

Carcinoma of the Esophagus in Tamil Nadu (South India): 16-year Trends from a Tertiary Center

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Abstract

Background. In the Western world, esophageal adenocarcinoma has surpassed in incidence squamous cell carcinoma. **Aim.** To determine the trend changes in histology and site distribution of esophageal malignancy between 1989 and 2004 in a southern state of the Indian subcontinent. **Method.** A retrospective study on 994 patient records with esophageal carcinoma esophagus. Age, gender, clinical presentation and duration of illness were recorded in a prestructured proforma. The site of the tumor was classified as upper, mid, lower esophagus and esophagogastric junction. The 16 year study period was divided into four equal cohorts. Statistical analysis was performed using the chi-square test and the one way ANOVA wherever appropriate; $p < 0.05$ was considered significant. **Results.** Squamous cell carcinoma was the most common malignancy, seen in 912 (92%) patients. 82 patients (8%) had adenocarcinoma. 65 of these 82 patients (79%) had an esogastric junction malignancy and 17 (21%) a tumor in the distal third of the esophagus. No time trends were discernible with regard to the clinical presentation, frequency, mean age or gender. However, an increase in the number of patients below the age of 40 was noted ($p=0.008$). In squamous cell carcinoma of the esophagus, there was an overall increase in the mean age of occurrence ($p=0.05$), but no significant changes in the gender ratio. The lower esophageal cancers outnumbered the midesophageal cancers in the 4th cohort and the former represent the most common site of malignancy. **Conclusion.** Squamous cell carcinoma is the most common type of esophageal cancer in the Indian subcontinent, located with a predilection in the distal third. Adenocarcinoma is uncommon and affects more frequently men younger than 40.

Key words

Esophagus - squamous cell carcinoma – adenocarcinoma - time trends

Introduction

Esophageal cancer is the 15th most common cancer in developed countries and 4th in the developing world (1). The incidence of esophageal adenocarcinoma (AC) has shown a dramatic increase in several populations over the past 25 years (2,3). This increase may be due to a true rise in the disease burden itself (4), an overdiagnosis due to an increased screening for dyspepsia, reflux disease and Barrett's esophagus (5,6) or due to a reclassification of AC of the gastric cardia (7-9). The highest reported increase at 10% per annum has been from the USA (10,11). Among the Asian countries, China (12) and Singapore (13) have reported an increasing number of esophageal AC.

The present retrospective study aimed to determine trend changes in histology and site-specific distribution of esophageal malignancy between 1989 and 2004 in the Indian subcontinent. Our institution is a major tertiary referral center for gastrointestinal diseases, referrals being open to the entire population of Tamil Nadu, a state in South India. During the study period the number of referrals and endoscopies performed has been constant.

Methods

Endoscopy records of 994 patients with carcinoma of the esophagus, either squamous cell (SCC) or AC, diagnosed between 1989 and 2004 were retrieved. Age, gender, clinical presentation, duration of illness and site of lesion were recorded in a prestructured proforma. Rarer types of esophageal tumors and gastric cancers infiltrating the esophagogastric junction (EGJ) and lower esophagus were excluded from the analysis.

For site-specific location of the tumor, the esophagus was divided into three equal segments based on the distance between the cricopharynx and the esogastric junction (EGJ). When the tumor extended beyond one segment, the centre

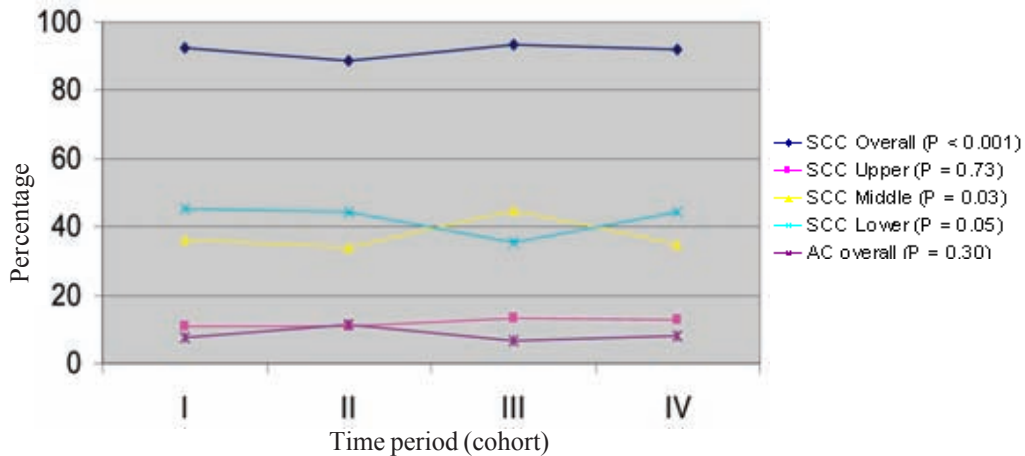


Fig.1 Subsite and histology specific trends.

