

EPIDEMIOLOGY OF ESOPHAGEAL CARCINOMA IN SOUTHERN PART OF INDIA- A SINGLE CENTRE STUDY

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Abstract

Background: Oesophageal carcinoma is least studied because of high morbidity and mortality. The aim is to study the histological pattern, risk factors distribution in oesophageal carcinoma (EC) in southern India over a while. **Materials and Methods:** Data was collected retrospectively of 102 patients with EC from June 2013 to May 2018 for 5 years and 112 patients from June 2018 to May 2023 for 5 years in the Department of Medical Gastroenterology in the Government Thoothukudi Medical College. **Results:** In the first period, there were 102 patients with EC; 69 (67.6%) were males, and 33(32.4%) were females, with median age of 58.96 years. Risk factors being tobacco in 89.2%, hot beverages in 95.1% and alcohol in 34.3% patients. EC was in upper two-thirds in 65.7%, followed by 35.3% in lower one-third of the oesophagus. Squamous cell carcinoma(SCC) was in 69.6% and Adenocarcinoma (AC) was in 30.4%. In the second period, there were 112 patients with EC; 75 (66.9%) were males, and 37(33.0%) were females, with median age of 59.69 years. Risk factors being tobacco 91.9%, hot beverages in 94.6%) and alcohol in 34.3%). EC was in upper two-thirds in 66.1%, followed by 33.9% in lower one-third of the oesophagus. SCC in 74.1% and AC was in 25.9%). **Conclusion:** Squamous cell carcinoma is more common than adenocarcinoma in southern India with upper two third being more common than lower one third. No changes were seen in epidemiology over years.

INTRODUCTION

Oesophageal carcinoma is one of the most common gastrointestinal malignancies worldwide, along with stomach, pancreatic, hepatobiliary and colorectal carcinomas. There is limited literature on the epidemiology of oesophageal carcinoma in South India. EC has high morbidity and mortality. Previous publications have provided various data on EC, including histological type, incidence, and risk factors for a certain region or country. Oesophageal cancer is the 8th most common cancer (3.2%) globally and the 6th most common cause of cancer-related mortality (5.3%). In India, oesophageal cancer is the 6th most common cancer, with an

incidence of 4.8% and a mortality of 6.9%.^[1] It is 6th most common cancer in females and 5th most common in males.

Squamous cell carcinoma (SCC) and adenocarcinoma (AC) are the histological types of oesophageal cancer; others are sarcomas, small cell carcinoma, melanomas, leiomyosarcomas, carcinoids and lymphomas which occur in rare incidences. The most common form of oesophageal cancer worldwide is SCC.^[2] SCC originates from the stratified squamous epithelium lining the oesophageal mucosa. In contrast, AC arises in the distal oesophagus from columnar glandular metaplastic epithelium, called Barrett's oesophagus, which undergoes dysplastic changes in the future.

Barrett's oesophagus increases the risk of developing EC by 50-100 times.^[3-6] For different types of oesophageal cancer, the risk increases with age; the highest incidence is 6th decade of life.^[7] EC incidence is higher in China compared to the United States. A "cancer belt" of EC, primarily squamous cell cancers, extends from the Middle East to northeast China.^[8,9] Nutritional deficiencies can develop by chronic alcohol use, poverty, and lack of an adequate food supply, but diet does not explain the whole picture. External carcinogens are necessary to affect the result.^[10,11]

Various studies have found multiple risk factors for developing EC. Most risk factors are implicated in acting directly on the oesophagus. They are tobacco use, consumption of alcoholic beverages, achalasia, GERD, Barrett's, lye ingestion, and high-temperature foods.^[12] The risk factors that act systemically are micronutrient deficiencies and obesity. EC risk factors like smoking, alcohol, and high BMI also significantly increase the risk of developing systemic diseases like diabetic mellitus, cardiovascular diseases and cancers like gastric, pancreas and lung cancers. Nutritional deficiencies may develop due to low socioeconomic status, alcohol use disorder, and inadequate food supply. External carcinogens are necessary to finally affect the pathogenesis, as diet does not explain the whole picture. Multiple studies have found an inverse correlation between the socio-demographic index and EC. A low socio-development index indicates multiple variables, such as poor water quality and indoor air pollution. Few recent studies have highlighted opium consumption as a risk factor for EC. Low socioeconomic status is associated with SCC oesophagus. Many recent studies have postulated that obesity is a risk factor for developing AC oesophagus. Obesity increases intraabdominal pressure GERD, predisposing to GERD. Obesity develops an environment for tumourogenesis by providing high levels of adipokines and other inflammatory cytokines. The rising incidence of oesophageal AC worldwide is thought to be due to the increasing prevalence of obesity.^[13,14]

As there are fewer studies in south India studying the epidemiology of oesophageal carcinoma over a while, we conducted to study the histological pattern of oesophageal carcinoma (EC) in the southern state of India and to evaluate the relation of age, sex, and substance abuse in oesophageal carcinoma over a while.

