Introduction

Esophageal cancer (EC) is the eight most common cancer worldwide, accounting for 3.2% of total new cases in 2012.\(^1\) About 80% cases of EC worldwide occur in less developed regions.\(^2\) According to GLOBOCAN 2012 estimate, in India, there were 42,000 new cases of EC, the incidence being 4.13% of all new cancer cases, and 39,000 deaths were caused due to EC.\(^3\)

Acharya Tulsi Regional Cancer Treatment & Research Institute, Bikaner, Rajasthan is a regional cancer center witnessing a large number of cancer patients from northwest India. Despite various advances in the treatment of EC, it is one of the least responsive tumors to cancer therapy, and the overall prognosis remains poor. The ratio between mortality to incidence is about 0.88, more than 80% of the cases die within 2 years of diagnosis even in developed nations.\(^4\) It is the nation’s most common malignancy involving the gastrointestinal tract.\(^5\) In North America and Western Europe, alcohol and tobacco use are the major risk factors for squamous cell carcinoma (SCC), accounting for 80-90% of cases.\(^6\) Diets of scant amounts of fruits, vegetables, and animal products are associated with increases in SCC.\(^7\) Other risk factors associated with EC include Plummer-Vinson syndrome (a condition characterized by iron-deficiency anemia and low riboflavin levels), achalasia, and...
tylosis. In India, EC is being reported in increasing numbers from Assam, Kashmir, Tamil Nadu, Karnataka, and Kerala. No literature is present from northwest India about the etiopathology of EC. Therefore, it is important to understand various aetiopathological factors associated with EC to find out various schemes for primary prevention of the disease. In this clause, we have reviewed the sociodemographic parameters of the patients with EC who visited the oncology department of our center in the last 10 years.

Materials and Methods

This is a retrospective analysis of medical records of the cancer patients registered in the regional cancer center of northwest India from January 2003 to December 2012. Thus, the data is derived from a hospital-based registry. Being a retrospective study, no ethical approval was required for the study as all the patients were treated with the standard departmental protocol. For extracting the data, the computerized data, hard copies of the files, and also the radiotherapy files of the patients were reviewed. A total of 55,242 patients with a variety of malignancies were registered in the 10-year duration. Out of this, 3,667 were diagnosed to have EC. The sociodemographic parameters including age, gender, locality, socioeconomic status, religion, education, occupation, and the addiction patterns of the patients were studied. The site of the disease and the histology were also recorded. Nonsmokers were defined as having smoked fewer than 100 cigarettes in their lifetime or less than one cigarette per day for 6 months or more. All others were counted as smokers for the purpose of recording in the history sheet. To assess alcohol consumption, subjects were asked about their usual intake of beer, wine, and liquor from the age at which they started drinking at least one alcoholic beverage per month. A never drinker was defined as having consumed less than one drink per month. Modified BG Prasad classification was used to assess the socioeconomic status of the patients as per the institutional policy. To calculate odds ratio (OR) for smoking, the data of Global Adult Tobacco Survey (India) was used to define the control population. The data from Global Survey on Alcohol and Health data by World Health Organization (WHO) region was utilized to calculate OR for alcohol abuse. All the recorded data was entered in Windows Excel sheet and imported to the statistical software to perform the calculations. Statistical calculations were performed used Statistical Package for Social Sciences (SPSS) for windows version 20.0 (IBM Corp., Armonk, USA).

Results

Out of 55,742 patients registered in our hospital, 3,667 were diagnosed to have EC. 53.4% patients were males with male:female ratio of 1.15:1, indicating almost similar incidence of EC in males and females of northwest India. The mean age was 54.6 ± 11.7 years; 66.2% of the patients were illiterate and 48.6% belonged to the low socioeconomic status; 41% cases were of >60 years age, while 3.4% of the patients were of ≤30 years; and 76% of the patients came from the rural areas. The primary location of the disease was 19.4, 43.9, and 28.9% in upper, middle, and lower third of the esophagus, respectively. Squamous cell histology was identified in 75.6% of the patients, while 18% patients had adenocarcinoma. Undifferentiated carcinoma was found in 6% cases. Most of the patients (54%) were involved in the farming works. Table 1 depicts the various sociodemographic parameters and risk factors of the study patients. Smoking was identified as a risk factor in 48% of the patients with bidi as the most commonly (26%) smoked form of the tobacco, 25% of the patients were addicted to alcohol, while 11% had the habit of chewing tobacco. Only 11% patients were classified as patients without any addiction. Strong associations was observed between smoking and EC (OR = 5.7, 95% confidence interval (CI) = 5.3-6.1). Alcohol abuse was also associated with increased risk of EC (OR = 2.7, 95% CI =2.1-3.3).

