

Study of Risk Factors for Esophageal Cancer in Khorramabad City From 2012 - 2014

Soroush Shamsifar,¹ Saba Sepahvand,^{2,*} Sadegh Rezapour,³ and Mahin Adeli⁴

¹Student Research Committee, Department of Medical, Medical School, Lorestan University of Medical Sciences, Khorramabad, IR Iran

²Department of Nursing and Midwifery, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, IR Iran

³Department of Medical, Lorestan University of Medical Sciences, Khorramabad, IR Iran

⁴Department of Biostatistics and Epidemiology, School of Health Sciences, Lorestan University of Medical Sciences, Khorramabad, IR Iran

*Corresponding author: Saba Sepahvand, Department of Nursing and Midwifery, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, IR Iran. Tel: +98-336638220, E-mail: Sabasepahvand92@gmail.com

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Abstract

Background: Esophageal cancer is of major concern worldwide, ranking sixth as the most common cause of cancer mortality. Lifestyles such as cigarette smoking, alcohol consumption, and poor dietary habits have been suggested to be associated with the carcinogenesis of esophageal cancer.

Objectives: This study aimed to determine the factors affecting and associated with esophageal cancer in Khorramabad city from 2012 to 2014.

Patients and Methods: This is an analytical study of 48 patients with esophageal cancer, including 80 controls. The patients were selected on the basis of a census. The data were collected using a questionnaire, and Chi-square, t-test, and one way ANOVA analyses were performed using SPSS 19.

Results: In this study, 57.8% males and 42.2% females participated, while the mean age of the patients was 68.46 years old, and the mean age of the healthy individuals was 59.79 years old. The findings of this study showed a family history of cancer, anemia, and smoking, and associations with education, occupation, socioeconomic status, blood group, consumption of hot drinks, as well as a history of gastroesophageal reflux. In addition, there was a significant relationship, but no significant association, between alcohol consumption and esophageal cancer.

Conclusions: According to the results of this study, the necessary measures to modify the risk factors, such as educational programs and changing food consumption patterns in the subjects, are effective, and can reduce the risk of esophageal cancer.

Keywords: Esophageal Cancer, Risk Factors, Khorramabad

1. Background

Today, cancer is considered to be one of the major health problems worldwide, and the importance of this disease in our country has been growing daily. Cancer is the third most common cause of mortality, and accounts for the second largest group of non-transmissible chronic diseases (1).

Two major histological types of esophageal cancer have been defined: esophageal squamous cell carcinoma (ESCC) and esophageal adenocarcinoma (EAC). While EAC has emerged as the major type in some Western countries, in Asia, ESCC is the predominant type, while EAC remains rare (2).

The so-called "Asian esophageal cancer belt" encompasses areas such as Turkey, Iran, and Kazakhstan, as well as northern and central China, with an estimated esophageal squamous carcinoma rate of more than 100 cases/100,000 people per year. Another area with a high incidence

of squamous cell carcinoma is southeastern Africa, with rates similar to those observed in Eastern countries. In the United States, from 1975 to 2004, the age-adjusted incidence in white males has increased from 5.76 to 8.34 cases/100,000 people per year at the expense of the adenocarcinoma histological subtype. Nevertheless, squamous carcinoma remains the most common subtype in American black males; however, adenocarcinoma is one of the few cancers that contributes to increased mortality from cancer among all American men (3).

The alarmingly high incidence of ESCC and its equal sex distribution in Iran highlights the likelihood of a very strong environmental risk factor as the main culprit (4). Gross nutritional deficiencies and unbalanced diets have long been suspected to play roles in ESCC risk, particularly in high-risk regions of the world where tobacco smoking and alcohol consumption are not very common (5, 6). Several studies have evaluated the effects of micronutrients, such as beta-carotene, folate, vitamin C, and vitamin E, on

the risk of ESCC (7, 8).

Factors that increase or decrease the EC risk include bad habits (tobacco use, alcohol consumption, opium consumption, drinking yerba mate, consumption of hot drinks, consumption of carbonated soft drinks, and eating pickled vegetables), nutritional deficiencies (low intake of fresh fruit and vegetables, and vitamin and mineral deficiencies), medications (non-steroidal anti-inflammatory drugs, medications that relax the lower esophageal sphincter, and H₂ receptor antagonists), infections (*Helicobacter pylori* and human papillomavirus), chemical carcinogens (polycyclic aromatic hydrocarbons, nitrosamines, and acetaldehyde), physiological or pathological predisposing conditions (gastroesophageal acid reflux, hiatal hernia, achalasia, gastric atrophy, and poor oral health), occupational exposure (silica and asbestos), and low socioeconomic status (9).

