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Demographic profile of Cancer Esophagus, a study conducted in a tertiary care center, Srinagar, Kashmir, India

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ABSTRACT

Background: - Esophageal cancer (EC) is a highly virulent disease with an aggressive clinical course. It is endemic in many parts of the world, particularly in the developing nations. EC shows one of the widest geographical variations among all malignancies and is the eighth most common cancer worldwide. "Kashmir valley" has a high incidence of EC, which almost parallels the infamous "EC belt" of Central Asia. Squamous cell carcinoma remains the predominant histology of the developing world but over the years, western data suggests an increase in the incidence of adenocarcinoma.

Objective: - The aim of the present study was to analyze the demographic spectrum of esophagus cancers in Kashmir valley.

Material and Method:- This was a retrospective study, So all patients were included who had Histopathologically confirmed esophagus neoplasm registered at Regional Cancer centre of Government Medical College Srinagar Kashmir between 2015 to 2018. All the patient characteristics including age, sex, clinical presentation, anatomical site, histopathological type, stage of the disease and including metastasis, treatment received in each case was studied in detail.

Results:- Total of 122 patients with histopathologically confirmed as esophageal cancers formed the study population, of these 18(15%) cases were upper esophageal cancer followed by 68 patients (56%) in middle esophageal cancer and 36 patients (29%) had lower esophagus cancer(EC), overall majority of patients 71 (58%) presenting stage III followed by 24 cases (19.6%) had stage II. The male to female ratio in esophagus cancers was 1.2:1. The majority of the patients in both the sexes were above 60 years of age. In esophagus cancers dysphagia were the chief complaints in 68% of the patients, followed by odynophagia in 18% of the patients followed melena in 7.4% of the patients however 6.6% presented with recurrent vomiting.

Conclusion: Old age, male sex, within an endemic geographical region seem to be the prime determinants affecting EC prevalence in a given population. Early detection will reduce the number of death of esophagus cancer patients. A significant number of esophagus cancer patients in Kashmir present with locally advanced stage, with dysphagia as a major clinical presentation. Most of the cases were elderly that is more than 64 years of age and about 90% of cases were diagnosed by upper gastro intestinal endoscopy..

Keywords: Esophagus cancer, Demography, Squamous cell carcinoma

INTRODUCTION

Esophageal cancer is the eighth most common cancer worldwide and the sixth most common Cause of cancer death [1]. In Asian countries, it is commonly found in the "*Asian esophageal cancer belt*", bounded by eastern Turkey and east of Caspian Sea through northern Iran, northern Afghanistan, and southern areas of the former Soviet Union, such as Turkmenistan, Uzbekistan, and Tajikistan, to northern China and India. In high incidence areas, the occurrence of esophagus cancer is 50–100-fold higher than that in the rest of the world. The trend of esophagus cancer remains steady in most countries in

recent decades. The disease is rare before age of 40 and incidence peaks at 70–80 years of age according to National Central Cancer Registry of China[2.] In most countries, ESCC is a male-predominant disease. It is the most common malignancy in Kashmir valley [3.] About 87% of all esophageal cancers globally are squamous cell carcinomas (SCC), with the highest incidence rates in populations within south-Eastern and Central Asia, Eastern Africa, and South America. Only 11% of all esophageal cancers are esophageal adenocarcinoma (EAC), with an elevated burden seen in Northern and Western Europe, Oceania, and Northern America[4.] Esophageal cancer staging is currently performed according to the 8th edition of the AJCC manual and follows the TNM classification[5]. .Esophageal carcinoma accounts for approximately 6% of all GI malignancies worldwide with most cases occurring in males, at a rate of 4:1 relative to females[6.]

Various factors, including tobacco consumption, unhealthy diet and diet deficient in trace elements, alkalinity of soil, genetic aberrations, and socio-economic status, have been implicated in the etiology of EC[7]. Low socioeconomic position has been shown to be associated with an increased risk of all these cancers, regardless of whether it is measured by educational level, income, occupation[8]. The outcome of EC has been dismal even with the advent of modern surgical and radiotherapy techniques, targeted molecules and newer chemotherapeutic agents, owing primarily to the late presentation of the disease. This study has been undertaken for a better understanding of the association between clinical profile and disease parameters in patients with cancer esophagus.

Methods

This retrospective study was carried out in the Department of radiation oncology, Government Medical College, Srinagar, Kashmir, India during the period of November 2015 to December 2018. Patients with esophageal cancer carcinoma from all ages and both sexes were included in the study. Clinically suspected esophageal carcinoma subsequently proved to be non-malignant lesions after histological examination; non-Hodgkin lymphoma and other non epithelial tumors of the esophagus were excluded from this study.

