

Esophageal Cancer in Northeast of Iran

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Background: Esophageal cancer is the 7th most common cancer in Iran. The northern part of the country shows the highest incidence for this malignancy. In this study we present some epidemiological and clinicopathological characteristics of patients with esophageal carcinoma in this region.

Methods: In a cross sectional study, 238 Esophageal cancer patients were enrolled in a prospective study of neoadjuvant chemo-radiation treatment in a 4-year period (2006- 2009). In an oncology clinic their epidemiologic characteristics and clinicopathological findings were registered in a preplanned file. Data consisted of age, sex, race, occupation, residential location, smoking, addiction history, signs and symptoms, blood biochemistry profile, imaging and endoscopic findings. The data were analyzed with the SPSS software.

Results: The mean age of the patients was (55% female) 59 years. They were mostly Fars (63%) and Turkmen (13%). Seventy two percent were residents of rural area, 20% were smokers and 22.3% were opium addict and its analogues. Only 1.3% of patients consumed alcohol. The most common presenting symptom was dysphagia (93.7%), mainly grade III dysphagia (53%). Location of tumor in esophagus was in the middle third in 53.4% and lower segment in 44.5%.

Sixty five percent of the patients had an abnormal esophagogram. On endoscopic evaluation the most common types of tumors were polypoid, vegetative and fungoid, respectively. Mean tumor length was 5.7 cm. The most common histology type was squamous cell carcinoma (99.1%) which was moderately differentiated in 51.3% of these patients. No significant relationship was found between the grade of dysphagia with the macroscopic type and the pathologic grade of the tumor in this study.

Conclusion: Squamous cell carcinoma comprised more than 99% of all esophageal cancers in our patients and this histological type is the prominent type in the Northeast of Iran. Middle esophageal segment is the major site for this type of cancer which unfortunately most patients present with grade III. Dysphasia reflects the advanced stage of the disease.

Key Words: Esophageal neoplasm; Epidemiology; Iran

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Introduction

Esophageal cancer is the 7th most common cancer in Iran [1] and it also is among the ten most common cancers in the world [2]. It includes 1% of all malignancies and 6% of gastrointestinal malignancies worldwide [3]. It ranks as the sixth leading cause of cancer-related death [4]. Iran is a well-known region with a high prevalence for this cancer, mostly from the North and North East of the country [3].

In the national report of the registered cancer cases in Iran in 2007, esophageal cancer with an incidence rate (ASR) of 6.4% stood for the 7th most common cancer. Esophageal cancer is the 7th leading

cause of cancer related death in Iran and has the 7th highest Disability-Adjusted Life Years (DALYs) among all cancers in Iranian population which had been estimated to be about 15920 years in year 2002 [5]. Its prevalence is increasing as the population is getting old; its highest incidence rate is around the age of 60-80 [1]. However, according to a report by Yavari and et al. Iran's highest incidence was between the age of 50 and 70 based on their studied population [6]. Its prognosis is usually undesirable and median survival after esophagectomy for patients with localized tumor is 15-18 months, and 5-year survival rate is 20-25% [7].

The risk of esophageal cancer increases with constant exposure to stimulants, hot beverages, alcohol and smoking. It has a higher incidence rate in society with a low economical state, severe malnutrition, low vitamin, fruit and vegetable intake and also high consumption of alcohol and cigarettes. The unchangeable factors in this cancer include age, sex and hereditary background. In various studies conducted in China, relative risk of patients with a family history of esophageal cancer was around 2.9% of cases [8]. Its prevention is based on early diagnosis, special attention to modifiable risk factors, particularly tobacco, alcohol and fast food consumption.

The symptoms of esophageal cancer usually appear 3 to 4 months prior to diagnosis and such symptoms vary depending on initial involved segment of esophagus. Dysphagia is seen in more than 90% of cases while a weight loss over 5% of body weight occurs in 5% and its presence is associated with a worse prognosis [3]. Less common symptoms such as hoarseness, cough and progressive lesions with invasion to other organs result in symptoms such as hematemesis, hemoptysis, dyspnea and cough secondary to bronchoesophageal and tracheoesophageal fistula. Considering most studies on statistic for epidemiologic indexes in esophageal cancer are implemented in other parts of the world, we aim this study which is to determine epidemiologic index of esophageal cancer patients provides better information on epidemiological characteristic of such cases and also a reliable base for future complementary studies.

Materials and Methods

This is a cross-sectional prospective study based on medical history and other collected data from 238 esophageal cancer patients referred to Omid hospital between 2001 and 2010.

The criteria consisted of: 1. No distant metastases, 2. A Karnofski score of 70 and over for the performance status. At the beginning of study, informed consent was obtained from patients for neoadjuvant chemoradiation treatment.