MATERIALS AND METHODS

This hospital-based descriptive study was done in the Department of Medical Gastroenterology in Government Thoothukudi Medical College after getting approved by the ethical committee of the college. Data was collected from the departmental registry retrospectively, and 102 patients with oesophageal carcinoma from June 2013 to May 2018

(Group 1) for five years and 112 patients from June 2018 to May 2023 (Group 2) for five years were included in the study.

Inclusion Criteria

Data from all the patients, department of medical, gastroenterology Government Thoothukudi Medical College including both outpatients and in-patients with cancer oesophagus was collected and filled in preformed proformas. Contrast enhanced computed tomography (CT) scan of the chest and abdomen was done in patients who had endoscopically non-negotiable tumour to see the size and extent of the growth.

Exclusion Criteria

Patients with endoscopically non-negotiable tumours with absence of CT imaging. Patients with absence/inconclusive Histopathology report, patient who died before evaluation and patients who were discharged against medical advice before evaluation. Patients are classified into four groups based on the involvement of the oesophagus: upper one-third (Group A), middle one-third (Group B), lower one-third with oesophagogastric junction (EGJN) involvement (less than 2 cm) (Group C) and lower one third without oesophagogastric junction (EGJN) (Group D) involvement. The long segmental tumours are classified according to the maximum extent of the tumour. Contrast Enhanced Computed tomography (CE- CT) is used to study the patients with whom the tumour cannot be negotiated. The patients were classified into two time periods, and the distribution was studied on histological types, gender, location and risk factors.

Statistical Analysis

Data were collected in pre-structured proforma, and statistical analysis was done. Mean and standard deviation were calculated for quantitative data, and the ratio was calculated for qualitative data. The chi-square test and t-test was used to analyse the trend in the histologic type of the tumour, age, sex, and substance abuse. The significance level was 95% for all statistical analyses (P value <0.05).

RESULTS

Risk factors

In Group 1, out of the 102 patients, a history of tobacco was found in 91(89.2%) patients, drinking hot beverages was found in 97(95.1%) and alcohol in 35(34.3%) patients. In Group 2, out of the 112 patients, a history of tobacco was found in 103(91.9%) patients(P value-0.25), drinking hot beverages was found in 106(94.6%)(P value-0.43) and alcohol in 41(34.3%) patients(P value-0.5). There is no significance statistically (all P value>0.05) (Figure 1).

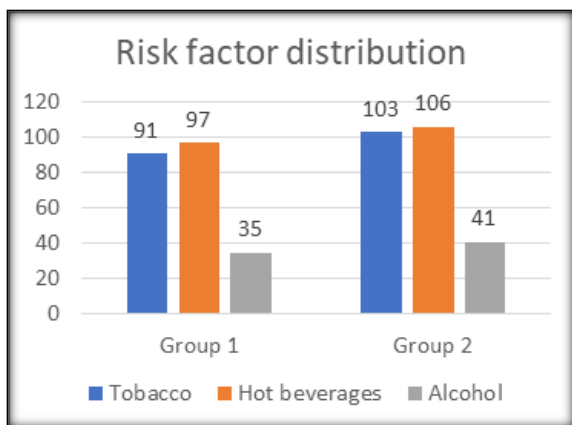


Figure 1: Distribution of Risk factor

Sex and age distribution

In group 1, there were 102 patients with oesophageal cancer; 69 (67.6%) were males, and 33(32.4%) were females, with M: F of 2.1:1, and the median age was 58.96 years compared to group2, there was a total of 112 patients with oesophageal cancer; 75 (66.9%) were males (P value -0.46), and 37(33.0%) were females (P value -0.46), with M: F of 2.0:1, and the median age was 59.69 years (P value -0.44), (Table 1). This was too statistically insignificant (all P value >0.05).

Site of the EC

In Group 1, the majority of the tumour was in the upper two-thirds, 67 (65.7%), followed by 35(35.3%) patients in the lower one-third of the oesophagus. In Group 2, the majority of the tumour was in the upper two-thirds, 74 (66.1%), followed by 38 (33.9%) patients in the lower one-third of the oesophagus (Table 1).

