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RESEARCH ARTICLE

SOCIODEMOGRAPHIC, CLINICAL AND PATHOLOGICAL PROFILE OF ESOPHAGEAL CANCER IN A TERTIARY CARE CENTER

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ABSTRACT

Background: Esophageal cancer (EC) is a highly virulent disease with an aggressive clinical course. It is an 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. **Aim and Objective**: To analyze the clinicoepidemiological profile of EC in Kashmir. **Materials and Methods**: Profile of 345 patients, who presented to our outpatient department between July 2016 and July 2020, was analyzed, in a cross-sectional study with regards to their demographic and clinical profile. **Results**: EC is still a predominant disease of developing nations, affecting mostly the elderly and rural population. Advanced disease is seen mostly in the population of low socio-economic status and males outnumber females at every stage of the disease. Various demographic parameters seem to affect the presenting stage of the disease. **Conclusion**: Old age, male sex, and low socio-economic status coupled with peculiar dietary habits within an endemic geographical region seem to be the prime determinants affecting EC prevalence in a given population. **Key words**: Epidemiology, Esophageal cancer, Incidence, Kashmir valley

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INTRODUCTION

Esophageal cancer (EC) is the eighth most common cancer worldwide with a case fatality rate of 90% (Kamangar *et al*., 2006). It is one of the malignancies with highest geographic, ethnic, and gender variations (Corley and Buffler, 2001). The high incidence areas of Linxian, China, Russia, and the Caspian region of Iran report incidences as high as 100/100,000 persons, whereas it is relatively uncommon in the United States, where the lifetime risk of being diagnosed with the disease is reported to be <1%(3).In India, in states such as Karnataka, Tamil Nadu, Kerala, and Assam, EC is the most common gastrointestinal (GI) malignancy (4). EC has a high prevalence in Kashmir valley, but there are no population-based data available on its incidence (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). It is the most common malignancy in Kashmir valley (7).

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Overall squamous cell carcinoma (SCC) is the most prevalent histology of EC worldwide (8,9) but the last 20 years have witnessed an increase in the incidence of adenocarcinoma (ADC). This increase is more rapid than that for any other cancer (10). There has been no consensus on the exact role of risk factors as causative agents in EC. 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(11,12). SCC is predominantly seen in upper two-thirds of esophagus unlike ADC, which is seen in lower one-third. 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 risk factors, clinical profile, and disease parameters in patients with cancer esophagus

MATERIALS AND METHODS

This study was conducted in the Department of Radiation Oncology, Government Medical College Srinagar, from July

2016 to July 2020. A total of 345 patients who had histological documentation of EC were enrolled in the study. Data were then analyzed for clinico-demographic information such as age, sex, residence, dietary habits, tobacco or alcohol consumption, performance score, presenting symptoms and signs, and their correlation with disease parameters such as tumor location, histology, endoscopic morphology, grade, and stage of the disease. Patients were staged clinically or pathologically depending on the surgical status. Staging investigations included endoscopy, endoscopic ultrasound, and contrast-enhanced computed tomography scans including appropriate metastatic evaluation wherever indicated. TNM American Joint Committee on Cancer 2011 classification system was used for staging. Endoscopic morphology of the tumors was classified according to the "Guidelines for Clinical and Pathologic Studies on Carcinoma of the Esophagus."(13).

