# High Prevalence of Esophageal Cancer in South East of Iran

# Mohammad Ali Mashhadi,<sup>1</sup> Kazem Nezam,<sup>2</sup> Ali Reza Bakhshipour,<sup>2</sup> Tahere Fajharian Ttorbati,<sup>3</sup> Ali Reza Ansarimoghaddam<sup>4</sup>

<sup>1</sup>Associated professor of Internal medicine, Hematologist & Oncologist, Zahedan University of Medical Science, Zahedan, Iran <sup>2</sup>Assistant professor of Internal medicine, Gastroentrologist Zahedan University of Medical ScienceZahedan, Iran <sup>3</sup>Gastroenterology & Liver disease Department, School of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran <sup>4</sup>Epidemiology Department, Health Promotion Research Center, Zahedan University of Medical Sciences, Zahedan, Iran

**Correspondig author:** Mohammad Ali Mashhadi, MD, Hematologist- Oncologist Department of Hematology & Oncology Ali Ebne Abitaleb Hospital, Zahedan, Iran Tel.: 09153411445 Email: dralimashhadi@yahoo.com

#### Abstract

Introduction: Esophagus cancer is most common GI malignancies in Zahedan. This investigation was undertaken to define the epidemiology, and prognostic factors relevant to patients with Esophagus cancer in this region.

**Methods**: We did a retrospective review of 175 patients with Esophagus cancer who presented to Ali Ebne Abitaleb Hospital and Khatam Alanbia Hospital in 2005-2010. Data analysis was done using the Kaplan-Meier method.

**Results:** The majority of the patients were male (70%) and 30% in female, and the mean age of them was 48.5 years. The vast majority were Iranian and from Baluch ethnicity group. 166 patients were Iranian population and in Balouchs ethnic group (118 cases) is more common than Sistani (49cases), and 9 patients were Afghan. Most of the cancer cases reported a history of Tobacco consumption (82 %) and the most common type of tobacco use was PAAN or Nass which is a combination of tobacco, lime, water, menthol and oil. Squamous Cell Carcinoma was the most commonly type of cancer (97%) in the region and adenocarcinoma was the second most common and the median survival time of patients was 13 months. Dysphagia and weigh lose were the most frequently encountered symptoms at the time of presentation. At the time of diagnosis early stage disease was found in 22%, locally advanced in 54% and metastatic in 24% of all cases. Any patients didn't have a family history of Esophagus cancer.

**Conclusion:** Clinical and epidemiological pattern of esophageal cancer in South-East of Iran is partially differed with other parts of the county as well as also other parts of the world which is important for both clinicians and health policy makers. Esophagus cancer is the most common GI malignancies in Zahedan. And this pattern is difference with other region in Iran, that, gastric cancer is most common GI malignancies according to previous of our study.

Key words: Esophageal cancer, Epidemiology, Clinical pattern, South East of Iran

#### Introduction

Esophageal cancer is one of the 10 most common cancers and the sixth most common cause of cancer deaths worldwide. It is the third most common gastrointestinal malignancy after gastric, colorectal and hepatocellular cancers. Esophageal cancer displays unique epidemiological features that distinguish it from other malignancies. It shows marked geographical variation, with exceptionally high rates (some of the world's highest for any cancer) ranging from 3 per 100000 per year reported in Western countries to 140 per 100000 reported in Central Asia.(1-3) Esophageal cancer is one of the most virulent tumors with a dismal prognosis, despite the recent advances in early diagnosis and treatment. It has one of the lowest possibilities of cure, with a 5-year survival rate of approximately 10%; these rates are second only to hepatobiliary and pancreatic cancers.(4)

### **Patients and methods**

A retrospective review of all the 175 cases seen at the Hospitals of Zahedan, from 2006 to 2010 was done. International Classification of Disease-10 was used for coding. Data were analyzed using SPSS (Release 10.05, standard version, copyright ©SPSS; 1989- 99). Descriptive analysis was done for demographic, clinical and pathologic features. Results were expressed as means±standard deviation and percentage.

In this study we looked at the following parameters: signs and symptoms, risk factors, laboratory data, imaging modalities, histology, and status of the disease, overall survival and various prognostic factors of the disease.

#### Results

Out of the 175 cases reviewed, a male preponderance was observed (70% males versus 30% females). The mean age at the time of diagnosis was 48.5 years.(20- 81) Figure 1, 166 patients were Iranian and in Balouchs ethnic group is more common (118 cases) than Sistani, and 9 patients were Afghan.

