Original article:

Correlation between Histopathological Findings and Endoscopy in Esophageal Cance: Results in Khorramabad, Iran, Western Iran

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Abstract

Background: Esophageal cancer is a cancer arising of the esophagus and during the past two decades, the epidemiology and treatment strategies for esophageal cancer have changed markedly in the Western Iran.The aim of this study is to investigate the clinical signs, endoscopy findings, and family history of esophageal cancer in the Khorramabad, Iran. ***Methods:*** In this cross-sectional research conducted during 1 year in 2015,96 patients had been diagnosed with esophageal cancer by endoscopy and pathological findings. The data collected through a multipart questionnaire includingage, sex, marital status, education, occupation, address and ethnicity, background as to smoking, alcohol consumption and history of gastric and esophageal cancers. The data were analyzed using chi-square test or Fisher exact test. ***Results:*** According to findings of this study, the most common clinical signs in the patients were Anorexia (53.1) and Weight Loss (62.5). The most common anatomical site of tumor in male was in the distal esophagus (41.3%) and middle esophagus in female patients (32%), which was statistically significant (P=0.047). ***Conclusions:*** In this study, distal esophageal cancer was more common. Abetter identification of Effective factors on esophageal cancer would result in better control and management of this disease.

Keywords: Familial background; Esophageal cancer; Khorramabad; Iran

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Background

Cancer is adisease indicating abnormal growth of cells with the potential to attack or spread to other parts of the body[1]. In 2015, circa 90.5 million people had cancer[2]. About 14.1 million new cancer cases occur in a year (not including skin cancers other than melanoma)[3]. It causes about 8.8 million deaths (15.7%) of total human deaths[2]. Esophageal cancer is a cancer occurs in esophagus the food pipe creation cancer between the throat and the stomach [4]. Clinical symptoms often include dysphagia and weight loss. Other symptoms may involve odynophagia, a hoarse voice, enlarged lymph nodes around the collarbone, dry cough, and possibly coughing up or hematemesis[5]. The two major subtypes of the cancer are squamous-cell carcinoma (SCC) and esophageal adenocarcinoma (EAC) that, spread across the world[6]. A number of less common types also occur[5]. SCC occurs from the epithelial cells that line esophagus[7]. Since 2012, esophageal cancer was the eighth most common cancer globally with 456,000 new cases per year[8]. Iran is one of the known regions with a high occurrence of esophageal cancer. Most of the patients in Iran have been reported from the north and northeast areas of the country. In one of the studies by the Iran Cancer Institute, 9% of all cancers

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and 27% of gastrointestinal cancers were esophageal carcinomas. Sex ratio (Male/Female) was 1.7/1. The distal site of esophagus is involved more often than the other parts[9]. Rates of esophageal cancer vary widely across countries, with about half of all cases occurring in China. It is more common in men than in women[7]. It generally occurs in fairly poor people, which often causes latediagnosis[9]. Five-year survival rates are around 13% to 18 %[9].Since cancers constituted the most serious health issue in the worldand also the Epidemiological and Environmental specifications of the disease are different in a geographical regions, this study can give us information for screening programs and providing early diagnosis of the disease. The present study goal to investigate the clinical presentations, endoscopies findings, and family history of esophageal cancer in the city of Khorramabad, Western Iran.

Materials and Methods

3.1. Source of Data

In this cross-sectional research, the study population consists of all patients who had referred to the ShohadaAshayer Hospital and gastrointestinalsupraspecialists' offices in Khorramabad during 1 year in 2015, who were diagnosed with esophageal cancer by endoscopy and pathological findings. The study included only the patients who resided in the city and its suburban areas. The sample size was 96 people using the census. In this study, patient's inclusion criteria to study was living in Khorammabad and around the areas, identification of esophageal cancer on upper endoscopy (EGD) and confirmed by pathology reports. Exclusion Criteria from the study was incomplete information, undocumented information and lack of access to pathology reports. The data collected through interviews patients and entourage using a multi-part questionnaire. The first section of the questionnaire was included age, sex, marital status, education, occupation, address and ethnicity and also questions regarding the patient's background as to smoking, alcohol consumption, drug and narcotic abuse and the cancers of the digestive system among immediate relatives. The second section of the questionnaire was included characteristic of tumors based on endoscopy and pathology reporting of esophageal tumor involved anatomical site of the tumor, type of pathology of tumors that this information collected on endoscopy and confirmed by pathology reports. The Thirdsection of the questionnairewas included clinical symptoms in patientsAdditionally, the presence of mucosal lesions indicates that esophageal cancerafter multiple biopsies taken of lesions, and cancer information was recorded. All gastrointestinal endoscopic procedures in cancer patients were performed in hospitals by expert endoscopists.

