnosed with gastric cancer, this cancer is still the second cancer-related cause of fatalities worldwide.[5, 6] In Iran, gastric cancer is the second most common cancer after lung cancer.[7-9] In recent years, the number of people affected by this disease and its mortality rates have increased in Iran, so that gastric cancer has the second place in terms of mortality.[10-12]

Some environmental factors such as smoking, alcohol consumption, infection with the Helicobacter pylori, and obesity have been recognized as the risk factors.[5, 13] These factors alone cannot account for the high rates of affliction with this disease, and hereditary risk factors must be taken into account, too. Some studies have reported that people with a familial background of cancer development are 1.5 to 3.5 times more likely to develop gastric cancer.[14]

Given the fact that various studies have emphasized the role of familial backgrounds of cancer as an important risk factor in the development of gastric cancer, and since the studies carried out in Iran in this regard have been limited in number,[15] the present study was conducted with the objective of studying the relationship between the development of gastric cancer and the presence of a familial background of digestive tract cancers among the first-degree relatives of the participants in Khorramabad, Iran.

Methods

In the present case-control research, all the patients who had referred to the Shohada Ashayer Hospital and a digestive tract sub-specialist's office in Khorramabad in 2012 and had been diagnosed with gastric cancer via endoscopy and pathological studies were enrolled in the study. In the present research, only patients residing in Khorramabad and its suburban areas were studied. The census taking sampling method was used. 84 patients diagnosed with gastric cancer were selected as the volume of the sample. The control group that matched the experimental group in terms of age and sex were selected from among those referring to the ophthamological and dermatological clinics of the Shohada Ashayer Hospital, provided that they had no backgrounds of chronic physical and mental illnesses.

The data collection instrument used in this study was a questionnaire that included items related to the demographic information of the patients, and also questions regarding the patient's background as to smoking, alcohol consumption, drug and narcotic abuse, and the cancers of the upper and lower digestive system among first-degree relatives. The same data were collected from the members of the control group. All the diagnostic studies for the diagnosis of the disease were carried out by a digestive tract sub-specialist.

All patients signed written consents regarding their participation in the study. The data were analyzed using SPSS19. Descriptive statistical methods, the Chi-square test, and the Fisher's exact test, were used. In order to determine the intensity of the relationship between familial backgrounds of upper and lower digestive tract cancers and the development of gastric cancer, the odds ratio estimate was used with a confidence interval of 95%. Additionally, multivariate analysis (logistic regression) was used to determine the significance levels of the relationship of variables which had shown a significant relationship in bivariate analysis.

Results

In the present research, 84 patients suffering from gastric cancer and 84 people in the control group were studied. The mean age of the patients was 65.4±10.7 and the mean age of the control group members was 63.3±11.3. No significant difference was observed between the patients and the control group in term of mean age (P_value=0.71). The youngest patient was 40 years old and the oldest was 88 years old. 64.3% of the patients were male and 35.7% were female, while the same figures in the control group were 61.9% and 38.1% respectively. The sex ration (male over female) of the patients suffering from gastric cancer was 1.8 over 1. 81% percent of the patients were married and 44.1% percent of them were illiterate. 51.7% of the patients were city dwellers. The frequency distribu-

tion of the demographic characteristics of the patients and the control group is presented in **Table 1** in detail. 23.8 percent of the patients reported a background of smoking, the same figure in the control group being 10.7 percent. Based on the Chi-square test, this difference was statistically significant (P_value=0.025). Additionally, 11.9 percent of the patients had background of narcotic use, and the same figure was 3.6 percent in the control group. This difference was significant, too (P_value=0.043). The part of the stomach in which the most cases of gastric tumor were observed was the cardia (21.4%) (**Table 2**). The highest occurrences of the tumors based on type belonged to adenocarcinomas (92.8%), GIST tumors (4.8%) and lymphomas (2.4%) as determined by the pathological studies. Additionally, most cases of adenocarcinoma were of the intestinal type. Two patients reported having suffered other forms of cancer previously (2.4%). The main objective of this study was to investigate the relationship between gastric cancer and having a familial background of superior and inferior digestive tract cancers among

first-degree relatives and to determine the intensity of this relationship. In this regard, 12 patients (14.3%) reported a familial background of gastric cancer among their first-degree relatives (**Figure 1**). The same figure in the control group was 3 cases (3.6%) and based on the Chi-square test, this difference was statistically significant (P_value=0.015). The intensity of the relationship was determined using the odds ratio, which was calculated to be 4.5 (CI=2.2-8.1) (**Table 3**). 40% of the gastric cancers in the first-degree relatives, was reported to have occurred in the patients' brothers.