Dysphagia was the most frequently encountered symptom at the time of presentation, seen in 85.2% of the cases. Obstruction, seen endoscopically or on computed tomography scans, was present in 5 % of patients. 75 percent of the patients gave a history of weight loss. Tobacco use was found in 82 % of the patients and less than 1% of the patients had a history of alcohol use.

#### Discussion

This single institution study of a South-East Iran population has looked at the demographic features, risk factors, survival data and prognostic indicators of esophageal cancer.

Table- 1: Patients	characteristics.
Sex	Male

Sex	Male	Female
	122 (70%)	53 (30%)
Age	48.5	20-81
Site of Malignancy	Upper (29%),	
	Middle(23%), Lower	
	(48%)	
Dysphagia	85.5%	
Weight loss	75%	
Obstruction	5%	
Tobacco use	82%	
Stage	Early(22%),	
	Locally advance (54%)	
	Metastatic (24%)	

Such a study has not been reported from this region before. Prevalence of esophageal cancer is high in Iran, accounting for 5% of all cancers in men within our institution, from where these data were retrieved.(5, 6) Esophagus cancer is the most common GI malignancies in Zahedan.(7) And this pattern is difference with other region in Iran, that, gastric cancer is the most common GI malignancies. Esophageal cancer is the most cancer of 5 top cancer in male population and second most frequent malignancy in patients of south east of iran.(7)

The average age at diagnosis in our patients was 48.5 years, median age being 60 years (range 20-81). The median age at presentation is 72 years according to data from Scotland.(8)

The male to female ratio was 2:1. Male to female ratio is 3:1 according to data from the United States.(9) The majority of our patients had special habits of chewing tobacco, and a risk factor for this cancer, especially squamous cell carcinoma, the most common histology here. The European data for sex ratio varied from 1.9:1 in Scotland to 16.3:1 in Calvados, France.(10) Around the rest of the world the incidence of esophageal cancer is four to six times higher in men than in women for all age groups, except is China, northern Iran and South-East Iran where the ratio is about 2:1.(11)

Dysphagia was the most common presenting complaint, seen in 80.2 % of the patients. Weight loss was the other more common feature at presentation, notable in 85.2 % of our patients. Data from another region showed that only 42% of the patients had weight loss at presentation. Sixty-five percent of the esophageal lumen must be involved before patients notice dysphagia.(12, 13)

Smoking increases the risk of developing squamous cell carcinoma of the esophagus by five-fold to 10fold, and of developing adenocarcinoma by twofold. Alcohol has an additive, and perhaps synergistic effect, where the risk increases to as high as 100-fold.(14-17)

Tobacco use, seen in 82% of our patients, is a major risk factor for esophageal cancer. This is in contrast to the European data, as Negri et al,(18) reported that 61% of esophageal cancer was attributable to smoking in Italy. The forms of tobacco are different here; these include chewing tobacco (named PAAN Combination of tobacco, lime, water, menthol, oil. Nass, Tambaku) and bidi smoking, which are common in Balouch, Pakistani and Indian populations and are considered a risk for developing this malignancy.(19, 20)

Drinking alcohol is rare in our part of the world. Only less than 1% of our cases had a history of

#### Mohammad Ali Mashhadi

alcohol usage. This is much less than in Italian data, where it accounted for 39% of the cases. It is also possible that other dietary factors may be playing a role in the high incidence of esophageal cancer, like drinking of very hot beverages such as tea, which are again extremely common in this region.

These have been described in other studies done in Iran and India,(21, 22) which has a lifestyle and dietary practices similar to those in this part of Iran.

Squamous cell carcinoma of the esophagus (97%) was the predominant histology seen in our study, with adenocarcinoma (3%) being less in proportion. These data are consistent with data from most of Asia.(23, 24)

These figures are different from those found in the developed countries where adenocarcinoma is the more abundant type, primarily because of a high frequency of Barrett's esophagus.(25) Adenocarcinoma constitutes about 50–60% of the cases of esophageal carcinoma in the West.(26, 27) Other studies showed which SCC ic most common Esophageal cancer in belt of esophageal cancer.(28, 29, 30)

In other part of Iran (Fars province) esophageal cancer is the third most GI cancers after stomach and colon cancer. In this region the incidence of every histologic subtype were squamous (78.4%), adenocarcinoma (21.6%) and 1.7% undetermined carcinoma,(31) but in our study esophageal cancer was the most common GI cancers and squamous histology was the mainly histology with more than 95% incidence.(7)

The prevalence of esophageal cancer in south east of Iran (Zahedan, Sistan & Balouchestan) is very high like to esophageal cancer belt.(32)

The north western of iran is one of the most common region of esophageal cancer, in this region the incidence rate of squamous cell cancer is very high (81%), and 16% showed adenocarcinoma histology,(33) and differ to our results with more than 95% squamous histology.