3.2. Statistical Analysis

Collecting information, the data from each of the returned questionnaire were coded and entered into the statistical package for the Social Sciences (SPSS) version 19 software and then, descriptive statistics were used to describe the collected information, such as the average indicators, standard deviation, percentage and otherdescriptive statistics, Fisher's exact test and the chi-square test were used for data analysis.

3.3. Ethical considerations

This study has been approved in the ethic committee of Lorestan University of Medical Sciences.

Results

A total of 96 patients suffering esophageal cancer were enrolled during 2015. The mean (± SD) age of patients was 68.91±10.06 years old. The minimum age of the patient was 37 years old and the maximum age of patients was 88 years old. In overall, 19 numbers (19.8 %) of patients were aged< 60 years of age and 77 numbers (80.8 %) of patients were ≥ 60 *years* old. There were 46 (47.9 %) male and 50 (62.1 %) female patients. Most patients (99 %(were married and 1% were single. Most patients had an educational level of Illiterate (83.3 %). Among the cases of study, 47 patients (49 %) were the housewife and 28 patients (29.2 %) were farmer and 62 numbers (64.6 %) of patients were Lur and 34 numbers (35.4 %) of patients were Lak (Table1).

Table 1: Frequency distribution of demographic characteristics of patient with esophageal cancer

Variable		Absolute Frequency (N)	Relative Frequency (%)	Total
Age	< 60	19	19.5	96(100)
	≥ 60	77	80.8	
Sex	Male	46	47.9	96(100)
	Female	50	52.1	
Marital status	Married	95	99	96(100)
	Single	1	1	
Education	Illiterate	80	83.3	96(100)
	Junior high school and lower	9	9.4	
	Senior high school	4	4.2	
	Academic	3	3.1	
Occupation	Unemployed	3	3.1	96(100)
	Employee	6	6.3	
	Free	11	11.5	
	Housewife	47	49	
	Worker	1	1	
	Farmer	28	29.2	
Ethnicity	Lur	62	64.6	96(100)
	Lak	34	35.4	

Regarding family history of esophageal cancer in the first-degree family, the results showed that 13 (13.5 %) patients reported a positive family history of esophageal cancer and 19 (19.8 %) reported other cancers, also, 16 (13.5 %) reported gastric cancers. In detail, 46 (47.9 %) of patients reported a background of smoking and No one has reported alcohol consumption (Table 2). Additionally, Analysis of the anatomical site of esophageal cancer revealed which, the more commonly location of esophageal cancer was in the distal, distal and cardiac, middle and Progsimal of the esophagus (40.6 %, 28.1 %, 22.9 %, 8.3 %, respectively) (Table 2).

Table 2: Frequency of anatomical site of esophageal cancer by age, sex, ethnicity, smoking history and history of gastric and esophageal cancer inimmediate relative

Variable \ Anatomical Site Of tumor		prog simal N(%)	Middle N (%)	Distal N (%)	Distal and Cardia N (%)	Total N (%)	P-value
Age	< 60	5 (26.3)	2 (10.5)	5 (26.3)	7 (36.8)	19 (100)	0.006*
	≥ 60	3 (3.9)	20 (26)	34 (44.2)	20 (26)	77 (100)	
Sex	Male	6 (13)	6 (13)	19 (41.3)	15 (32.6)	46 (100)	0.047*
	Female	2 (4)	16 (32)	20 (40)	12 (24)	50 (100)	
Ethnicity	Lur	6 (9.7)	13 (21)	25 (40.3)	18 (29)	62 (100)	0.867
	Lak	2 (5.9)	9 (26.5)	14 (41.2)	9 (26.5)	34 (100)	
History of other cancers in the individual	Yes	2 (10.5)	4 (21.1)	3 (18.8)	10 (52.6)	19 (100)	0.032*
	No	6 (7.8)	18 (23.4)	36 (46.8)	17 (22.1)	77 (100)	
History of Gastric cancer in immediate Family	Yes	3 (18.8)	2 (12.5)	6 (37.5)	5 (31.3)	16 (100)	0.318
	No	5 (6.3)	20 (25)	33 (41.3)	22 (27.5)	80 (100)	
History of esophageal cancer in immediate Family	Yes	0 (0)	1 (7.7)	7 (53.8)	5 (38.5)	13 (100)	0.262
	No	8 (9.6)	21(25.3)	32 (38.6)	22 (26.5)	83 (100)	
Smoking history	Yes	4 (8.7)	9 (19.6)	16 (34.8)	17 (37)	46 (100)	0.303
	No	4 (8)	13 (26)	23 (46)	10 (20)	50 (100)	