5 patients (6%) reported that one of their first-degree relatives had suffered from esophageal cancer. This figure in the control group was 2 (2.4%). Based on the Fisher's exact test, this difference was not statistically significant (P_value=0.24) (**Table 4**).

Finally, 10 patients (11.9%) reported a background of colon cancer among their first-degree relatives (**Figure 2**). The same figure was 2 (2.4%) in the control group. There was observed a significant difference between

Table 1. Frequency distribution of the demographics of the patients and the control group.				
Type of variable		**Patients n (%)**	**Control group n (%)**	**P value**
Age groups	40-59	22 (26.2)	18 (21.4)	
	60-79	56 (66.7)	63 (75)	0.37
	>80	6 (7.1)	3 (3.6)	
Sex	Male	54 (64.3)	52 (61.2)	0.74
	Female	30 (35.7)	32 (38.1)	
Marital status	Married	68 (81)	73 (86.9)	0.61
	Single	16 (19)	11 (13.1)	
Educational attainment	Illiterate	37 (44.1)	30 (35.7)	
	Junior high school or less	34 (40.5)	41 (48.8)	
	High school or High school diploma	8 (9.5)	9 (10.7)	0.32
	University	5 (5.9)	4 (4.8)	
Occupation	Office employee	2 (2.4)	3 (3.6)	
	Laborer	4 (4.8)	6 (7.2)	
	Self-employed	20 (23.8)	23 (27.4)	
	Unemployed	10 (11.9)	13 (15.5)	0.16
	Housewife	30 (35.7)	28 (33.3)	
	Farmer or Stockbreeder	18 (21.4)	11 (13)	
Place of residence	Urban areas	48 (57.1)	56 (66.6)	0.48
	Rural areas	36 (42.9)	28 (33.4)	

Table 2. Frequency distribution of the anatomical position of the gastric cancer in the studied patients.

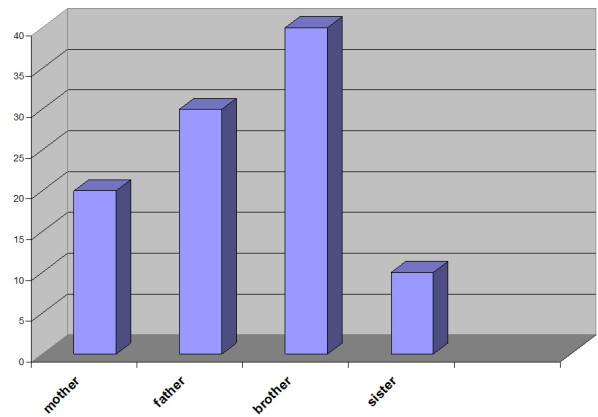| The anatomical position of the tumor	Absolute frequency (number)	Relative frequency (percentage)
Cardia	18	21.4
Cardia and fundus	10	11.9
Cardia and lesser curvature	2	2.4
Lesser curvature	8	9.5
Body and antrum	10	11.9
Lesser curvature and antrum	4	4.8
Antrum	16	19
Antrum and pylorus	12	14.3
Pylorus	4	4.8
Total	84	100

Figure 1. Frequency of gastric cancer among the first-degree relatives of gastric cancer patients.

Table 3. A comparison of the frequency of the familiar history of gastric cancer among the first-degree relatives of the patients and members of the control group.

Study groups	Familial background of gastric cancer					
	Positive n (%)	Negative n (%)	Sum n (%)	P-value	OR	95% Confidence Interval
Patients	12 (14.3)	72 (85.4)	84 (100)	0.015	4.5	2.21-8.16
Control group	3 (3.6)	81 (96.4)	84 (100)			

Table 4. A comparison of the frequency of the familiar history of esophageal cancer among the first-degree relatives of the patients and members of the control group.

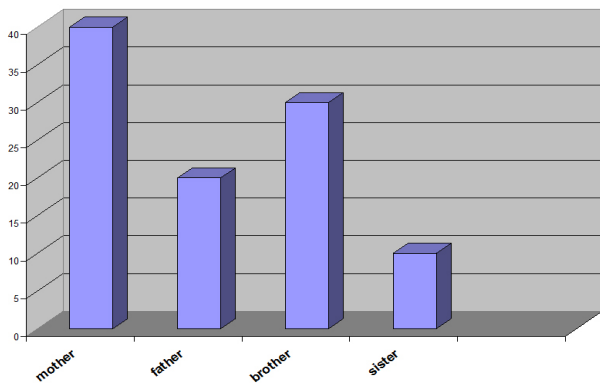| Study groups	Familial background of esophageal cancer					
	Positive n (%)	Negative n (%)	Sum n (%)	P-value	OR	95% Confidence Interval
Patients	5 (6)	79 (94)	84 (100)	0.24	3.96	0.48-7.61
Control group	2 (2.4)	82 (97.6)	84 (100)			

Figure 2. Frequency of colon cancer among the first-degree relatives of gastric cancer patients.

the two groups based on the Fisher's exact test (P_value=0.017) (**Table 5**). Most cases of colon cancer (50%) had reportedly occurred in the mothers of these patients.