In Group 1, 36(35.3%) patients are in the upper one-third, 30(29.4%) in the middle one-third, 16(15.7%) patients in the lower one-third with EGJN and 19(18.6%) patients in the lower one third without EGJN involvement compared to 33(29.5%) patients are in the upper one third, 41(36.6%) in the middle one third, 20(17.9%) patients in lower one third with EGJN and 18(16.1%) patients in lower one third without EGJN involvement in the second group. Here, there is an increase in the number of patients in the middle one-third of the oesophagus (Figure 2).

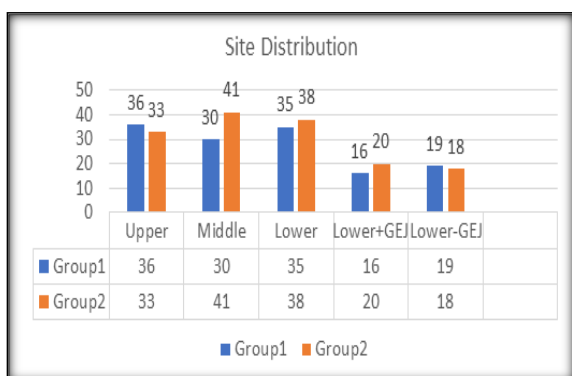


Figure 2: Location- wise distribution of the malignancy and time trend

In Group 1, 61(59.8%) patients needed CECT to categorise since the endoscope cannot pass across the EC compared to Group 2, 67(59.8%) patients had EC, which cannot be negotiated across the endoscope, which was statistically insignificant (P value=0.5).

Histological distribution

In Group 1, squamous cell carcinoma was the histological type involved in 71(69.6%) patients, adenocarcinoma was detected in 31(30.4%) patients compared to squamous cell carcinoma (SCC) involving in 83(74.1%) patients, and adenocarcinoma (AC) was detected in 29(25.9%) patients in the second group. There is an increase in the SCC in the second group, mainly in the middle one-third. In the group 2, 29(40.8%) patients had SCC in the middle third compared to 41(49.4%) patients in the second group, which is statistically insignificant (P value=0.14) (Figure 3).

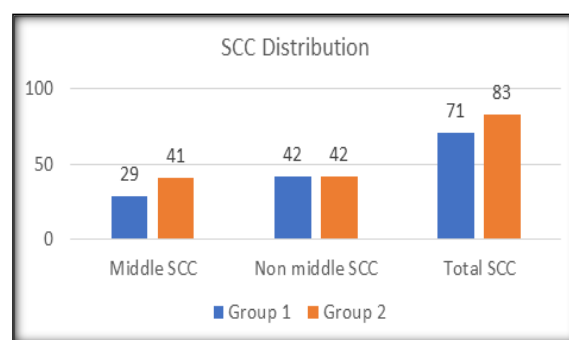


Figure 3: Oesophageal SCC distribution

In the first group, there are 13(41.9%) patients with AC involving EGJN and 18(58.1%) without EGJN compared to 19(65.5%) patients with AC involving EGJN and 10(34.5%) without EGJN in the second group. Here, there is an increase in the number of patients with AC involving EGJN, which is statistically significant (P value=0.03) (Figure 4).

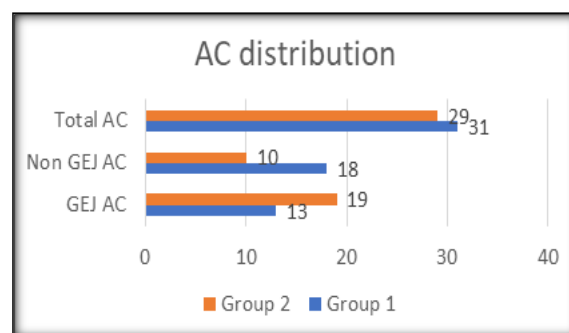


Figure 4: Oesophageal adenocarcinoma distribution

DISCUSSION

Oesophageal carcinoma is a disease with high morbidity, mortality and poor prognosis. Most patients present with advanced disease when only palliation is available. A nationwide campaign is required to generate public awareness about this dreaded disease and identify the high-risk

population. Our study included a total of 214 oesophageal carcinoma patients who were grouped into two time periods. Variables data, including risk factors, age, sex, tumour location, and histology, were collected, and distribution was studied.