* Level of significance: < 0.05

The most common of esophageal cancer occurred in the distal esophagus and cardia gastric in patients under 60 years of age and were located in the distal and middle esophagus in patients over 60 years old. The most cases of esophageal cancer had reportedly occurred in the progsimal esophagus in the patients under 60 years old (26.3 %) and in the patients over 60 years of age (3.9 %) which, based on the outcome of the chi-square test this difference was statistically significant. (P= 0.006). Additionally, According to results of the study, the more case of esophageal cancer was located in the distal esophageal in male patients (41.3 %) and the most common of the tumor were located in the middle esophageal in female patients (32 %) which, this difference was statistically significant (P= 0.047) .In the patients with the history of other cancers, the most common of esophageal cancer occurred in the distal esophagus and cardia of gastric (52.6 %) and in other patients it is located in distal esophagus (46.8 %). According to chi-square test, there were significant differences between the history of another anatomical site of esophageal cancers in the patients and other patients, too. In terms of the relationship between the anatomical site of the tumor and ethnicity, smoking history and In terms of the relationship between the anatomical site of the tumor and ethnicity, family history of esophageal and gastric cancers in the first-degree family, was not statistically significant difference (Table 2).

In terms of tumor pathology, the more commonly were adenocarcinoma esophagus 47(49 %) and then SCC 43 (44.8 %) and other (6 %) (Table 3). The pathological types of esophageal cancer were SCC in female (50 %) and adenocarcinoma in male(60.9 %), which was statistically significant (P= 0.013). furthermore, most common type of pathological of esophageal cancer was adenocarcinoma in the patients

under 60 years old (42.1 %) and the pathological were SCC in the patients 60 years of age and older (46.8 %) which was statistically significant (P= 0.012). Also, the relative between the history of Gastric cancer in immediate Family and the patients which have not the immediate relative with esophageal cancer were statistically significant. The most common type of gastric cancer was SCC (42.1 %), whereas, themorecases of gastric cancer in other patients were adenocarcinoma (51.9 %) which, was statistically significant (P= 0.011) (Table3).Furthermore, the conclusion that there is no statistically significant difference between pathological of esophageal cancer and Ethnicity, Smoking history and history of gastric cancer in an immediate relative (Table 3).

Table 3: Frequency of tumor pathology by age, sex, ethnicity, smoking history and history of gastric and esophageal cancer inthe immediate relatives and history of other cancers in the patients

Anatomical Variable / Location Of tumor		Scc N(%)	Adenocarcinoma N (%)	Others N (%)	Total N (%)	P-value
Age	**< 60**	7 (36.8)	8 (42.1)	4 (21.1)	19 (100)	0.012*
	≥ 60	36 (46.8)	39 (50.6)	2 (2.6)	77 (100)	
Sex	**Male**	18 (39.1)	28 (60.9)	0 (0)	46 (100)	0.013*
	Female	25 (50)	19 (38)	6 (12)	50 (100)	
Ethnicity	**Lur**	28 (45.2)	30 (48.4)	4 (6.5)	62 (100)	0.986
	Lak	15 (44.1)	17 (50)	2 (5.9)(	34 (100)	
History of other cancers in the individual	**Yes**	8 (42.1)	7 (36.8)	4 (21.1)	19 (100)	0.011*
	No	35 (45.5)	40 (51.9)	2 (2.6)	77 (100)	
History of Gastric cancer in immediate Family	**Yes**	8 (50)	8 (50)	0 (0)	16 (100)	0.517
	No	35 (43.8)	39 (48.8)	6 (7.5)	80 (100)	
History of esophageal cancer in immediate Family	**Yes**	3 (23.1)	8 (61.5)	2 (15.4)	13 (100)	0.130
	No	40 (48.2)	39 (47)	4 (4.8)	83 (100)	
Smoking history	**Yes**	18 (39.1)	23 (50)	5 (10.9)	46 (100)	0.160
	No	25 (50)	24 (48)	1 (2)	50 (100)	

* Level of significance: < 0.05

As demonstrated in Table 4, shows thatthe more common of clinical signs were weight loss, anorexia,and dysphagia.