of the lesion was taken as the point of reference and the site of the tumor classified accordingly. The site of the tumor was categorized as upper, middle, lower esophagus and EGJ. EGJ tumors were defined as tumors over the esophagogastric junction. In those with an obstructed lumen, the site was noted after dilatation. Cases where dilation was not successful were excluded from the analysis.

For the site specific trend study, the 16 year period was divided into four cohorts, i.e. 1989–1992, 1993–1996, 1997–2000, and 2001–2004. The patient distribution according to the histopathology, site, age group and gender were expressed as a percentage of the total number of patients in each cohort. Statistical analysis was performed using the chi-square test and the one way ANOVA wherever appropriate and p values < 0.05 were considered significant.

Results

Squamous cell carcinoma was the most common malignancy seen in 912 (92%) patients. The remaining 82 (8%) had an AC.

Trends in adenocarcinoma

Sixty-five of the 82 patients with AC had an EGJ malignancy and in 17 the lesion was in the distal third of the esophagus. None involved the middle or upper third of the esophagus. No time trends were discernible over the four successive cohorts with regard to the clinical presentation, frequency (Table I, Fig.1), mean age (Table II) or gender predilection (M:F ratio 3.6:1) (Fig 3). However, a significant increase in the number of patients below the age of 40 years was noted (p=0.008) (Fig 2).

Trends in squamous cell carcinoma

Time trends in clinical presentation

There were no significant differences in the presenting symptoms or in the physical signs in the four cohorts.

Time trends in age

Overall, there was an increase in the mean age of occurrence (p=0.05). However, this was not significant on site or gender specific analysis (Table II). SCCs of the esophagus, both overall and site specific were significantly higher above the age of 40 in all the four cohorts. There was a statistically significant reduction in the number of patients below the age of 40 in those with middle third malignancy (p = 0.002) (Fig 2). Irrespective of the site or the cohort, women were affected at an earlier age than men.

Time trends in gender predilection

The overall male:female ratio was 2.16. The gender ratio for upper, middle and lower third SCC was 1.73, 2.08 and 2.35 respectively, and the changes observed were not statistically significant (Fig 3).

Time trends in site distribution

There was an increase in the overall number of cancers during the initial three cohorts and a significant fall during the fourth. This trend was maintained for SCC involving the middle third. The trend showed a distinct reversal for the distal third tumors, i.e. a decline in the initial three cohorts followed by a rise during the fourth. Thus, in the fourth cohort, lower esophageal cancers outnumbered the mid esophageal cancers and appeared to be the commonest site of esophageal malignancy (Fig. 1). No change in trend was noted for upper esophageal cancer, which remained constant at a porportion of 12.3%.

Table I Subsite specific trends of carcinoma esophagus

Site	Total No. (%)	1989-92	1993-96	1997-2000	2001-04	p
Total	994	196(19.72%)	233 (23.5%)	323 (32.5%)	242(24.3%)	<0.001
SCC overall	912 (91.8%)	181 (92.3%)	207 (88.8%)	301(93.2%)	223(92.1%)	< 0.001
upper	120 (12.1%)	21 (10.7%)	25 (10.7%)	43 (13.3%)	31 (12.8%)	0.73
middle	379 (38.1%)	71 (36.2%)	79 (33.9%)	144 (44.6%)	85 (35.1%)	0.03
lower	413 (41.6%)	89 (45.4%)	103 (44.2%)	114 (35.3%)	107 (44.2%)	0.05
AC overall	82 (8.2%)	15 (7.7%)	26 (11.2%)	22 (6.8%)	19 (7.9%)	0.30