RESULTS

345 patients with histological documentation of EC were enrolled over a period of 4-year from July 2016 to July 2020. The study included 212 males (61%) and 133 females (39%) in the ratio of 1.5:1. Median age of the patients was 62, and mean age was 58 years. The majority of the patients (51%) in both the sexes were above 60 years of age; with males and females constituting 52% and 50% of patients in their respective groups. 268 (77%) patients were from a rural background, of these 156 (58%) were males and 112 (42%) females. Around 45% patients belonged to "Kuppuswamy Socio-economic Class" scale (KSS) IV and V,(14). which was statistically significant (0.002). Non vegetarian diet was consumed by 339 (98%) patients of whom 208 (61%) were males and 131 (39%) females, and the association was statistically significant (P = 0.003). 60 patients (18%) consumed smoked meat. 288 (83%) patients consumed tobacco of which 194 (67%) were males and 94 (33%) females; 235 (81%) belonged to rural areas while rest 53 (19%) to urban areas. 36 (12%) patients consumed more than one form of tobacco. In all the forms of tobacco consumption, males outnumbered females except "hookah" smoking which was prime mode of tobacco consumption in 57% females which was significant statistically (P = 0.0002). Only six (0.01%) patients consumed alcohol of which none was female. The majority of the patients in both the genders; 98 (46%) males and 70 (52%) females had "Eastern Cooperative Oncology Group" performance score (PS) of "I" at presentation (Table 1). Overall dysphagia was the most common presenting symptom in both the sexes (78%), with 162 (76%) males and 109 (81%) females but patients with tumors located<20cm had odynophagia as the prominent symptom (57%) (Table 2). Weight loss was the most common finding in males 129 (60%) as well as females 75 (56%) (Table 3). Overall lower one-third (30-40 cm) was the most common site of disease location in both the sexes accounting for 161 (46%) of the total patients (which included 97/212 [45%] males and 64/133 [48%] females). Endoscopic morphology as classified by "JSED" revealed 5 males and 4 females in superficial carcinoma (tumor limited to mucosa, submucosa, and in-situ carcinoma) and 336 patients (207 males and 129 females) in advanced carcinoma. Of the advanced carcinomas, majority (171) (50%) patients had "ulcerated and localized" morphology. Ulcerative localized was the predominant morphology in all the stages (44%, 58%, 49%, and 48% in Stages I, II, III, and IV, respectively).

Table 1. Patient characteristics

Patient parameters	Male	Female
Gender	212	133
Age		
<40	7	2
40-60	94	65
>60	111	66
Residence		
Rural	156	112
Urban	56	21
Dietary habits		
Smoked non-veg	47	13
Cooked non-veg	161	118
Dried veg	1	1
Cooked-veg	3	1
Tobacco consumption		
Cigarette	54	0
Hookah	79	77
Snuff	30	12
Combination	31	5
No consumption	18	39
Alcohol consumption		
Yes	6	0
No consumption	206	133
Performance score		
0	60	33
I	98	70
II	52	26
III	2	4

Table 2. Patient symptomology

Presenting symptoms	<20	20-25	25-30	30-40
Odynophagia	19	8	1	0
Vomiting	2	4	8	3
Dysphagia	11	15	100	145
Hamatemesis	0	5	8	1
Malena	0	1	2	6
Loss of appetite	1	3	1	1

Table 3. Correlation of clinico -demographic profile with stage

Patient Parameters stage I	stage II		stage III	stage IV
Gender				
Male	25	41	114	32
Female	18	60	42	13
Residence				
Rural	28	68	136	36
Urban	15	33	20	9
Socio-economic class				
I	11	11	7	8
II	14	31	28	5
III	9	27	43	6
IV	5	26	55	19
V	4	6	23	14
Presenting sign				
Anemia	14	27	53	9
Clinical lap	0	0	13	9
Weight loss	29	74	90	11
Abdominal lump	0	0	0	16
Endoscopic level				
<20	4	11	15	3
20-25	7	12	13	4
25-30	12	46	47	15
30-40	20	32	81	23
Histological grading				
G1	27	29	20	2
G2	6	55	104	15
G3	10	17	31	26
G4	0	0	1	2
Endoscopic appearance				
0-I	4			
0-II	2	1		
0-III	1	1		
Protruding	9	12	40	5
Ulcerative and localized	16	58	77	21
Ulcerative and infiltrating	7	15	22	8
Diffusely infiltrating	4	14	17	11

Table 4. Correlation of endoscopic level and metastatic level

Endoscopic level		Liver	Lung	Bone	Brain
<20		0	1	1	1
20-25		0	2	2	0
25-30		3	10	2	0
30-40		19	4	0	0

SCC was the most common histology with 340 patients, and only 5 patients had ADC. Overall Stage III was the most common presenting stage with a total of 156 (45%) patients, comprising of 114 (53%) males and 42 (31%) females. 136 patients (87%) of the Stage III patients were from a rural background and over half 136 (51%) of patients from rural background had Stage III disease while as, majority 33 (43%) of urban patients had Stage II disease. Males predominantly presented with T3 disease (42%) while females with T2 disease (51%). N1 was the predominant nodal stage in males (46%) as well as females (67%). Stage IV was more common in, males (15%), rural population (13%), and patients with "KSS" scale of IV and V (Table 3). On the whole, liver was the most common presenting site for distant metastasis with 22 (49%) patients, followed by lung 16 (38%), bone 5 (11%), and brain metastasis 1 (0.02%) patients. 19 (87%) of the patients with liver metastasis had a primary site located at 30-40 cm (Table 4).