Table 4: Frequency of clinical signs of esophageal cancers in the patients

Type symptoms	Yes N (%)	No N (%)	Total N (%)
Anorexia	51 (53.1)	45 (46.9)	96 (100)
Weight Loss	60 (62.5)	36 (37.5)	96 (100)
Gastrointestinal bleeding	7 (7.3)	89 (92.7)	96 (100)
Anemia	20 (20.8)	76 (79.2)	96 (100)
Nausea	7 (7.3)	89 (92.7)	96 (100)
Vomit	31 (32.3)	65 (67.7)	96 (100)
Abdominal pain	28 (29.2)	68 (62.5)	96 (100)
Dysphagia	51 (53.1)	45 (46.9)	96 (100)

Discussion

In the present study, we investigated the clinical presentations, endoscopy findings, family history of esophageal cancer in the city of Khorramabad in Lorestan city, Iran. Given the fact that, ShohadaAshayer Hospital is the only referral center for subspecialty health services in gastrointestinal diseases in the province, the information regarding the epidemiology of esophageal cancer obtained by this study is of value. In terms of age, this study showedthat the mean age of patients was 68.91, which, it was higher than the other studies [10, 11], but lower than the mean age were in the studies in the Western World (mean age of 61 years)[12]. Studies done in Iran have reported different statistics so that the mean age of the patients in our study was lower than the mean ages in studies done at the Towhid Hospital, Sanandaj city, Kurdistan province, western Iran[13]. Most cases of thestudywere male which was similar to the results of the studies conducted in Azerbaijan, Khorasan, Gilan, Mazandaran, Golestan, and Kurdistan [14], but in another study, 50.5% of patients in Golestan were female[15]. In this study, there was a statistically significant difference between the mean of age tumor pathology with anatomical site of esophageal cancer according to last studies have shown thatthe chance of getting esophageal cancer is low at younger ages and increases with age. Less than 15% of cases are found in people younger than age 55 [16] which this resultis matched with our findings. In the present study, 47.9% of patients reported a background of smoking which there is no statistically significant difference. This result was consistent with the results of a study on esophageal cancer in Spain which, the results of study have shown that not significantly associated with a risk of esophageal cancer[17].On the other hand, the results of study have shown, positive association between smoking and esophageal cancer[18].According to family history of esophageal cancer, Gastric cancer and other cancers in immediate relatives, the results of study showed that13(13.5%), 16(13.5%) and 19(19.8%) of patients respectively, a family history of diseases in immediate relative which was statistically significant that this result shown that, a genetic factors In addition, environmental factors may affect to development of esophageal cancer in society. Therefore, family history can be a potential way to identification people at risk of cancer. Many studies have supported an association between genetic factors and gastrointestinal cancer risk[19, 20]. In one study that examined the relationship between family history and esophageal cancer, the results indicate that, Family history of esophageal cancer increases the risk of esophageal squamous cell carcinoma[19].In this study, the result has shown that, the most common anatomical sites of esophageal cancer occurred in the distal esophagus and cardia of gastric (52.6%) and other patients were in the distal esophagus (46.8%) which, is consistent with the results of study in Ardebil showed that, the more common of anatomical sites of esophageal cancer werecardia of gastric and distal esophageal21. In the present of study, the most common clinical presentations wereanorexia, weight loss and dysphagia. Findings from the studies conducted in Philadelphia [22] and New York [23] also reported these clinical signs as the more common with slight differences in the percentage of each sign. However, retrosternal pain was reported more common sign of esophageal cancer in Tanzania[24].

Finally, given the increasing rates of esophageal cancer in Iran, particularly in Lorestan Province, is counseled that further complementary studies should be conducted to identify the underlying causes and predisposing factors of esophageal cancer. A better identification of these agents can result in better control and management of the diseases.

Conflict of interests

The authors declare no conflict of interests.

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References:

1. Thomas N. Seyfried and Leanne C. Huysentruyt.On the Origin of Cancer Metastasis. *Crit Rev Oncog*. 2013; **18(**1-2): 43–73.
2. GBD 2015 Disease and Injury Incidence and Prevalence Collaborators.Global, regional, and national incidence, prevalence, and years lived with disability for 310 diseases and injuries, 1990–2015: a systematic analysis for the Global Burden of Disease Study 2015. *Lancet*.2016 Oct 8; **388**(10053): 1545–1602.
3. Zadnik V, PrimicZakelj M, Lokar K, Jarm K, Ivanus U, Zagar T. Cancer burden in slovenia with the time trends analysis. *Radiology and Oncology*. 2017; **51**(1):47-55.
4 Ellis A, Risk JM, Maruthappu T, Kelsell DP. Tylosis with oesophageal cancer: Diagnosis, management and molecular mechanisms. Orphanet Journal of Rare Diseases. 2015; 10:126.
5. Ferri, FF, ed. (2012). "Esophageal Tumors". Ferri's clinical advisor 2013. Philadelphia, PA: Mosby (Elsevier). pp. 389–391.
6. Otterstatter MC, Brierley JD, De P, et al. Esophageal cancer in Canada: Trends according to morphology and anatomical location. *Canadian Journal of Gastroenterology*. 2012; **26**(10):723-727.
7. Zhang Y. Epidemiology of esophageal cancer. World Journal of Gastroenterology : *WJG.* 2013; **19**(34):5598-5606.
8. GLOBOCAN 2012. Lyon: IARC. Available online: http:// globocan.iarc.fr/
9. Ghavamzadeh A, Moussavi A, Jahani M, Rastegarpanah M, Iravani M. Esophageal cancer in Iran. *SeminOncol*. 2001 Apr; **28**(2):153-7.
10. Alema O, Iva B. Cancer of the esophagus: histopathological sub-types in northern Uganda. *African Health Sciences.* 2014; **14**(1):17-21.
11. E. Bollschweiler, R. Metzger, U. Drebber, S. Baldus, D. Vallböhmer, M. Kocher, A. H. Hölscher; Histological type of esophageal cancer might affect response to neo-adjuvant radiochemotherapy and subsequent prognosis. *Ann Oncol* 2009; **20** (2): 231-238.
12. Siewert JR, Stein HJ, Feith M, Bruecher BLDM, Bartels H, Fink U. Histologic Tumor Type Is an Independent Prognostic Parameter in Esophageal Cancer: Lessons From More Than 1,000 Consecutive Resections at a Single Center in the Western World. *Annals of Surgery.* 2001; **234**(3):360-369.
13. Veisani Y, Delpisheh A, Sayehmiri K, Rahimi E. Demographic and Histological Predictors of Survival in Patients With Gastric and Esophageal Carcinoma. Iranian *Red Crescent Medical Journal.* 2013; **15**(7):547-553.
14. Parvin S, Firouz S.A study of 415 cases of esophageal carcinoma in northwest of Iran. *Med J Malaysia.* 2003 Aug; **58**(3):429-31.
15. Aghcheli K, Marjani HA, Nasrollahzadeh D, Islami F, Shakeri R, Sotoudeh M, et al Prognostic factors for esophageal squamous cell carcinoma--a population-based study in Golestan Province, Iran, a high incidence area. *PLoS One.* 2011; **6(**7):e22152.
16. Hamouda A, Forshaw M, Rohatgi A, Mirnezami R, Botha A, Mason R. Presentation and survival of operable esophageal cancer in patients 55 years of age and below.*World J Surg.* 2010 Apr; **34**(4):744-9.
17. Vioque J, Barber X, Bolumar F, et al. Esophageal cancer risk by type of alcohol drinking and smoking: a case-control study in Spain. *BMC Cancer*. 2008; **8**:221.
18. Cook MB, Kamangar F, Whiteman DC, et al. Cigarette Smoking and Adenocarcinomas of the Esophagus and Esophagogastric Junction: A Pooled Analysis From the International BEACON Consortium. *JNCI Journal of the National Cancer Institute*. 2010; **102**(17):1344-1353.
19. Chen T, Cheng H, Chen X, Yuan Z, Yang X, Zhuang M, et al. Family history of esophageal cancer increases the risk of esophageal squamous cell carcinoma. *Sci Rep.* 2015 Nov 3; **5**:16038.
20. Ghanadi K, Shayanrad B, Ahmadi SA, Shahsavar F, Eliasy H. Colorectal cancer and the KIR genes in the human genome: A meta-analysis. *Genomics data*. 2016 Dec 31; **10**:118-26.
21. Haghighi P, Nasr K. Gastrointestinal cancer in Iran. *J Chron Dis.* 1971; **24:** 625-33.
22. Schlansky B, Dimarino AJ Jr, Loren D, Infantolino A, Kowalski T, Cohen S. A survey of oesophageal cancer: pathology, stage and clinical presentation. *Aliment PharmacolTher.* 2006 Mar 1; **23(**5):587-93.
23. Gibbs JF, Rajput A, Chadha KS, et al. The changing profile of esophageal cancer presentation and its implication for diagnosis. *Journal of the National Medical Association*. 2007; **99**(6):620-626.
24. Mchembe MD, Rambau PF, Chalya PL, Jaka H, Koy M, Mahalu W. Endoscopic and clinicopathological patterns of esophageal cancer in Tanzania: experiences from two tertiary health institutions. *World journal of surgical oncology*. 2013 Oct 4; **11**(1):257.