OESOPHAGEAL CANCER IN NORTHERN AREAS OF PAKISTAN

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Background: Oesophageal carcinoma is the leading cause of death from cancers. Most of the oesophageal carcinomas are either squamous cell carcinomas or adeno-carcinomas. The cervical oesophagus is an uncommon site of the disease. There is an increase of 15–20 percent mortality rate over the past two to three decades, during which time the histologic pattern of the disease has also changed significantly. **Objective:** The objective of this study was to see the incidence of oesophageal carcinoma in different sex and age groups, in the Northern Areas of Pakistan. **Method:** This was a retrospective study over a period of 7 years which was designed to assess age and sex incidence for oesophageal carcinoma in Northern Areas of Pakistan. A total of 69 already diagnosed carcinomas of the oesophagus were included in the study, all these cases were from Malakand Division of Northern Pakistan. All specimens were stained and examined microscopy. The demography of the disease and type of carcinoma were evaluated. **Results:** Out of 69 diagnosed cases of oesophageal carcinomas, squamous cell carcinoma was the found in 64 (92.5%) while adenocarcinoma was seen in 5 (7.5%) cases. Out of 64 squamous cell carcinomas, moderately differentiated carcinomas were the most common 34 (49.2%). **Conclusion:** Most of the oesophageal carcinomas were squamous cell carcinomas and were mostly biopsied from the lower 1/3rd of the oesophagus. The mean age of patients was 42 years in males (M) and 53 years in females (F). F:M was 1:3. All patient presented in advanced stage with dysphagic symptoms. No *in situ* or mucosal carcinoma was identified in this study. Radiological assessment also showed late stages of the disease.

Keyword: Oesophageal carcinoma, incidence, type, demography

INTRODUCTION

Most of the oesophageal carcinomas are either squamous cell carcinomas or adeno-carcinomas.[1–3] It is the 7th leading cause of death from cancers in America.[1] On rare occasions other carcinomas, melanocarcinomas, carcinoid may develop in the oesophagus as well.[1,2] Approximately three quarters of all adenocarcinomas are found in the distal oesophagus, whereas squamous cell carcinomas are more evenly distributed between the middle and lower third.[1–3] Oesophageal carcinoma is the most common tumour in African Bantus[3]. Squamous cell carcinoma is more common in china and other oriental countries.[2–4] The cervical oesophagus is an uncommon site of the disease. [1–4]

The pathogenesis of oesophageal cancer remains unclear.[2,3,5] Data from studies suggests the oxidative damage from factors such as smoking or gastro-oesophageal reflux, which causes inflammation, increase cell turnover and may initiate a carcinogenic process[1]. Once cancer develops it may spreads rapidly. The sub-mucosal cancers (T1) are seen in 14 to 21% of patients, while involvement of muscularis proper (T2) is seen in 38 to 60% of patients, in which most carcinomas are associated with positive lymph nodes.[1,4] At the time of diagnosis more than 50% of patients have either un-resectable tumour of or have radio-graphically visible metastasis.[1] Early *in situ* carcinoma have five year survival rate of up to 83.5%, intra-mucosal 79.4% and sub-mucosal carcinomas show a five year survival up to 16.3%.[1,6] Radiological early mucosal lesions can be identified by stiffening of the mucosa and failure to collapse completely once the peristaltic wave has passed.[7]

Smoking is associated with an increased risk of both squamous cell carcinoma and adenocarcinoma of the oesophagus. Nitrosamines in contact with the oesophageal mucosa directly correlates with the amount and duration of smoking.[1,4–6] Other risk factors for squamous cell carcinoma includes alcohol, gastro-oesophageal reflux, achalsia, caustic injury to the oesophagus, tylosis, Plummer-Vinson syndrome, history of head and neck cancer, history of breast cancer treated with radiotherapy and frequent consumption of extremely hot beverages.[2,3,6] Genetic abnormality of chromosome 17q25 has been strongly associated with squamous cell carcinoma.[3] Beside the smoking other risk factors for adenocarcinoma of the oesophagus includes Barrett's oesophagus, obesity, radiation therapy for breast cancer and use of drugs which relaxes the oesophageal sphincter such as beta-blockers, anti-cholinergics and aminophyllines.[1,5,6] Genes and their protein products that may have a role in the development of this cancer includes cyclooxygenase2,

Bd-2, p53, p16, p27, cyclin D1,Rb gene, erb-b2, α-catenin, and β-catenin.[1,2,6]

There is an increase of 15–20 percent mortality rate over the past two to three decades, during which time the histologic pattern of the disease has also changed significantly.[1,3,6] It has been noted for unexplained reasons that the incidence of squamous cell carcinoma is decreasing while that of adenocarcinoma has increased significantly.[1,2,5,6]

Patients of carcinoma oesophagus generally presents for dysphagia or odynophagia at the time of diagnosis. Symptoms of weight loss, dyspnoea, cough, hoarseness of voice and retrosternal pain reflect presence of extensive un-resectable stage of carcinoma oesophagus.[1–3,5] Similarly signs of pleural effusion, hepatomagaly or left supra-clavicular lymph-adenopathy indicate advance stage of the disease.[1,3]

Diagnosis is generally made by endoscopic biopsy or barium meal swallow or CT scan. The over all prognosis is poor and survival rates of 4–14 years have been noted in different studies.[1,7,8]

MATERIAL AND METHODS

Sixty-nine already biopsy proven cases of oesophageal carcinoma were included in this study. All were endoscopic biopsies done over a period of seven years (2001–2008). The specimens were received in 10% formalin. These were further processed in formalin, dehydrated in alcohol, cleared in xyline and then embedded in paraffin wax. Four micron thick sections were taken, stained with hematoxylin and eosin (H & E). All the slides of the relevant cases were reviewed. The relevant data of age, sex, histological type and grade of the carcinoma were recorded from the laboratory data. The H&E stained slides were re-assessed microscopically. Major complaints of the patient were noted from the laboratory request forms.