A retrospective study was conducted to find the Information regarding age, sex, clinical presentation, anatomical site, histopathological type, stage of the disease and including metastasis. The diagnoses of esophageal cancer performed by upper gastrointestinal (UGI) endoscopy and CECT scan and confirmed by biopsy of tumor. Records of patients who had complete UGI endoscopy examination till the duodenum, presence of tumor in the esophagus and biopsy showing squamous cell cancer, were scrutinized. The tumor was classified according to the World Health Organization classification and the tumor staging was done using TNM classification. Baseline investigations were done to assess the patient's fitness for surgery. Treatment modalities included surgery, neoadjuvant or adjuvant chemotherapy and radiotherapy.

Statistical analysis

Descriptive analysis was used to report the study results. Categorical data were summarized as percentages. We analyzed the cancer characteristics according to age and sex. The aim of the present study was to analyze the demographic spectrum of esophagus cancers in Kashmir valley

RESULT

Total of 122 patients with histopathologically confirmed as esophageal cancers formed the study population. The male to female ratio in gastric cancers was 1.2:1. The majority of the patients (57%) in both the sexes were above 60 years of age; with males and females constituting 54% and 45% of patients in their respective groups. The age group varied from 16 to 80 years with most common age group in esophageal cancer was more than 64 years, followed by age group 45-64years. Less than 45 years were in age group constituted 5% of the cases (6 patients). Majority of patients had ECOG performance score I (48%) followed by II (31%) shown in table 1.

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Table1:- Demographic profile

Age	N	%
<45	6	5
45-64	46	38
>64	70	57
Gender		
Male	62	51
Female	60	49
Performance score		
0	14	11
I	58	48
II	38	31
III	12	10
PRESENTING SYMPTOMS		
Dysphagia	83	68
Melena	9	7.4
Recurrent vomiting	8	6.6
Odynophagia	22	18
Total	122	100%
BMI (*kg/m2*)		
<25	54	44
25-30	46	38
30+	22	18

Clinical presentation, anatomical sites, histological patterns and tumor stage

The duration of symptoms at presentation ranged from one month to 6 month with mean duration of 3 months. In esophagus cancers dysphagia was the chief complaints in 68% of the patients, followed by odynophagia in 18% of the patients followed by melena in 7.4% of the patients however 6.6% presented with recurrent vomiting .There were 122 cases of carcinoma esophagus, of these 18(15%) cases were upper esophageal cancer followed by 68 patients (56%) were in middle esophageal cancer and 36 patients (29%) had lower esophageal cancer shown in table 2. The different sites measured by clinical upper gastro endoscopy and radiological imaging.

Pathologically squamous cell cancer was observed in 98% of the cases and 1% had adenocarcinoma and 1% had sarcoma. According to TNM staging in esophageal cancers, overall majority of patients 71 (58%) presenting stage III followed by 24 cases (19.6%) had stage II and 10 cases (8%) had stage IVb, however 16 patients (13%) were in stage I and 6 patients (3.4%) had stage IVA cancer. In both males

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and females, G2 was the most common histological grade. Overall, liver was the most common presenting site for distant metastasis, followed by lung, and brain metastasis in one patient, as shown in Table 3.

Table 2:-Esophagus site and TNM CLASSIFICATION

Esophagus Site	N	<45		45-64		>64	
		N	%	N	%	N	%
Upper	18(15%)	-	-	6	5	12	10
Middle	68(56%)	4	3	26	21	38	31
Lower	36(29%)	2	2	14	11	20	17
	122(100%)	6	5	46	37	70	58
Gender							
Male	66(54%)	3	2.5	26	21	37	30
Female	56(46%)	3	2.5	20	16	33	27
TNM STAGING							
Stage		I		II	III	IVA	IVB
Total	122(100%)	1(0.8%)		24(19.6%)	71(58%)	16(13%)	10(8%)

Table 3: Correlation of endoscopic level and metastatic site

Endoscopic level	Liver	Lung	Bone
<20	0	1	1
20-25	0	1	0
25-30	1	1	0
30-40	5	0	0

Treatment modalities: - Treatment plan was made according to the stage of presentation assessed by clinical examination, radiological findings. Operability and type of surgery was assessed by the operating surgeon by clinical examination and examination under anesthesia. Neoadjuvant, adjuvant chemotherapy and radiotherapy was given according to protocols.