Epidemiological studies in Western countries have shown that smoking and alcohol consumption are important risk factors for esophageal cancer in low incidence areas. A relatively recent nested case-control study with large samples in Linxian (China) showed different results: tobacco smoking was associated with a significantly elevated risk, with a two-fold increase among long-term smokers. Evidence from Shanghai (East China) showed that smoking and alcohol consumption contributed to the risk of esophageal cancer, and a study in the Chaoshan area (South China) found fermented fish sauce to be an important risk factor (10).

Because early detection increases the survival rate and reduces the cost of treatment, it should be possible to prevent and avoid the risk factors for these cancers, as well as provide a timely diagnosis of its causes. Therefore, this study aimed to determine the prevalence of risk factors for esophageal cancer in Khorramabad city.

2. Objectives

The aim of this study was to determine the effects of the risk factors on patients with esophageal cancer.

3. Patients and Methods

This descriptive-analytical study was conducted to assess the impact of risk factors on esophageal cancer in the city of Khorramabad, from 2012 to 2014. The studied population was comprised of all of the patients admitted to the hospitals of Shohada-ye-Ashayer, Shahid Rahimi, and Tamin-e-Ejtemaee, and the pathology laboratories of Khorramabad city that detected their esophageal cancers by conducting pathological assessments from 2012 until 2014.

The control subjects were randomly selected from patients without esophageal cancer admitted to the hospitals of Shohada-ye-Ashayer, Shahid Rahimi, and Tamin-e-Ejtemaee. Finally, 48 cases and 80 controls were studied, adding up to 128 samples living in Khorramabad city and its suburbs. The objective and purpose of this study was explained to the participants after obtaining their written consent, and they were informed that the questionnaires would remain anonymous and completely private. The data on the questionnaire was collected by interview, and included the demographic data (age, sex, education level, occupation, history of smoking, economic status, family history of cancer, alcohol consumption, history of anemia, consumption of hot drinks, and gastroesophageal reflux) and the food frequency questionnaire (FFQ) from the nutrition society of Iran, which has had its validity and reliability confirmed to assess the food habits and consumption of the participants. The questionnaire included 69 types of food, with the serving sizes, which are usually consumed by Iranians. The subjects were asked to report the rate of consumption of each type of food, as well as the frequency of their consumption with regard to the number of days, weeks, and months in the last year. The data were analyzed after the completion of the sampling and coding, and the final data were analyzed using SPSS 19. The descriptive statistics, including the frequency tables, graphs, frequency, mean, and standard deviation, were used to analyze the data, and the K-square statistical test was used to evaluate the relationship between the quality of the independent variables and prevalence of esophageal cancer. The independent t-test or one-way analysis of variance (ANOVA) was carried out to assess the relationship between the quantitative independent variables and the occurrence of esophageal cancer.

4. Results

A total of 48 cases and 80 controls were investigated in this study. The mean ages of the patients and controls were 68.46 and 59.79 years old, respectively. Out of 128 samples, 57.8% were male and 42.2% were women, while most of the participants were married. In this study, the majority of the patients lived in the village (plain), while the non-patients lived in the urban areas. In addition, 62.5% of the patients had weak economic situations, while the majority of the non-patients (60%) enjoyed moderate economic situations. Moreover, 62.5% of the cases and 17.5% of the controls had a history of smoking, while 4.2% of the patients and 2.5% of the non-patients were alcohol consumers. However, there was no significant relationship between the risk of esophageal cancer and alcohol consumption. The results showed that 52.08% of the patients had a

history of anemia, but in the control group, 20% reported a history of anemia. This finding indicates that anemia was more prevalent in the patient group.

Of the patients, 83.33% consumed hot drinks, while in the control group, 16.67% consumed hot drinks, and these results showed a significant correlation between the consumption of hot drinks and esophageal cancer. Moreover, the results showed that 52.08% of the patients had a family history of cancer, of which 25% had a family history of upper gastrointestinal cancer, which reflects the positive impact of genetic factors on esophageal cancer. Furthermore, 77.08% of the patients reported a history of gastroesophageal reflux, and in the control group, 12.5% had a history of gastroesophageal reflux; thus showing a significant relationship between the risk of esophageal cancer and the history of gastroesophageal reflux. All of the risk factors affecting esophageal cancer can be seen in [Table 1](#).