RESULTS

Out of 69 oesophageal carcinoma cases, squamous cell carcinoma was the found in 64 (92.5%) patients while adenocarcinoma was seen in 5(7.5%) of patents which are more elaborated with grads in Table-1. Out of 64 squamous cell carcinomas, moderately differentiated carcinomas were the most common 34 (49.2%).

Table-1: Types and grade of oesophageal carcinoma

Histological types and grades	Number	%
Squamous cell carcinoma	**64**	**92.5**
Well differentiated squamous cell Carcinoma	17	24.6
Moderately differentiated squamous cell Ca	34	49.2
Poorly differentiated squamous cell Ca	13	18.8
Well differentiated Adenocarcinoma	**5**	**7.2**

Table-2: Demography of oesophageal Carcinoma

Site of involvement by Ca	Number	%
Upper third	2	2.8
Middle third	13	18.8
Lower third	54	78.4
Total	69	100

Most common site of involvement for oesophageal carcinoma was lower 1/3rd 54 (78.4%). This includes both squamous cell and adenocarcinomas.

Table-3 shows that female to male ratio for carcinoma oesophagus is 1:3, and is seen at earlier ages in male as compared to female. Mean age for male was 42 yrs and for females it was 51 yrs.

Table-3: Age and sex distribution

Age Groups (Yrs)	Squamous cell Ca		Adenocarcinoma	
	Male	Female	Male	Female
11–20	-	-	-	-
21–30	-	-	-	-
31–40	14	2	-	-
41–50	25	3	2	
51–60	6	6	-	1
61–70	2	5	-	2
71–80	-	1	-	-

DISCUSSION

There is wide variation in the demography of the tumour as well. The tumour is located in the proximal third in 6%, middle third in 21%, and distal third in 73% of the patients.[6] In an another study involvement of upper third was 1.18%, mid third 9.4% and lower third including gastro-oesophageal junction was 89.3%.[9]

Squamous cell carcinoma is the most common malignancy of esophagus.[2,3] There is marked geographical variation in its incidence.[2] The incidence of adenocarcinoma is on the rise in western countries and America.[6,8] In one study 73% adenocarcinomas were noted versus 37% squamous cell carcinomas.[10] Good prognosis is seen in the well differentiated cancers and in early lesions.[6,11–13]

Over the last decade an epidemiological change have been noted in the pattern of oesophageal cancer in western world, i.e., the incidence of adenocarcinoma now exceed that of squamous cell carcinoma.[6] Adenocarcinoma of the oesophagus and gastro-oesophageal junction are rapidly increasing in incidence and have a well described sequence of carcinogenesis: Barrett's metaplasia-dysplasia-carcinoma sequence.[12]

Mean age varies in different studies, from 55.5 years[5], 63.1 years[2], to 67 years[11]. There is wide variation in female to male ratio of squamous cell oesophageal carcinoma, and is seen from 1:1.6[2] to 1:9.8[3]. In case of adenocarcinoma the incidence F:M was 1:6.4.[2]

For detection of early lesions (*in situ* and mucosal carcinoma) any leukoplakia or Barrett

oesophagus should be biopsied or assisted by radiological procedures.[7,14] In one study it was pointed out that increasing incidence of late stages of carcinoma is at least partly a consequence of failed medical approach to the precursor conditions of gastro-oesophageal reflux disease and Barrett's oesophagus.[15] Interpretation of biopsies is considerably enhanced if these are taken with larger forceps.[16]

In our study all the patients presented in advanced stages of the disease and clinically for dysphagia. Those who were assisted by barium meal swallow and CT scan, also revealed late stage of the disease. Squamous cell carcinoma was the most common type (92.7%). We found that 2.8% carcinomas were in the proximal third of the oesophagus, 18.8 % in the middle third and 73.2% in the lower third of the oesophagus. Female to male ratio was 1:3. The mean age incidence for male was 42 years and for female it was 53 years. In situ or mucosal carcinomas were not noted.

CONCLUSION

In the northern areas of Pakistan the squamous cell carcinoma is the commonest malignancy of oesophagus and presents generally at later stages of the disease. It most commonly affected the lower third of the oesophagus. It presented at an earlier age in males (mean age 42 yrs) as compared to female patients (mean age 53 years).

There was not a single case of *in situ* or mucosal carcinoma in our study which could be due to infrequent endoscopic biopsies for oesophageal problems.

RECOMMENDATION

Oesophageal carcinoma had its earlier appearance in male patients as compared to the females in the northern areas of Pakistan, could it be attributed to dipping snuff or exposure to some other carcinogen. We recommend an epidemiological study for such an early age onset in male patients in this area.

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