Retrospective Review of Esophageal Carcinoma: 3-Year Experience from a Tertiary Care Teaching Institute

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ABSTRACT

Introduction: Esophageal carcinoma, one of the common malignancies, generally presented in advanced stage makes these neoplasms less curable and highly lethal. Having such poor prognosis, it is significant to understand various patient and tumor facts related to treatment outcome of esophageal cancer, which varies regions wise. The present retrospective study also seeks to focus on current description of patterns and trends of tumors in esophageal cancer patients attended in a tertiary care hospital in a northern state of India and their treatment outcome.

Materials and Methods: Records of esophageal carcinoma patients over a period of 3-years were reviewed retrospectively. These records were analysed for incidence, demographic pattern, different treatment modalities and their response evaluation.

Results: A total 439-patients of esophageal carcinoma were identified. The median age at presentation was 47-years and males slightly outnumbered females. Among all the tumors, lower thoracic esophagus involvement was most predominant and most common presentation was dysphagia. Squamous cell carcinoma constituted the predominant histopathological type. Majority of patients presented in advanced stage and treated with combined modalities approach of radiation therapy, chemotherapy and surgery. Overall average survival was 13-months. Clinically, the response at last follow-up was CR in 19%, PR and PD in 33% each.

Conclusion: Despite its high prevalence in north India and poor survival rate, less initiative has been taken to increase awareness in preventing these cancers. Understandings of socio-demographic patterns and tumor characteristics may improve treatment outcome in these patients and improve quality of life. Further studies are needed in different regions of India, to get more treatment options which may convert the current scenario of palliative intent in to radical one in patients of esophageal carcinoma.

Keywords: Esophageal carcinoma, retrospective study, socio-demographic profile, dysphagia, squamous cell carcinoma

INTRODUCTION

Esophageal carcinoma is not among the uncommon cancer occurring in world. It has a higher incidence to mortality ratio, despite the fact that multidisciplinary approach has been taken in management of these cancers. Along with cancer management by combined modalities of surgery, radiation and chemo therapy; care of nutrition status of patient is of paramount importance to improve quality of life. To outline a good treatment strategy in patients of esophageal carcinoma, it is important to know region wise different socio-demographic profile and tumor characteristics and their impact on treatment...
outcome. A few studies in different regions of India have already investigated these parameters in patients of esophageal cancer. The current study also focuses on patients of esophageal cancer presented in the department of radiation oncology in a tertiary care teaching hospital of Haryana to analyse their socio-demographic profile, tumor characteristics, different treatment schedules and their impact on survival rates.

MATERIALS AND METHODS

We retrospectively reviewed records of the patients with esophageal cancer who registered in Department of Radiation Oncology PGIMS Rohtak, Haryana, a tertiary care teaching hospital and regional cancer centre over a period of 3-years from January 2016 to December 2018. Records were analysed using software (MS Excel 2016) to obtain socio-demographical profile in terms of age, gender, origin, addiction status and tumor characteristics like histopathological subtypes, sites of primary lesion & different presenting symptoms and different treatment schedules with regard to surgery, radiation therapy, chemotherapy or combined modality along with their response evaluation.

RESULTS

Total 439-patients of esophageal cancer were registered, which constituted approximately 4.2% of total cancer patients in above hospital. The age of the patients ranged from 23 to 88 years with median age at presentation being 47-years. Greater part of the cases (53%) was seen in fifth and sixth decade of life (table 1). Overall, male (n=300) predominance was seen, male to female ratio being 2.1:1. The year wise distributions among both sexes were displayed in figure 1.

<table>
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<tr>
<th>Table 1: Distribution of Patients according to age</th>
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<td>Age groups (years)</td>
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Figure 1: Year-wise distribution of esophageal carcinoma among male and female

Majority of the patients belonged to rural origin, rural to urban ratio being 4:1 and 70% (n=310) of the total patients, irrespective of gender, were farmer. In general, 69% patients had a history of tobacco intake in the form of bidi or hookah smoking, while 47% were alcoholic; only 16% patients were recognized as having no addiction (figure 2).
Mean duration of symptoms was four months. Dysphagia was the most common presenting symptoms (85%) followed by vomiting (12%) and loss of weight (8%). Histopathologically, squamous cell carcinoma (87%) constituted the largest group followed by adenocarcinoma (11%). A few rare neoplasms (2%) were also encountered like 4-cases of small cell neuroendocrine tumor, 3 cases of gastrointestinal stromal tumor (GIST) and 1-case each of lymphoma (esophageal mucosa-associated lymphoid tissue lymphoma) and angiosarcoma, which are treated as per rare entity clinical trial. Lower thoracic esophagus including gastroesophageal junction was the commonest site of presentation (43%) followed by middle thoracic and cervical esophagus in 29% and 22% cases respectively (figure 3).