Table 1. Risk Factors of Esophageal Cancer^a

Risk Factors	No	Yes
History of anemia		
Case	23 (47.92)	25 (52.08)
Control	64 (80)	16 (20)
History of GERD		
Case	11 (22.92)	37 (77.08)
Control	70 (87.5)	10 (12.5)
Family history		
Case	23 (47.92)	25 (52.08)
Control	62 (77.5)	18 (22.5)
History of smoking		
Case	18 (37.5)	30 (62.5)
Control	66 (82.5)	14 (17.5)
Hot drink		
Case	8 (16.67)	40 (83.33)
Control	72 (90)	8 (10)

^aValues are expressed as No. (%).

The type of pathology in the case group was 46.6% squamous cell carcinoma (SCC) and 35.5% adenocarcinoma (AC), showing a higher prevalence of SCC. The tumor location of 50% of the patients was in the middle, 14.6% in the upper, and 35.4% in the lower part of the gastroesophageal region, which shows a higher incidence of tumors in the middle region. Moreover, the food pattern was different between the two groups, and there was a significant relationship between the risk of esophageal cancer and an individual's diet, using a significance level or inde-

pendent t-test of $P < 0.001$. The mean and standard deviation of the dietary patterns in the two groups are shown in [Table 2](#).

5. Discussion

The findings of this study showed that there are significant relationships among the level of education, employment, economic status, and an increase in the esophageal cancer risk. In this study, most of the patients were unemployed, illiterate, and had a poor economic status, which indicates that this disease exists at a higher rate in the lower socioeconomic groups. The results obtained are in agreement with the findings of other countries, which also show that poor socioeconomic status is a risk factor for esophageal cancer (11).

It has long been known that EC is a disease of poor and socially disadvantaged people. In his 1939 paper, Watson wrote, "... it should be noted that a large percentage of the patients in this series [of 771 EC cases] are of the station in life that is definitely below average, and further, that 9 out of 10 patients with this disease are in the lower middle class socially, and on the whole financially insecure" (12). Since then, a large number of epidemiological studies have confirmed that the risk of EC is higher in populations with lower socioeconomic status (SES) (13-19).

In the US, a correlation between the SES of patients and the histology of esophageal cancer has been demonstrated. Those patients with a higher SES had a higher incidence of esophageal adenocarcinoma, whereas the squamous cell carcinoma was more frequently found in those patients with a lower SES (16). The results of Nourafkan et al. (20), as well as Azami et al. (21), confirm these findings. It seems that a high SES can have a significant impact on the access level of healthcare services, as well as an increased level of public health.

In this study, the patients had more positive family histories when compared to the non-patients. In a number of books and scientific articles, a family history of the development of many diseases, including cancer, and in particular esophageal cancer, is cited as a risk factor (22). Studies conducted in China and Iran have shown that the affliction risk of SCC in the close relatives of patients with esophageal cancer is more than double those who have no family history of esophageal cancer (9).

The results also showed that there is a significant relationship between the consumption of hot drinks and the risk of esophageal cancer, and this association has been reported in several studies conducted in different parts of the world (5, 23-27). In addition, several previous studies have assessed the temperature preferences for beverages, and those from the United Kingdom have reported

Table 2. The Mean and Standard Deviation of the Dietary Pattern in the Two Groups

Group	Number	Average	Standard Deviation	P Value
Food pattern				< 0.100
Case	48	117.75	8.36	
Control	80	109.51	9.54	

an average temperature preference of 56 - 60°C among healthy populations (28-33). Another study reported a significantly higher tea drinking temperature in seven participants with esophageal disorders (mean 62°C, range 53 - 73°C), compared to 50 controls (mean 56°C, range 47.5 - 65°C, $P < 0.001$) (29). Another study reported a mean temperature of 69.5°C (SD 6.5°C) for drinking yerba mate among 1,388 inhabitants in southern Brazil, a moderate to high incidence area for esophageal squamous cell carcinoma (30). Case-control studies in Iran (14) and Singapore (34) have shown that drinking tea and coffee raises the risk of esophageal cancer. In addition, based on the latest case-control study conducted in Gonbad-e Qabus (Iran), one of the most important causes of esophageal cancer is the consumption of very hot tea, which increases the risk of esophageal cancer to 10% (35).