The most common site of malignancy was the lower esophagus (48%). The middle esophagus was involved in 23% and the upper esophagus in 29% of cases.

Despite the most common site being the lower esophagus, the most common histology was squamous cell carcinoma; this speaks for the low probability of Barrett's esophagus as an etiology of esophageal carcinoma in our population.

Western data show that the lower esophagus was involved in 30% of cases, whereas 60% and 10% arise from the middle and upper third of the esophagus, respectively.(28, 29)

# Conclusion

The predominant histology in our patients with esophageal carcinoma was squamous cell carcinoma (97%). The overall median survival was 13 months.

Although Esophagus cancer is the most common GI malignancies in Zahedan,(7) and this cancer is the first most common malignancy in male population with malignancy and second most frequent in female population. This pattern is difference with other region in Iran. Other significant point was the usage of a specific type of tobacco that named PAAN or NAAS.

## Refernces

1. Blot WJ. Epidemiology and Genesis of Esophageal Cancer. In Roth JA, Ruckdeschel JC, Weisenburger TH (eds): Thoracic Oncology. Philadelphia, PA: Saunders 1995; 278.

2. Blot WJ, McLaughlin JK. The Changing Epidemiology of Esophageal Cancer. Semin Oncol 1999; 26: 2.[ISI][Medline]

3. Blot WJ. Esophageal Cancer Trends and Risk Factors. Semin Oncol 1994; 21: 403-410. [ISI][Medline]

4. Wong R, Malthaner R. Esophageal Cancer: A Systematic Review. Curr Probl Cancer 2000; 24: 297-373.[Medline]

5. Malik IA, Khan WA, Khan ZK. Pattern of Malignant Tumors Observed in a University Hospital: A Retrospective Analysis. J Pak Med Assoc 1998; 48: 120- 122. [Medline]

6. Roohullah, Khursheed AK, Burdey GM et al. Cancer of Esophagus: Ten Years Experience at CENAR, Quetta. J Ayub Med Coll Abbottaba 2001; 13: 4-7.

7. Mashhadi MA, Zakeri Z, Abdollahinejad MJ. Cancer Incidence in South East of Iran: Result of a Population Based Cancer Registry. Shiraz E Medical Journal; 2010, Vol. 11, No. 3.

8. Park KG, Brewster DH. Epidemiology. CRAG Publication, NHS Quality Improvement, Edinburgh, UK, Scottish Audit of Gastric and Esophageal Cancer. Report 1999- 2000.

9. National Cancer Institute PDQ Internet Information for Esophageal Cancer. http://cancernet.nci.nih.gov/cgi.bin/srchcgi.exe?DB ID=pdq&TYPE=search&UID=208+00089.

10. Botterweck AA, Schouten LJ, Volovics A, et al. Trends in Incidence of Adenocarcinoma of the Esophagus and Gastric Cardia in Ten European Countries. Int J Epidemiol 2000; 29: 645-654.[Abstract/Free Full Text] 11. Sons HU. Etiologic and Epidemiologic Factors of Carcinoma of the Esophagus. Collective Review. Surg Gynecol Obstet 1987; 165: 183-190.[ISI][Medline]

12. Ojala K, Sorri M, Jokinen K, Kairaluoma M. Symptoms of Carcinoma of the Esophagus. Med J Aust 1982; 1: 384- 385.[ISI][Medline]

13. Ojala K, Sorri M, Jokinin K et al. Symptoms and Diagnostic Delay in Patients with Carcinoma of the Esophagus and Gastric Cardia: a Retrospective Study of 225 Patients. Postgrad Med J 1982; 58: 264-267.[ISI][Medline]

14. Castellsague X, Munoz N, De Stefani E, et al. Independent and Joint Effects of Tobacco Smoking and Alcohol Drinking on the Risk of Esophageal Cancer in Men and Women. Int J Cancer 1999; 82: 657.[CrossRef][ISI][Medline]