The relationship between the occurrence of gastric cancer (P_value=0.034) and colon cancer (P_value=0.047) among first-degree relatives and the occurrence of gastric cancer in the patients themselves was shown to be statistically significant using a multivariate analysis (logistic regression, Enter method), and having factored out the effect of other variables such as age, sex, occupation, a history of smoking, and using narcotics.

Table 5. A comparison of the frequency of the familiar history of colon cancer among the first-degree relatives of the patients and members of the control group.

Study groups	Familial background of colon cancer					
	Positive n (%)	Negative n (%)	Sum n (%)	P-value	OR	95% Confidence Interval
Patients	10 (11.9)	74 (88.1)	84 (100)	0.017	5.54	2.11-10.81
Control group	2 (2.4)	82 (97.6)	84 (100)			

Discussion and Conclusion

In the present research, 84 gastric cancer patients who had referred to the Shohada Ashayer Hospital during one year were studied. Given the fact that the afore-mentioned hospital is the only center providing digestive tract sub-specialty services, this study can provide valuable information regarding the epidemiology of gastric cancer, the relationship between the occurrence of gastric cancer and familial backgrounds of digestive tract cancers, and age distribution of the patients as risk and susceptibility factors for gastric cancer.

In terms of sex, this study like other studies[14, 16, 17] showed that this disease is more prevalent among males and the male to female ratio among the patients was 1.8. The findings of the present study indicated that the age distribution of gastric cancer in the Lorestan province is similar to that of European and North American countries. The results of the studies conducted in these countries and in different areas of Iran suggest the prevalence of this disease in the seventh and eighth decades of life.[1-3, 17]

This study showed that the single most affected area of the stomach was the cardia in most patients. Some studies during the 1960s, 80s and 90s indicated that the distal areas of the stomach were most affected[18-20] by this type of cancer, while recent studies suggest more proximal involvement,[21, 22] which support the findings of the present study.

In the present study, 14.3 percent of the patients mentioned a history of gastric cancer among their first-degree relatives, the same figure being 3.6 percent among the members of the control group. The likelihood of the development of gastric cancer was 4.5 times higher among people with a familial history of gastric cancer. This issue indicates that genetic factors, together with envi-

ronmental factors, can contribute to the development of colorectal cancers. In other words, familial history can be considered as the key in identifying susceptible individuals. Many studies have shown the presence of the link between genetic factors and the incidence of gastric cancer.[23, 14]

Moreover, this study demonstrated the presence of a significant relationship between a history of colon cancer among first-degree relatives and the occurrence of cancer. This finding matches the results of the study conducted by Amundadottir et al[24] in Italy. Other studies carried out all over the world indicate the existence of a significant relationship between the occurrence of gastric cancer and a familial background of colon cancer.[14, 23, 25] These differences may be explained by the differences between the research methods. In fact, the study of familial backgrounds using the patients' or control group self-reports may have some faults and imperfections. This issue suggests the necessity of more comprehensive investigations using genetic tests.

The findings of the present study also point out that there is no significant relationship between a familial history of esophageal cancer among the first-degree relatives and the incidence of gastric cancer. These findings correspond with the results of other studies.[14, 23, 24] Of course, lack of a statistically significant relationship between gastric cancer and a familial history of esophageal cancer cannot negate the possibility of the existence of a genetic link between these two types of cancer (gastric and esophageal). In order to further support the above findings, more studies need to be conducted on a wider scale.

Therefore, given the relationship between a familial history of digestive tract cancers and the incidence of gastric cancer, the importance of screening with the objective of early identification of malignancies and the prevention of the progress of diseases becomes increasingly clear. Screening patients and healthy individuals requires fol-

lowing specific guidelines, some of which will be mentioned below:

1. Screening should not have any complications and side-effects.

2. It must be easy to use in healthy individuals.

3. The number of false negatives and positives must be low.

4. It should be cost-effective.

5. It should be socially acceptable.

6.It should be accepted by people who undergo screening.

Acknowledgments

Conflict of interests

The authors declare no conflict of interests.

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