



PRESENTATION DELAY IN OESOPHAGEAL CARCINOMA : EXPERIENCE IN A TERTIARY HEALTH CENTRE

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ABSTRACT

INTRODUCTION: Esophageal carcinoma is one of the high prevalent and deadliest malignancies worldwide with very aggressive nature and poor survival rate. Esophageal cancer, among all malignancies, shows one of the widest geographical variations in terms of histological subtype. North Eastern region of India which is a part of oesophageal cancer belt, represents the highest incidence of oesophageal squamous cell carcinoma. Dysphagia is the cardinal symptom of oesophageal cancer yet many patients present late. There is only 14% five year survival despite recent advances in the treatment techniques. A few months delay before final treatment may have an impact on the stage of cancer and thereby on patient's prognosis. **OBJECTIVE:** The primary aim of this study was to analyse the time delay from the first symptom to treatment in oesophageal cancer and to analyse the relationship between the delay and stage at the time of definitive treatment. **MATERIAL AND METHODS:** 50 patients were analysed retrospectively and prospectively between September, 2015 and August, 2016 at Assam Medical College, Dibrugarh. Patients were interviewed at their first presentation to our hospital. Dates were recorded according to the patient's recollection, written information in the doctor's records during diagnosis process, and the hospital files. Details from the patient's first symptoms and course of diagnosis and treatment were recorded. The overall delay in months was recorded from appearance of the first symptoms to the date when the patient was started with definitive cancer specific treatment (end point), and this delay was divided as: (1) time of appearance of the first symptom to first contacting the health care system (patient delay). (2) Time from first contacting the healthcare system to histopathological diagnosis (histopathological delay). (3) Time from histopathological diagnosis to the end point (treatment delay). Statistical analysis: Data analysed using SPSS ver. 16 (SPSS Inc., Chicago, Ill., USA). **RESULTS:** The median age of presentation was 54.6yrs. The first symptoms were progressive dysphagia in all the patients (100%), abdominal or chest pain, regurgitation and odynophagia. The mean delay from first symptom to end point was 360.4 days. Total symptom- to-treatment was due to: patient delay (86%) - histopathological delay (5.3%) treatment delay (8.7%). **CONCLUSION:** Duration of delay is very long in patients. Most of the cases presents at advanced stage of disease. Patient delay is the most important factor, community education programs may help in their early presentation to the hospital for better QOL.

KEYWORDS :

INTRODUCTION:

Oesophageal cancer is the 7th most commonly occurring cancer in men and the 13th most commonly occurring cancer in women. [1] According to GLOBACON 2018 data, oesophageal cancer together with gastric cancer are included in most commonly diagnosed malignancies worldwide with more than 1.5 million new cancer cases and 1.3 million cancer related deaths. Worldwide 572,000 new cases of oesophageal cancer were diagnosed in 2018 and squamous cell carcinoma remains the most common subtype of oesophageal cancer globally (84% of all cases). About 70% of all esophageal cancers occurred in male gender. [2] Cancer statistics show that Asian countries have some of the highest age-standardized incidence rates (ASR) of esophageal cancers in the world with a very high concentration of cases in the in Iran and in China.[3-6]

80% of overall global burden of oesophageal squamous cell carcinoma was concentrated in Asia, whereas majority of all oesophageal adenocarcinoma cases occurred in Eastern Asia followed by Northern America and Western Europe. [2]

In India, oesophageal cancer is sixth most common malignancy in terms of incidence and deaths with 4.5% of all newly diagnosed cases and 5.9% of all cancer related death in 2018. [7]

Assam along with the North east region, a part of oesophageal cancer belt, has the highest incidence of oesophageal cancer where it is the second leading cancer in men and third leading cancer in woman. [8,9]. Traditional dietary habits in this region, which is very peculiar compared to other parts of India play as a major risk factor for development of oesophageal cancer. [10]