At the time of initial presentation 110-patients (25%) were locally advanced and 97-patients (22% of total) had metastatic disease. Most common metastatic site was liver and lungs (9% each).
patients (n=197) and 92-patients (21%) received definitive concurrent chemoradiation. Among the 197-patients received induction chemotherapy, 96-patients (22% of total patients) underwent radical surgery and 90-patients received definitive chemoradiation. 150-patients (34% of total patients), having poor performance status, were considered for palliative therapy at initial evaluation and 124-patients among them (28% of total patients) and 7-patients of induction chemotherapy recipient group received palliative radiotherapy. 9-patients did not report for treatment after initial evaluation and rest of the patients (n=17, 4% of total patients) received only palliative chemotherapy. Radical dose used predominantly was 40 gray in 20 fractions over 4-weeks. Palliative schedule was given either 20 gray in 5 fractions over 5 days, 30 gray in 10 fractions over 2-weeks or 8 gray single session mainly in very poor general condition. Most common concurrent chemotherapeutic drugs used were intravenous 5-flourouracil and platinum compound (carboplatin or cisplatin), whereas combination chemotherapy with paclitaxel plus carboplatin regimen was used in neoadjuvant and palliative only settings.

Overall average survival was 13-months. Clinically the response at last follow-up was as follows: CR in 19%, PR & PD in 33% each and death in 13% patients (figure 4). In view of the progressive disease and poor general condition of the patient, 16% were given therapeutic trial with oral cyclophosphamide tablet. Among all, 74-patients need feeding jejunostomy in due course of disease for survival.

**DISCUSSION**

Esophageal carcinoma, one of the common malignancies, creates a major concern for the oncologist due to its less curable rate. It is ninth most common cancer constituting 3.1% of all cancer cases and sixth most common cause of mortality constituting 5.5% cancer related deaths worldwide in 2020. [1] In India esophageal cancer ranks fifth in incidence and mortality with 4.8% and 6.9% respectively in 2020. [2] In the last few decades, there is a changing trend in the incidence and pattern of esophageal cancer. In the developed nations of western region, there is a slight decrease in total incidence of esophageal cancer and the main burden has changed from more squamous cell carcinoma to more adenocarcinoma. [3] This change in histopathological patterns attributed to certain factors, like high body mass index, obesity and increase cases of gastro-esophageal reflux disease. Whereas in developing countries like India and other
Asian countries, incidence of esophageal cancer is still in rising trends and although cases of adenocarcinoma have increased, still squamous cell carcinoma contributes the lion’s share. Some rare histopathological subtypes like small cell carcinoma, sarcoma, adenoid cystic and mucoepidermoid carcinoma, melanoma and gastro-intestinal stromal tumor also occurred in esophagus with very less incidence, but clinically these are indistinguishable from typical squamous and adenocarcinoma. Different risk factors, both modifiable and non-modifiable, contribute to the development of esophageal carcinoma; most dreaded of which is smoking. Smoking is a risk factor for both squamous and adenocarcinoma, alcohol added synergistic effect to it; 90% of squamous and half of adenocarcinoma occurs due to excessive smoking. Other modifiable risk factors include chronic exposure to irritants, excessive intake of pickled vegetables, alcohol, soft drinks and spicy foods, obesity; whereas age, gender, genetical predisposition are immutable risk factors. Published article on Indian population showed that socioeconomic status has a dramatic impact on esophageal cancer, poor socioeconomic status with low body mass index (BMI) contributes more to squamous cell carcinoma while rich socioeconomic status leading to high BMI and obesity causes more adenocarcinoma. Overall, incidence of esophageal carcinoma increases with ages, people in their 6th and 7th decades are more affected with an appreciable male predominance and this was well proved on patients of Indian origin.

Progressive dysphagia is most common complaint, leading to considerable weight loss, generalized weakness. Advanced stage diseases may present with neck node involvement, hoarseness of voice, recurrent lung infection due to trachea-esophageal fistula and sometimes even with signs of distance metastasis. Dysphagia for long time leading to poor nutritional status is a major cause for apprehended outcome in most of these patients. At the time of initial presentation, more than half patients presented with metastatic disease, half of the rest have locally advanced disease and less than 20% presented with curable disease. Overall regional nodal involvements in esophageal cancer differ in squamous and adenocarcinoma. Cervical, thoracic and abdominal, all stations can be involved in both histology types depending upon tumor location and stage of primary lesion. Common sites of distant metastasis are liver, lungs and bones; adrenal gland and brain metastasis are also seen in a few patients. Contrast enhanced computed tomography of thorax and abdomen (CECT) and endoscopic ultrasound (EUS) are the two most common diagnostic modalities having good positive predictive value in assessing accurate T (primary tumor) and N (regional node) stage as well as to guide for biopsy for tissue confirmation; whereas whole body fluorine-18-labelled fluorodeoxyglucose positron emission tomography with computed tomography (PET/CT) scan is mandatory for metastatic workup and post-chemotherapy response assessment.