In addition, the results of this study showed that there is a significant relationship between smoking and the risk of esophageal cancer. Based on the available resources, among those people who regularly smoke, the risk of esophageal cancer increases 6.2 times (36). However, no significant relationship was found between alcohol consumption and esophageal cancer, indicating that these findings are consistent with the study of Azami et al. (21). The results of Navarro Silvera et al. investigation in the United States demonstrated the effects of smoking, wine, age, and income on developing this type of cancer (37). Moreover, the Hajian et al. study conducted in Babolsar, a northern city of Iran, showed a 19.3% positive smoking history, but only 7.9% were addicted (38). Overall, tobacco smoking and the consumption of alcohol are strongly associated with SCC and, to a lesser degree, with adenocarcinoma of the esophagus. Fortunately, alcohol consumption is not popular in Iran due to the religious beliefs of the people; however, smoking and drug abuse are most likely the important factors in this regard. As reported by Heeyng Kimm et al. in Korean men, alcohol and smoking are incidentally associated with an increased esophageal cancer risk, but they do not interact synergistically (39). In a study conducted by Vioque et al. in Spain, the consumption of alcohol and tobacco were both strong and independent risk factors for esophageal cancer. We found that heavy drinkers had a higher risk than heavy smokers, par-

ticularly for the esophageal SCC (40).

Our research showed a significant relationship between the history of gastroesophageal reflux and esophageal cancer. Rashidkhani et al. reported that a history of reflux symptoms was shown to be a risk factor for esophageal cancer (41). In a cohort study carried out by Pourshams et al. in northeast Iran, complaints of gastric esophageal reflux disease were widespread in the participants during the preparatory phase, and 31% of them complained of this problem at least once a week (42). The role of weekly symptoms of gastroesophageal acid reflux has also been confirmed as one of the major causes of esophageal cancer in northwest Iran (Ardabil) (43). Additionally, the study by Navarro Silvera et al. carried out in the United States also confirmed a strong correlation between esophageal cancer and the frequency of reported gastroesophageal reflux (GERD) (37).

Symptomatic gastroesophageal acid reflux is perhaps the strongest known risk factor for EAC. In a population-based case-control study from Sweden, Lagergren et al. showed a strong dose-response association of both the frequency and duration of reflux with EAC. In this study, any reflux was associated with an approximately 8-fold increase in risk, but the risk was increased up to 20-fold in those with very frequent and severe reflux (44). Several other studies published since then have confirmed a dose-response association between reflux and EAC (45-48).

In this study, the most common SCC tumors were in the middle one-third of the gastroesophageal region. The results of Azami et al. (21), Abdollahian et al. (49), Shhryary et al. (50), and Jan et al. (51) were largely consistent with our findings. Most of the studies, if not all, were performed in Asia, where the incidence of SCC is high (52). Esophageal SCC is the predominant histological subtype in Asia, while the incidence and mortality are higher in China than in Japan (2).

Moreover, our study results showed that the dietary patterns were different in each group, and that those dietary patterns have contributed to the development of esophageal cancer. This finding is consistent with the results of Rashidkhani et al., which also show a relationship between the dietary patterns and cancer of the esophagus (41). The research of Hu that was published in Sweden (53)

and a study carried out by Chen et al. both reported a relationship between dietary patterns and esophageal cancer (54). In a prospective study conducted by Malekshah in Golestan (Iran), a dietary role was confirmed (55) in the risk of esophageal cancer.

Interestingly, an evidentiary review by the World Cancer Research Fund and the American Institute for Cancer Research (WCRF-AICR) identified 4 cohort studies (all from China), 36 case-control studies, and 7 ecological studies on the associations between fruit intake and EC (56).

According to the results of this study, measures to modify the risk factors, such as educational programs and changing food consumption patterns, in those subjects at risk are effective, and can reduce the incidence of esophageal cancer. Moreover, the government and public media must provide more information to increase people's knowledge about esophageal cancer, especially about the signs and symptoms, as well as the needs of people with esophageal cancer as human beings.

There were some limitations in this study. For example, there was a lack of access to those patients who died, and a number of patients were not available for interviews due to the severity of the disease.

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Footnotes

Authors' Contribution: Study concept and design: Saba Sepahvand, Soroush Shamsifar, and Sadegh Rezapour; data gathering: Saba Sepahvand and Soroush Shamsifar; data analysis: Saba Sepahvand, Soroush Shamsifar, and Mahin Adeli; critical revision: Saba Sepahvand, Soroush Shamsifar, and Sadegh Rezapour; manuscript preparation: Saba Sepahvand.

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