It is also one of the most virulent tumours with poor prognosis and not more than 14% of the patients could survive longer than five years despite the recent advances in treatment techniques.[11, 12] The prognosis for patients with oesophageal cancer is closely related to the stage of the disease at the time of diagnosis. The outcome of this cancer is closely related to the American Joint Committee on Cancer (AJCC)

tumour-node-metastasis (TNM) staging system.[13] According to that, five-year survival rates for Stages I, II, III are 50-80%, 30-40%, and 10-15%, respectively. Stage IV disease treated with palliative therapy has a median survival of < 1 year. [14] Therefore, if the disease is diagnosed and treated early (stages I and II) the outcome may be considerably better as compared if diagnosed in the late stages (stages III and IV). It is important to consider that the median values of potential doubling time in oesophageal tumours is 4 - 5 days with a range of 2 - 20 days among the fastest of all types of tumours. [15] Therefore, a few months of delay may allow the tumour to grow exponentially. Hence, long delays in starting definitive treatment will have a negative effect on the patient's prognosis. [16] The early stages of oesophageal cancer. Since, a majority of patients present with advanced disease leading to a poor outcome, a fast diagnostic workup after the first consultation is important as a diagnostic delay may lead to delay in the start of definitive treatment. This factor may therefore have an impact on the stage of the oesophageal carcinoma and subsequently on the prognosis of the disease. We performed this study to, identify the time of delay from the first symptom-to-treatment of oesophageal cancer and to investigate the possible correlation between symptom-to-treatment delay and the stage of tumour at the time of presentation.

MATERIAL AND METHODS:

50 patients with cancer oesophagus were analysed retrospectively and prospectively between September, 2015 and August, 2016 at registered in the department. Patients were interviewed at their first presentation to our hospital. Dates were recorded according to the patient's recollection, written information in the doctor's records during diagnosis process, and the hospital files. Details from the patient's first symptoms and course of diagnosis and treatment were recorded. The overall delay in months was recorded from appearance of the first symptoms to the date when the patient was started with definitive cancer specific treatment (end point), and this delay was divided as: (1) time of appearance of the first symptom to first contacting the health care system (patient delay). (2) Time from first contacting the healthcare system to histopathological diagnosis (histopathological delay). (3) Time from histopathological diagnosis to the end point

(treatment delay).

Statistical analysis: Data analysed using SPSS ver. 16(SPSS Inc., Chicago, Ill., USA).

RESULTS:

The median age of presentation was 54.6yrs .The first symptoms were progressive dysphagia in all the patients (100%), abdominal or chest pain, regurgitation and odynophagia. The mean delay from first symptom to end point was 360.4 days. Total symptom- to-treatment was due to: patient delay (86%) - histopathological delay (5.3%) treatment delay-(8.7%).

TABLE 1: Genderwise distribution of patients.

GENDER	N	%
MALE	33	66
FEMALE	17	34

TABLE 2: Habbits of patients : Genderwise distribution (N=50)

S. NO	CHARACTERISTICS	MALES (N=33)		FEMALES(N=17)	
		N	%	N	%
1.	ALCOHOL YES NO	33	100	07	41
		00	00	10	59
2.	SMOKING YES NO	33	100	14	82
		00	00	03	18
3.	TOBBACO CHEWING YES NO	32	97	15	88
		01	03	02	12

TABLE 3: Breakdown of symptom to treatment delay

EVENTS (DELAYS)	MEDIAN (DAYS)	MEAN	PERCENTAGE
From the first symptom to treatment	20-564	360.4	86
Time of appearance of the first symptoms to the first contacting health care system	20-564	309.9	86
Time from first contacting health care system to histopathological diagnosis	5-321	19.1	5.3
Time from first histopathological diagnosis to end point	10-123	31.4	8.7

DISCUSSION:

In our experience, a majority of patients present with advanced disease leading to a poor outcome. This observation is in accordance with the study of Subasinghe D et al. [17] Amongst the well-recognized risk factors, smoking tobacco was found in most patients with SCC followed by alcohol consumption. In our study betel nut and tobacco chewing was strongly associated SCC, but our findings do not match with those from other study.[17]Alcohol ingestion was common amongst males in our study population, however this observation is not in accordance with other studies conducted earlier. Although less common than SCC, AC was still seen in 65% of our patients which differ from that reported by others[17]. AC has been closely linked to the rise in GERD in the developed world, where it has increased exponentially.[18-21] A greater percentage of patients smoked and drank alcohol in the SCC compared to AC patients was found in the study of Subasinghe D , which is in accordance with our study. Comparison between SCC and AC patients was also found difficult because of the small numbers of patients with the known risk factors in both groups. The association of lower social class (>80%) was well seen in patients with SCC. The association of GERD with obesity and a more affluent lifestyle predisposing to AC may affect patients in the higher social classes. This concept supports our observations as in our study most of the patients belonged to lower socioeconomic strata and were found to be suffering from SCC. However a study conducted in Sri Lanka do not support our observation there they had found the predominance of AC.[17] The most striking problem with our patients is the late presentation of disease, with almost 98% of patients presenting in locally advanced stage and with distant metastasis. Only a minority of patients had presented at early stage and were operable. This reflects the natural history of the disease which is often silent until dysphagia sets in. Utilization of health facilities is also low among poorer and less educated patients who often resort to traditional cures and alternative medicines before seeking a allopathic medical consultation, leading to delayed presentation for definitive treatment.[17]