Management of esophageal carcinoma is a multidisciplinary approach, definitive surgery with or without chemoradiation therapy remains the curative treatment. Endoscopic resection in very early mucosa-limited lesion showed calculated 5-year survival rate of 98%. For resectable locally advanced lesion, esophagectomy is the mainstay of treatment, choice of transthoracic or transhiatal depends upon surgeon. For unresectable locally advanced cases, chemoradiation is the standard of care, it may be followed by radical surgery if possible. Radiation in esophageal cancer should be given with recent more precise techniques like intensity modulated radiotherapy (IMRT), image guided radiotherapy (IGRT) and stereotactic body radiation therapy (SBRT) to spare surrounding normal tissue as much as possible. The dose ranges from 414 gray in preoperative settings to 50.4
gray in definitive management, with 1.8 to 2 gray per fraction. However, in developing countries with limited infrastructures like ours, 2-dimensional radiation by cobalt-60 teletherapy machine of dose up to 45 gray (to limit spinal cord tolerance dose) in neoadjuvant cases is also well established. Doublet chemotherapy consists of platinum compounds (cisplatin or carboplatin) and 5-fluoururcin or paclitaxel is used as concomitant chemotherapy with radical radiation. 

Chemotherapy alone is considered as secondary treatment adjunct to surgery and radiation therapy or in advanced metastatic disease or as salvage therapy in recurrent cases. For advanced and residual diseases, therapeutic trials with combination chemotherapy regimens have been tried. Different combinations of platinum compounds (cisplatin, carboplatin and oxaliplatin), taxanes (paclitaxel and docetaxel), fluoropyrimidines (fluouracil and capecitabine) irinotecan, methotrexate, ifosfamide (with mesna coverage) and cyclophosphamide has been explored in literature with improve tumor control and increase chances of survival. A few targeted agents like trastuzumab in HER-2 positive adenocarcinoma, ramucirumab and bevacizumab in junctional adenocarcinoma, nivolumab & pembrolizumab in PDL1 (programmed death-ligand 1) overexpressed tumor are well approved therapy with proved benefit. The role of some other targeted therapy like cetuximab, gefitinib and erlotinib, nimotozumab, panitimimum, sunitinib, entrectinib, larotrectinib in advanced, metastatic and recurrent esophageal cancer is evaluated in different studies but yet to established conclusively. Patient with very advanced disease and morbid general condition sometimes only require palliative treatment.

Prognosis of esophageal carcinoma in most of the part in world is still very improbable due to advanced stage of disease at presentation and very poor tolerance to radical treatment due to poor nutrition status. Management of nutritional status is of utmost importance, in order to provide adequate anticancer therapy. Per-ental nutrition through feeding jejunostomy is often required to provide proper nutrition.

In this retrospective analysis, male had majority of the cases and squamous cell carcinoma shared the major histological types which is well matched with similar studies done in other parts of India. Other parameters analysed in the study like background of patients (rural vs. urban), smoking habit, site of primary cancer (lower third more common) are also correlate well with previous Indian studies. The major limitation of this study is its retrospective nature. The follow up of these patients is continuing to get a proper idea regarding pattern of local and distal failure, which will be updated later.

CONCLUSION

In this retrospective analysis, different socio-demographic features of esophageal carcinoma patients, their tumor hallmarks, aspects of different treatment schedules had been evaluated. Overall patients were having poor prognosis and only 19% patients achieved complete response. In developing countries like India, majority of esophageal carcinoma patients presented with advanced disease and treatment outcome become disappointing. Despite radical surgery and chemo-radiation have beneficial role in complete cure of early disease; advanced stage, poor nutritional support and poor patient compliance makes the intent of treatment more palliative than radical one. In conclusion, careful monitoring of esophageal cancers in other institutions remain priorities to conclude proper nationwide demographic profile and it is recommended to establish the role of targeted therapies alone or with definitive chemo-radiation in advanced and metastatic esophageal cancer so as to prolong their survival and improve quality of life. More treatment options in future will convert the current scenario of palliative treatment to radical one in patients of esophageal cancer.
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