The risk of developing oesophageal carcinoma increases with age. In a study, Cummings LC et al. found a mean age of 67 years at diagnosis. The age-adjusted incidence of developing EC in blacks was about twice that of whites (8.63/100000 vs 4.39/100000, $P < 0.05$).^[7]

In low-risk areas like the USA, SCC oesophagus is more common in males than females (4:1), whereas it is 1:1 or even low in high-risk areas like China and Iran. In US studies, oesophageal AC is more common in males than females (8:1).^[15,16]

In a WHO study, oesophageal cancer is 2.4 times more common in males compared to females; however, it is 1.2 times more common in India in a study by Samarasinghe I.^[17]

Our study found a male-to-female ratio of 2.1:1 in Group 1 and a male-to-female ratio of 2.0:1 in Group 2. Our findings show male predominance, similar to other studies. The male predominance may be that males have multiple risk factors combined. Compared to other countries, Indian women have more incidence likely due to high consumption of regional hot beverages and tobacco.^[18,19]

Bidi and khaini are the most common forms of tobacco consumed. The latest ICMR data shows the highest Age-Adjusted Incidence Rate (AAR) of cancer in sites associated with tobacco use is reported in the East Khasi Hills district of Meghalaya. It is 161.3 per 100,000- males and 58.1 per 100,000-females. Andrici J Eslick GD found that consuming hot beverages and food items increases the risk of developing oesophageal cancer.^[20]

In Western studies, oesophageal carcinoma incidence is common in the sixth decade of life.^[7,28]

In our study, the median age for developing EC was 58.96 years in Group 1; in the second time period, the median age was 59.69 years. It is a decade earlier than Western studies.^[7,28]

Choksi D et al. found oesophageal SCC was more common than adenocarcinoma oesophagus. The study also showed a statistically significant increase in lower oesophageal carcinoma; most were adenocarcinoma oesophagus.^[21]

Bhame R et al. study showed squamous cell carcinoma oesophagus is three times more common than AC oesophagus.^[19]

Jose Tony et al. showed a statistically insignificant rise in the incidence of gastrooesophageal junction carcinomas, mainly oesophageal adenocarcinoma. However, there is no change in the histological distribution.^[22]

Noronha V. et al. study had the largest data in India, including 7874 patients with oesophageal carcinoma. 64.7% were men, with M: F of 2.5:1 and the highest incidence is the fifth decade of life. 4912 patients had tobacco and alcohol as risk factors, and there were oesophageal carcinoma in the middle third in 2942

(41.5%) patients. Squamous cell carcinoma 6413 (81.4%) patients had SCC histology, with the commonest site being the middle one-third, 2942 (41.5%) patients, followed by the lower-third in 2331 (32.8%).^[23]

It is similar to our study. In our study, there is an increase in the SCC in the second group, mainly in the middle one-third. In the first group, 29(40.8%) patients had SCC in the middle third compared to 41(49.4%) patients in the second group, which is statistically insignificant (P value=0.14). Also, there is an increase in the number of patients with AC involving EGJN, which is statistically significant (P value=0.03).

Cancer registries in Western countries show increased adenocarcinoma of the lower oesophagus. There were similar observations observed from a recent multinational study. The increasing incidence of oesophageal adenocarcinoma in the Western world can be attributed to the rising prevalence of obesity.^[24] Nonsteroidal anti-inflammatory drugs, selenium, alpha-difluoromethylornithine, and vitamin A are under investigation to prevent oesophageal carcinoma. Vegetable and fruit intake plays a preventive role, and raw vegetables are more protective than boiled vegetables.^[25,26]

The annual per cent change in the incidence of oesophageal carcinoma in Chennai is -0.3 in the ICMR report published in 2020. It highlights the decrease in the incidence of oesophageal carcinoma in major cities of India.^[27] Our study included patients of low socioeconomic status. Gradual improvement in health awareness among the population and better health facility availability may be a reason for the increasing detection rate, which may be a factor causing an increase in oesophageal carcinoma patients. Our study showed alcohol intake, drinking hot beverages, consuming tobacco as risk factors for developing oesophageal carcinoma. So, lifestyle modification to modify these risk factors can be helpful in preventing oesophageal cancer. Measures to modify these risk factors may help in forming preventive strategies for oesophageal carcinoma prevention. So our study may be helpful by identifying these risk factors and their association with oesophageal carcinoma in the development of effective preventive strategies to modify the risk factors causing oesophageal carcinoma in India.

CONCLUSION

Our study is one of the few studies in the southern part of India. The study highlights that oesophageal carcinoma occurs in southern India's fifth decade of life. Squamous cell carcinoma in the oesophagus is still far more common than adenocarcinoma in India. The upper two-thirds of the oesophagus is the most common site of oesophageal carcinoma in southern India. Drinking hot beverages, alcohol intake and tobacco consumption are still the risk factors for developing oesophageal carcinoma. GEJ

adenocarcinoma is increasing in trend, similar to Western countries.

Limitations

The study was retrospective and done in a single department in a government medical college where the patients mainly belong to low socioeconomic status, which causes bias in the study of risk factors as they are more exposed to risk factors.

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