Discussion

EC is a disease with poor prognosis with approximately half of the patients presenting with unresectable or metastatic disease, thus cure rate of more than 15% are seldom achieved. Most of the western literature has reported male to female ratio of 4:1. However, in our study, this ratio is 1.15:1, thus indicating a higher incidence of EC in females of northwest India. Using the interactive cancer atlas which is a project of the National Cancer Registry Programme, it was found that highest age adjusted incidence rate of EC (International Classification of Diseases (ICD)-10: C15) in females of India is in East Khaki Hills district of Meghalaya (10.8 per 100,000 population); while for males, it is 9.9 per 100,000 at the same place. However, for males, this figure is highest in Aizawl, Mizoram (26.7 per 100,000). Studies from south India have reported a ratio of 2:1. Another study from western India observed a ratio of 1.4:1. Kamangar et al., reviewed the epidemiological pattern of EC in northeastern India and reported 1:1 ratio in Golestan province. The epidemiologic feature of equally high incidence of EC among females is a rare one; such ratios have also been reported in Linxian, China. One common feature of these areas of the world with 1:1 male to female ratio is high registry reported rate of ≥100 per 100,000 population. Very high risks and this unusual incidence pattern may indicate the presence of a strong risk factor that is shared by both the genders. Thus, it can be inferred that the areas with high prevalence of EC have nearly equal ratio of females and males affected by the disease.
In our study, 3.46% patients were of ≤30 years. It has been found that EC is rare in individuals younger than age 30 in both low and high incidence areas; EC cases in those ≤30 years of age in northern China, northeastern Iran, and the Surveillance, Epidemiology, and End Results (SEER) registries in the US account for 0.7, 1, and 0.5% of cases, respectively. Another Indian study by Chitra et al., also reported similar age patterns with 5% cases below the age of 40 years with majority 62% cases of age group 41-60 year. In the US, the mean age of EC patients at diagnosis is 68 years, while it was 54.6 years in our study. In our study, about two-third of the EC patients were illiterate and half belonged to low socioeconomic status as per the modified BG Prasad scale. Sehgal et al., also reported that the majority (63%) cases were illiterate and 59.5% from lower socioeconomic status. Thus, our data are in agreement with already published literature. The occupation that had highest relation with EC was found to be farming. This may stem from the fact that most of the patients visiting our cancer center belong to the rural area with farming being their main occupation. Another plausible explanation of this observation may be the use of organophosphorus pesticides in farming practices in patients coming from Sriganganagar district of Rajasthan and patients of Punjab and Haryana. However, exact comment on this etiology is not possible in the absence of specifically designed studies investigating the level of organophosphates in the serum of these patients. Such studies will further provide insight into the carnal knowledge of pesticides with cancer.

In our study, 19.4% patients had the malignancy of upper third of the esophagus; 44% patients had middle and 29% had carcinoma of the lower esophagus. In 7.6% of the patients, insufficient data were available to locate the exact site of the lesion. In another study by Giri et al., the percentage of patients with upper, middle, and lower third cancer was 9.66, 40.57, and 49.76%, respectively. In our study, 18% patients had adenocarcinoma, while 75.6% had SCC. In 6.4% cases, the histology revealed undifferentiated carcinoma. Western literature has reported alcohol and tobacco use to the major risk factor for SCC, accounting for 80-90% of the cases. In the present study also, the addiction of smoking was present in the majority (48%) of the patients. Alcohol abuse was reported by 25.3% of the patients. Western reports have also described the relative risk of EC in relation to the amount of alcohol and tobacco consumed, including a relative risk of 155:1 when consuming ≥30 g/day of tobacco with 121 g/day of alcohol. Esophageal SCC risk is 4.2 times higher in current smokers in Europe compared with never-smokers, a meta-analysis showed. Another meta-analysis showed that esophageal AC risk is 2.3 times higher in people with 40+ years of cigarette smoking, compared with never-smokers. In our study, the OR for smoking and risk of EC was estimated to be 5.7. Since 75.6% patients in our study had SCC, our data is