DISCUSSION

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Esophageal cancer is the eighth most common cancer worldwide and the sixth most common cause of cancer death [1].One of the high incidence areas of the "*Central Asian esophageal cancer belt*" is the Jammu and Kashmir State of India[9].whereas in Asian nations squamous cell cancer continues to be the major histological type[10]. Esophageal cancer is predominantly a disease of the elderly, where nearly one third of the diagnosed patients are more than 75 years of age[11]. The lifetime risk of EC is reported to be 0.8 for males and 0.3 for females and mean age of diagnosis is 67 years[12]. The present study included 122 patients of esophageal cancer. The mean age of presentation was 69 years in the western population. Most common age group in esophageal cancer was age of >64years. Our study was similar to a study conducted by **Chen WQ et al[2] that**, the risk of esophageal cancer increases with age; the median age at diagnosis for esophageal cancer is 70. In our study both male and females presented in elderly age group.

Esophageal cancer incidence rates vary wildly between men and women and across different countries a study conducted by Blot WJ et al, that Esophageal carcinoma accounts for approximately 6% of all GI malignancies worldwide with most cases occurring in males, at a rate of 4:1 relative to females[10] .The present study was similar that the male to female ratio in esophageal cancers was 1.2:1. Dysphagia is one of the earliest and predominant presenting symptoms of EC[13]. Nearly 68% of the patients in our study had dysphagia as the most common presenting symptom though patients with tumor located 20-30 cm and 18% of patient presented predominantly with odynophagia with tumor located 30-40cms. Cancer esophagus is invariably associated with weight loss in nearly two-thirds of patients[14]. 70% of our patients had associated weight loss.

Nearly three-fourths of all adenocarcinoma (ADCs) are found in the distal third of esophagus, whereas SCCs are more evenly distributed throughout the distal two-thirds[15] **,** however, in our study, distal one-third (30-40 cm) was the most common site in both the sexes. Higher incidence of distal EC in west may primarily be attributed to a higher incidence of ADCs. SCC still is the predominant histological subtype in Asian nations where most of the cases occur in middle or lower third[12]**.** Only 2 cases of ADCs and 2 cases of sarcomas were registered in our study population.

In a study conducted on nearly 400 EC patients in Japan, two most frequent morphological types were "ulcerative localized" and "ulcerated infiltrative" type (JSED Types 2 and 3)[16].The appearance of lesions during endoscopy has been reported to be helpful in assessing the likelihood of lymph node metastasis. In particular, flat lesions are said to metastasize less likely to a lymph node than a depressed or elevated lesion[17] **.** In our analysis, ulcerative localized was the most common morphology and SCC was the most common histology in all the stages implying no correlation between endoscopic morphology and stage. Histological grade is known to affect lymph node metastasis. In a study by Bollschweiler *et al.*[18] it was reported that G1/G2 histology was associated with a lower rate of lymph node metastasis compared with G3 in early EC. Our analysis revealed G2 to be the most common tumor grade overall, with the majority of G2 patients in Stage III.

Approximately one-third of EC patients are loco-regionally advanced at presentation[13]. Stage III was the most common presenting stage in our study with around 58% patients. Close analysis revealed that 80% of esophageal cancer presented with advanced Stage (III and IV) .

Obesity is a growing problem in modern societies and has been associated with a range of diseases, .A few study reveals that BMI >30 have a 3-fold risk of cancers of the esophagogastric junction, and esophagus. Majority of patients in present study had BMI <25 , It is unlikely that in this study BMI measurement or recall was impacted by disease development because BMI was queried soon after diagnosis and was defined based on usual adult weight excluding the year before diagnosis.

Limitations

The limitations of our study are, more often the patients are referred to outside state, and most of patients were registered and treated at other cancer center Skims, Kashmir valley. Hence, our study group may not exactly reflect the prevalence and incidence of esophagus cancer in the whole population in this region. Despite these limitations, our institution being a major oncological center in

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this region, it may reflect the nature of the disease burden in this population and emphasizes the significance of early diagnosis by proper and timely evaluation, and management of the disease.

Conclusion

Old age, male sex, within an endemic geographical region seems to be the prime determinants affecting EC prevalence in a given population. Early detection will reduce the number of death of esophageal cancer patients. A significant number of esophagus cancer patients in Kashmir present with locally advanced stage of disease, probably due to late clinical presentation. In our centre, major clinical presentation was dysphagia and weight loss. Most of the cases where diagnosed by upper gastro intestinal endoscopy .Esophagus cancers are observed at an elderly age group that is more than 64 years of age. People should be educated for an early consultation for symptoms and high risk individuals should be encouraged for screening. The health programs about esophagus cancer should be carried out in open places to give more information about this cancer to the public.

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