15. Zhang ZF, Kurtz RC, Sun M, et al. Adenocarcinomas of the Esophagus and Gastric Cardia: Medical Conditions, Tobacco, Alcohol and Socioeconomic Factors. Cancer Epidemiol Biomarkers Prev 1996; 5: 761.[Abstract]

16. Kabat GC, Ng SK, Wynder EL. Tobacco, Alcohol Intake, and Diet in Relation to Adenocarcinoma of the Esophagus and Gastric Cardia. Cancer Causes Control 1993; 4: 123.[CrossRef][ISI][Medline]

17. Vaughan TL, Davis S, Kristal A, Thomas DB. Obesity, Alcohol, and Tobacco as Risk Factors for Cancers of the Esophagus and Gastric Cardia: Adenocarcinoma versus Squamous Cell Carcinoma. Cancer Epidemiol Biomarkers Prev, 1995; 4: 85.[Abstract]

18. Negri E, La Vecchia C, Franceschi S et al. Attributable Risks for Esophageal Cancer in Northern Italy. Eur J Cancer 1992; 28A: 1167-1171.[CrossRef][ISI][Medline]

19. Bhurgri Y, Bhurgri A, Hassan SH et al. Cancer Incidence in Karachi, Pakistan: First Results from Karachi Cancer Registry. Int J Cancer 2000; 85: 325-329.[CrossRef][ISI][Medline]

20. Jayant K, Deo MG. Oral Cancer and Cultural Practices in Relation to Betel Quid and Tobacco Chewing and Smoking. Cancer Detect Prev, 1986; 9: 207- 213.[ISI][Medline]

21. Siddiqi M, Kumar R, Fazili Z et al. Increased Exposure to Dietary Amines and Nitrate in a Population at High Risk of Esophageal and Gastric Cancer in Kashmir (India). Carcinogenesis, 1992; 13: 1331- 1335.[Abstract/Free Full Text] 22. Sankaranarayanan R, Duffy SW, Padmakumary G, et al. Risk Factors for Cancer of the Esophagus in Kerala, India. Int J Cancer 1991; 49: 485-489.[ISI][Medline]

23. Law S, Wong J. Changing Disease Burden and Management Issues for Esophageal Cancer in the Asia-Pacific Region. J Gastroenterol Hepatol 2002; 17: 374–381.[CrossRef][ISI][Medline]

24. Puttawibul P, Chanvitan A, Pornpatanarak C, Sangthong B. Esophageal Carcinoma in Southern Thailand. J Med Assoc Thai, 2001; 84: 1-5.[Medline]

25. Jemal A, Thomas A, Murray T et al. Cancer Statistics, 2002. CA Cancer J Clin 2002; 52: 23-47.[Abstract/Free Full Text]

26. Blot WJ, Devesa SS, Kneller RW, Fraumeni JF Jr. Rising Incidence of Adenocarcinoma of the Esophagus and Gastric Cardia. J Am Med Assoc 1991; 265: 1287- 1294.[Abstract]

27. Hesketh PJ, Clapp RW, Doos WG, Spechler SJ. The Increasing Frequency of Adenocarcinoma of the Esophagus. Cancer 1989; 64: 526-530.[CrossRef][ISI][Medline]

28. Saenko AI. The Epidemiology of Cancer in Central. Asia. Vopr Onkol, 1975; 21(11): 40-4.

29. Kirakbaev M. Malignant Neoplasms among Ethnic Groups in the Kazakh SSR. Vopr Onkol 1978; 24(6): 100-104.

30. Tran GD, Sun XD, Abnet CC, Fan JH, Dawsey SM, Dong ZW, et al. Prospective Study of Risk Factors for Esophageal and Gastric Cancers in the Linxian General Population Trial Cohort in China. Int J Cancer 2005; 113(3): 456-63.

31. Bagheri Lankarani K, Mowla A, Asadian F, Tabei SZ, Hahin. Changing Epidemiology of Esophageal Cancer in Fars Province, Iran. Iranian Journal of Medical Science. 2002; 27(1): 4-10.

32. Marjani A , Kabir MJ , Semnani S . Stomach Cancer Incidence among Males in Golestan Province, Iran. Indian Journal of Gastroentrol 2007; 26: 299- 302.

33. Pedram A, mahmodiou R, Enshayi A, Sepehrvand N. Esophageal Cancer in Northwestern Iran. Indian Journal of Cancer. 2011, 48(2): 165-169.