The collected data included age, sex, race, occupation, residential location, addiction history, alcohol and smoking habits, dysphagia grading (I, II, III, IV, V), weight loss, nausea and vomiting, lack of appetite and paraclinic tests: CBC, liver function tests, sonography or CT scan of abdomen, barium swallow and also anatomic location of tumor, lesion type in endoscopy, lesion length and also type and grade of tumor pathology. All data were analyzed by the SPSS software, version 16.

Results

The mean age of the studied cases was 59 years. Twenty two point three percent of patients were younger than 50 years and 77.7% were older. Forty five percent were male and 55% female. Regarding the race, 63% were Fars, 13% were Turkmen and 24% were from other ethnic groups. Regarding the occupation, 30% were farmers, 45% were housewives and 25% had other jobs; they came mostly (72.3%) from the rural areas. Twenty percent (33.3% of males and 8.5% of females) had a history of smoking, 22.3% (31.5 of males and 14.6% of females) were addicted and 1.3% of patients had alcohol consumption (Table 1).

The most common anatomical site was the middle (53.4%), lower (44.5%) and upper (2.1%) segment of esophagus (Table 2). Considering clinical signs and symptoms, most patients (93.7%) complained about dysphagia over an average duration of 3.4 months. Also 24%, 53% and 23% of patients had grade I and II, III, IV and V dysphagia, respectively (Table 3).

Amongst patients whom their clinical symptoms were registered completely, 84% had weight loss i.e. 21% (1-5Kg), 17% (5-10Kg) and 16% more than 10Kg. Degree of weight loss was not precisely measured in 30% of patients. Nausea was recorded in 39% and vomiting in 27.7%. Before treatment, anemia, leukopenia and thrombocytopenia were detected in 39%, 2.1% and 0.6% of cases, respectively (Table 3). In addition 1.8% had abnormal liver function tests. Barium swallow results were abnormal in 65.5% and normal in 6.4%; it was not performed in 28.1% of cases. At the beginning of the study, all patients had an abdominal sonography with no metastases.

On endoscopy, 51.3% of lesions were polypoid, vegetative and fungoid while in 48.7% were ulcerative, ulcerovegetative and infiltrative. The mean lesion length according to endoscopy and barium swallow was 5.7cm; the tumor length was less than 5cm in 52.5% and more in 47.5% (Table 2).

The most common pathology was squamous cell carcinoma with 99.1% prevalence. According to tumor grading, 34.2% were well differentiated, 51.3% were moderately differentiated and 14.5% were poorly differentiated (Table 3).

Discussion

In this prospective cross sectional study, epidemiologic status of esophageal cancer was evaluated in a specific area i.e. the Northeast of Iran and cases were selected from patients who were referred to Omid hospital for undergoing

Table 1. Frequency and percentage of age, sex, race, living place, smoking, opium addiction

Patients demographic characters	Incidence(percent)	
Age	Under 50 year	53(22.3)
	Over 50 year	185(77.7)
	Total	238(100)
Sex	Male	108(45.4)
	Female	130(54.6)
	Total	238(100)
Race	Fars	149(62.9)
	Turkmen	31(13.1)
	Others	58(24)
Total	238(100)	
Living place	City	66(27.7)
	Village	172(72.3)
	Total	238(100)
Smoking	Yes	47(19.7)
	No	191(80.3)
	Total	238(100)
Opium addiction	Yes	185(77.7)
	No	53(22.3)
	Total	238(100)

Table 2. Incidence and percentage of lesions' types in endoscopy, site of tumor in mediastinal esophagus, length of lesion, pathology and tumor grade.

Patients pathology	Incidence(percent)	
Type of the lesion in endoscopy	Polypoid, vegetative, fungoid	122(51.3)
	Ulcerative, ulcerovegetative, infiltrative	116(48.7)
	Total	238(100)
Site of tumor in mediastinal esophagus	Upper	5(2.1)
	Middle	127(53.4)
	Lower	106(44.5)
	Total	238(100)
Tumor length	Less than 5 cm	125(52.5)
	More than 5 cm	113(47.5)
	Total	238(100)
Tumor pathology	SCC	236(99.1)
	Adenocarcinoma	2(0.9)
	Total	238(100)
Tumor grading	Well differentiated	81(34.2)
	Moderately differentiated	122(51.3)
	Poorly differentiated	35(14.5)
	Total	238(100)

neoadjuvant chemoradiation treatment. The goal and reason for selecting this study group was to ensure that their data are usually precisely registered in the form of a protocol. The reported data in this study included:

1. Age, sex, race, location, smoking and addiction history.

2. Tumor type according to endoscopy (length and location).

3. Prevalent clinical symptoms including dysphagia (and its grade), weight loss, anemia, nausea and vomiting.

Many esophageal cancer reports belong to regions of the world where this type of cancer is considered prevalent. The incidence rate in the Northern China, Iran, and Russia and around the Caspian Sea is 100 per 100,000 populations [3]. The mean age of the patients was 59 years in our study. In recent report from CDC in Iran

Table 3. Incidence and percentage of patients' symptoms and signs

Symptoms and signs	Incidence(percent)	
Grade of esophagitis	G1 & G2	57(24)
	G3	126(53)
	G4& G5	55(23)
	Total	238(100)
Weight loss	1-5	50(21)
	5-10	40(17)
	>10 kg	38(16)
	unknown	72(30)
	No	38(16)
	Total	238(100)
Anemia	Yes	93(39)
	No	145(61)
	Total	238(100)
Nausea	Yes	93(39)
	No	145(61)
	Total	238(100)
Vomiting	Yes	66(27.7)
	No	172(72.3)
	Total	238(100)

the highest incidence of esophageal cancer occurred between the ages of 60 and 80 [1]. The mean age at the time of diagnosis in U.S. is 69 years, whereas in our study the mean age was 10 years lower. Considering that these patients were candidates for preoperative chemoradiation protocol; this difference is partially related to bias in patient selection. In another study the mean age of 190 esophageal cancer patients chosen for chemoradiation protocol, was 65 years [9].

The effect of race on the incidence rate has been investigated in several studies. In Cumings et al. study which was performed on 1801 esophageal cancer (SCC) patients in U.S, the incidence rate was 5 and 1.3 in 100,000 in both white and black population respectively. However, adenocarcinoma had a higher incidence rate amongst the whites (8 vs. 3.3 in 100,000) [10]. Despite considerable distance between our center and Golestan province, 12% of cases were Turkmens who were referred for therapy from that region. Various studies have revealed that residents who are living around the Caspian Sea are at a greater risk for developing this type of cancer [9].

Possible reasons include a diet deficient in fruits, vegetables and animal proteins as well as dry and thick bread which consists of silica fibers; hot tea, smoking, drugs and burnt opium.

Smoking, drug and alcohol consumption are the main factors causing this type of cancer in western countries. However, few studies have shown no significant correlation between such factors and esophageal cancer [9].

In the current study 19.7% of affected cases were smokers and 22.3% were drug abuser. In Hajian et al. study in Babolsar, a northern city of Iran, 19.3% had a positive smoking history but only 7.9% were addicts [11]. Smoking tobacco and drinking of alcohol are strongly associated with SCC and to a lesser degree with adenocarcinoma of esophagus. Fortunately in Iran due to religious beliefs alcohol consumption is not popular, but smoking and drug abuse are most probably important factors. As reported by Heeyng Kimm and et al. in Korean men, alcohol and smoking are indecency associated with increased risk of esophageal cancer but they do not interact synergistically [12].

Considering the characteristics of developed tumors, it should be noted that adenocarcinoma has a very small portion in comparison to SCC in esophageal tumors in our country.

The incidence rate of adenocarcinoma has increased over the past two decades in western countries and at the moment it is more common than SCC, for example only 40% of esophageal cancers in U.S. are SCC. However in some regions of the world with a high incidence rate

for this type of cancer, SCC is more prevalent than adenocarcinoma [7]. In developed countries where adenocarcinoma has drastically increased, this cancer is associated with reflux and obesity [13, 14].

Amongst our 238 cases, adenocarcinoma was found only in two cases (0.9%). Other studies in Iran have also confirmed the predominance of SCC over adenocarcinoma. According to a study reported by Farhoudi et al. 86.3 % and 7.3% of cases showed SCC and adenocarcinoma respectively [15].

Also considering that the current study was performed on patients who had undergone surgery after chemoradiotherapy, only cases with mediastinal esophagus involvement were investigated. In 53.4% of patients, tumors were localized in the middle third of esophagus and 43.3% in the lower third as described by Hajian studies [11]. In Farhoudi study in Mashhad the lower third was also considered as the most common site [15]. In the current study, the lesion types considered as effective factors of prognosis and they were polypoid, vegetative and fungoid in 51.3% as well as ulcerative, ulcerovegetative and infiltrative in 48.7% of cases.

Conclusion

In summary, SCC comprised more than 99% of all esophageal cancers in our patients and this was also the prominent type in northeast of Iran. In our patients, the middle esophagus was the major site for this type of cancer. Also most patients with grade III dysphasia reflected the advanced stage of the disease.

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Conflict of Interest

The authors have no conflict of interest in this article.

Authors' Contribution

ASA and AK designed the study, literature review and writing up process. SG analyzed the data and entering the data and contributed in writing-up process. All authors read and proved the final manuscript.

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