In several specialized centers in Asia the advent and use of multimodality treatment with neoadjuvant chemoradiation and newer surgical approaches have resulted in better cure rates. [22,23]

Oesophageal cancer is a malignancy that is relatively common in Indian sub-continent and we found that the mean overall delay from the appearance of the first symptom to definitive treatment was 360.4 days which was far more as that of Sri Lanka. [17] Nearly more than ninty percent of the patients had an overall delay of more than three months and 8.5% of the patients had a delay exceeding one year. Delay from the appearance of the first symptoms to first contacting the healthcare system (patient delay) accounted for 96% of the total, histopathological delay and delay from the histological diagnosis to the start of definitive treatment accounted for 5.3% and 8.7%, respectively which is in accordance with the study of Sri Lankans[17] The median overall delay in the diagnosis in oesophageal cancer was 360.4 (20-564 days) days in our study, which was far higher than the median overall delay (3 months) found by some of the previous investigators. [24] Martin *et al.* in their study in UK had found more than four months of median delay from the first symptom diagnosis of the disease.[25]. Wittzig *et al.*,[26] in Germany and Wang *et al.*[27] in China had observed a shorter delay than our study. The reasons for these differences are numerous, some being, the knowledge and attitude of patients towards the symptoms and health seeking, the difference in the healthcare systems and different referral patterns. As we are developing country in South East Asia, in the state sector, we have limited facilities for diagnostic and staging investigations such as Upper GI endoscopy, CT, MRI, and endoscopic ultrasound. Even if available, the state health sector in our country being a free health provider, there may be a considerable 'waiting list' for these investigations. These results were also supported by other investigators. [17] Regarding oesophageal carcinoma, some investigators have found in their study that a shorter delay in the start of definitive treatment progressively decreases the degree of invasion and increases the survival rate, [28],[29] while others have proven that there is no relationship between delay and the stage of the tumour or mortality.[30-32] In addition to these findings, some researchers have indicated that shorter delay is associated with poor prognosis.

[33]The reason for the contradiction of the studies is not clear.

However, the results of the studies by Martin *et al.* and Wang *et al.*[25, 27] have suggested that a longer delay before definitive treatment of oesophageal cancer increases the stage of the cancer and thereby worsens the patients' prognosis. Almost all patients with oesophageal cancer have dysphagia and some (27%) report odynophagia at the time of diagnosis. [34] Weight loss is also common (57%) and is an independent indicator of poor prognosis if there is a loss of more than 10% body mass. [35] However, in our setting, all the patients presented with dysphagia with or without other symptoms. In our study the all the patients had loss of weight when they presented for the endoscopic examination. In addition to the TNM stage, multivariate analyses suggest that a weight loss of more than 10% of body mass, dysphagia, and advanced age are independent predictors of a poor prognosis. [35-38] According to our results it shows that a delay in diagnosis is mainly due to a delay in seeking medical attention (96%). Due to this, the majority of our patients presented at an advanced stage of the disease, which resulted in neoadjuvant therapy prior to surgery or palliative treatment. Another factor shown in our study is the notable delay in carrying out endoscopy and histology in 14% of the patients. At present our medical system faces an acute shortage of qualified histopathologists in the state sector, and most of the district and provincial hospitals do not have qualified histopathologists. There is also a relative dearth of endoscopists. Therefore, the specimens have to be sent to a central well-equipped laboratory for reporting, and this process may even take several weeks (if not months)to issue a report.

CONCLUSION:

The results of our study indicate that long delays in diagnosis and treatment of oesophageal cancer still occur in our set up. This is mainly due to patient delay, although non-availability of diagnostic facilities also appears to contribute in a notable way. Therefore, a community education program to increase the awareness regarding oesophageal cancer may help in reducing patient delay. This will also potentially identify the high-risk groups to be screened, and the disease can be identified at an early stage. Therefore, a national patient education program with establishment of regional centers of excellence is recommended.

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