| Table 1: Sociodemographic parameters and risk factors of the study patients |
|-----------------------------------|------------------|------------------|
| **Sociodemographic determinants** | **Number**       | **Percentage**   |
| Age (in years)                    |                  |                  |
| ≤30                               | 127              | 3.46             |
| 31-40                             | 166              | 4.52             |
| 41-50                             | 1,137            | 31.01            |
| 51-60                             | 734              | 20.01            |
| >60                               | 1,503            | 40.98            |
| Gender                            |                  |                  |
| Male                              | 1,961            | 53.47            |
| Female                            | 1,706            | 46.52            |
| Locality                          |                  |                  |
| Rural                             | 2,787            | 76.01            |
| Urban                             | 880              | 23.99            |
| Site of disease                   |                  |                  |
| Upper                             | 711              | 19.38            |
| Middle                            | 1,613            | 43.98            |
| Lower                             | 1,063            | 28.99            |
| Insufficient data                 | 280              | 7.63             |
| Socioeconomic status              |                  |                  |
| Upper                             | 23               | 0.62             |
| Upper middle                      | 237              | 6.46             |
| Lower middle                      | 352              | 9.59             |
| Upper lower                       | 1,271            | 34.66            |
| Lower                             | 1,784            | 48.60            |
| Religion                          |                  |                  |
| Hindu                             | 3,080            | 83.99            |
| Muslim                            | 510              | 13.91            |
| Christian                         | 38               | 1.03             |
| Others                            | 39               | 1.06             |
| Education                         |                  |                  |
| Illiterate                        | 2,426            | 66.15            |
| Literate                          | 1,241            | 33.84            |
| Occupation                        |                  |                  |
| Farmer                            | 1,986            | 54.16            |
| House work                        | 841              | 22.93            |
| Self-employed                     | 223              | 6.08             |
| Laborer                           | 470              | 12.81            |
| Service                           | 147              | 4.01             |
| Histology                         |                  |                  |
| Squamous cell                     | 2,772            | 75.59            |
| Adenocarcinoma                    | 660              | 17.99            |
| Undifferentiated                  | 235              | 6.41             |
| Risk factor                       |                  |                  |
| Smoking                           |                  |                  |
| Cigarette                         | 377              | 10.28            |
| Bidi                              | 963              | 26.26            |
| Combination of both               | 110              | 2.99             |
| Hukka                             | 312              | 8.51             |
| Alcohol                           | 927              | 25.28            |
| Tobacco chewing                   | 403              | 10.98            |
| Betel nut chewing                 | 219              | 5.97             |
| No habit                          | 412              | 11.23            |

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in agreement with the results of these meta-analyses. Esophageal SCC risk is 30-38% higher in people who consume around 1-1.5 units of alcohol per day, 2.6 times higher in those who consume around 1.5-6 units of alcohol per day, and 5.5 times higher in those who consume 6+ units of alcohol per day, compared with never-drinkers.\(^27\)\(^{28}\) Esophageal AC risk is not associated with alcohol drinking overall (versus not drinking).\(^29\)

**Conclusions**

Esophageal carcinoma is one of the important cancers prevalent in northwest India with a relatively higher incidence in females as compared to the findings of other studies. The etiology in majority of patients is linked to tobacco and alcohol, thus, modification of lifestyle with limiting the use of addictions may be an effective strategy in the prevention of this dreaded and mostly incurable disease. A nationwide campaign is required to generate public awareness about this dreaded disease along with identifying the high risk population. Besides, further research is needed to identify the causes of geographical variations in the incidence of EC and its relatively higher incidence in females of northwest India.

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