DISCUSSION

The incidence of EC is rapidly increasing worldwide(15). Nearly two third of ECs in the United States are ADCs,(16) whereas in Asian nations squamous cell cancer continues to be the major histological type(17) Esophageal cancer is predominantly a disease of the elderly, where nearly one third of the diagnosed patients are more than 75 years of age(18).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(19). The majority of the patients in our study were above 60 years age in both the sexes, with males outnumbering females in all age groups. About 90% of ECs worldwide occur in defined high incidence areas of low and middle-resource countries and economically deprived communities (20). Most of the patients in our study were males, from a rural background with a low socio-economic status. Dysphagia is one of the earliest and predominant presenting symptoms of EC (21). Nearly 80% of the patients in our study has dysphagia as the most common presenting symptom though patients with tumor located <20cm presented predominantly with odynophagia. Cancer esophagus is invariably associated with weight loss in nearly two-thirds of patients (22). 60% of our patients had associated weight loss.

Nearly three-fourths of all ADCs are found in the distal third of esophagus, whereas SCCs are more evenly distributed throughout the distal two-thirds; (23) 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 (23). Only five cases of ADCs 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(24).

Association of macroscopic appearance with histological types and subtypes was drawn, with polypoid types of "protruding superficial" and "advanced malignant" tumors reported to be "carcinosarcomas," "SCC" or "malignant melanomas." Plateau types of protruding tumors were usually "basaloid squamous" cell carcinomas, "adenoid cystic" carcinomas, "poorly differentiated" SCCs or ADCs. Predominantly, subepithelial types of protruding tumors were found to be small cell type undifferentiated carcinomas, basaloid SCCs or adenoid cystic carcinomas (24). 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 (25). 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., (26) 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. Low socio-economic status and general deprivation have been proposed to be one of the many factors for high incidence of EC in Asian nations (20). Close to half of the patients (44%) in our study had KS of IV and V and 88% of these (KS IV and V) patients were from rural background. Approximately one-third of EC patients are loco-regionally advanced at presentation (16). Stage III was the most common presenting stage in our study with around 45% patients. Close analysis revealed that 85% of the total advanced Stage (III and IV) patients came from rural areas.

Lymph node metastasis in the range of 0-3%(27) and 26-50%(28,29) have been seen in esophageal SCC invading the mucosal (T1a) and submucosal (T1b), respectively, whereas the rate of nodal involvement is 0-2% in cases of esophageal ADC invading the mucosa (T1a) and 27- 41% in ADC with submucosal invasion (T1b)(30,31). Lymph node metastasis is the single most important prognostic factor in EC (32). Evaluation of the lymph node metastasis risk in association with the invasion depth was previously deemed necessary to predict prognosis and decide on the therapeutic modality (28,30). The prevalence of nodal metastasis has been seen to correlate with T status and as per one data >50% nodal metastasis was seen with T2 invasion and all patients had lymph node metastasis with T4 invasion (33,34). In our study also, nodal stage was seen to increase with increasing T stage (T1 = 22%, T2 = 65%, T3 = 82%, and T4 = 100%). In the absence of nodal metastasis, the prognosis of EC has been seen to be related to T stage, histology, grade, and location of the tumor (25). Relevant to our data, most of the Stage IV patients were men with distal esophagus being the most common site and liver being the most common site of metastasis. Patients having T3 and T4 disease were the most common among Stage IV cases. We could not elucidate correlation between genetic factors and premalignant conditions with disease parameters of our patients due to lack of proper evidence for the same (35,36).

CONCLUSION

Old age, male sex, and low socio-economic status coupled with peculiar dietary habits within an endemic geographical region seem to be the prime determinants affecting EC

prevalence in a given population. The fact that improvised treatment modalities have not changed the outcome of EC necessitates focusing on primordial prevention and early detection at a genetic level as the majority of patients still present with a locally advanced or advanced stage. The role of clinical and demographic parameters depicts mixed results when compared with data elsewhere. Old age, male sex, low socio-economic status, smoking and non-vegetarian diet, positive correlation of T stage with N and M stage, proclivity of distal EC for distant metastasis were the variables consistent with other literatures, whereas increasing incidence of ADC, higher stage with increasing grade of tumor, association of endoscopic morphology with disease stage, prevalence of premalignant pathologies were non-corroborative with world literature

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