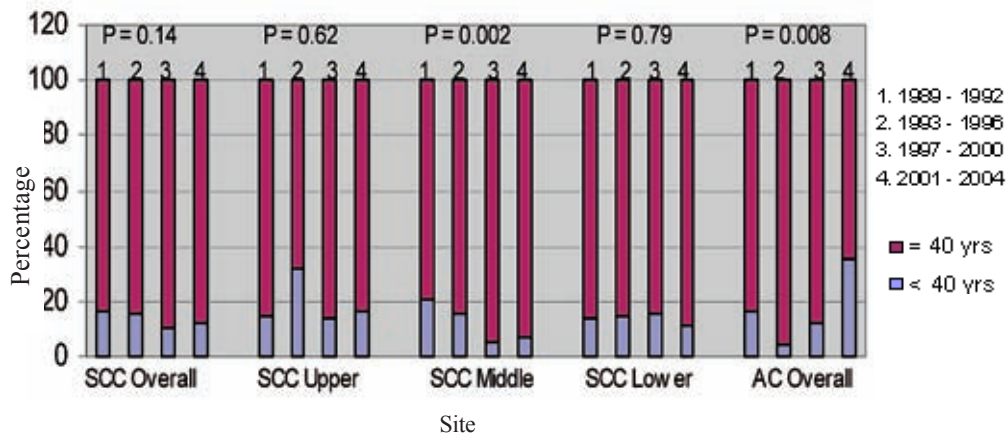


Fig.2 Trends in age group distribution (<40 yrs vs >40 yrs).

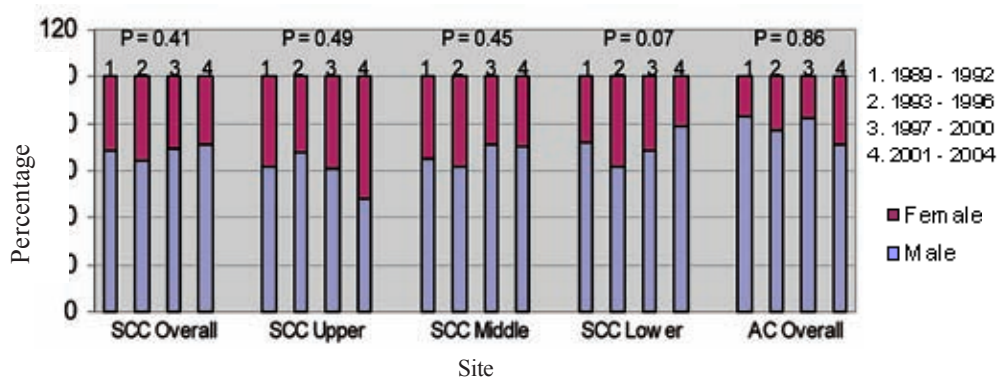


Fig.3 Trends in gender distribution.

Table II Site specific trends in mean age

Mean age	1989-92	1993-96	1997-2000	2001-04	p
SCC overall	53.9 ± 12.4	54.1 ± 11.2	56.4 ± 10.5	54.7 ± 11.4	0.05
upper	52.1 ± 10.4	50.6 ± 14.2	56.1 ± 12.1	53.9 ± 11.4	0.31
middle	54.2 ± 13.3	55.3 ± 12.1	57.1 ± 10.1	55.3 ± 10.6	0.31
lower	53.9 ± 11.8	53.3 ± 9.9	55.6 ± 11.8	55.2 ± 11.7	0.38
AC overall	54.3 ± 16.0	58.0 ± 8.7	55.6 ± 10.2	49.3 ± 13.5	0.20
Mean age – Men					
SCC overall	55.5 ± 12.6	54.7 ± 11.1	57.7 ± 10.8	55.8 ± 10.8	0.07
upper	52.5 ± 11.1	54.1 ± 13.8	56.3 ± 12.8	57.7 ± 8.4	0.65
middle	56.6 ± 13.4	55.9 ± 11.9	58.4 ± 10.0	57.2 ± 10.4	0.35
lower	55.1 ± 12.3	53.4 ± 10.3	57.1 ± 11.5	55.6 ± 10.9	0.26
AC overall	57.5 ± 13.6	59.8 ± 8.1	58.6 ± 7.7	50.5 ± 14.3	0.17
Mean age - women					
SCC overall	50.1 ± 11.3	53.1 ± 11.3	53.3 ± 10.9	52.0 ± 12.4	0.33
upper	51.4 ± 9.9	43.1 ± 12.5	55.7 ± 11.3	50.4 ± 12.9	0.11
middle	49.7 ± 12.1	54.9 ± 12.6	53.9 ± 9.7	50.7 ± 9.8	0.13
lower	51.0 ± 10.2	53.1 ± 9.3	52.4 ± 11.9	55.1 ± 14.5	0.56
AC overall	38.5 ± 23.3	51.8 ± 8.7	41.7 ± 9.6	46.3 ± 12.6	0.55

Discussion

Squamous cell carcinoma has remained the most common esophageal malignancy between 1989 and 2004. It is unlikely that it will be surpassed by AC in number in the near future.

This is in contrast to reports of an increasing incidence of AC from several countries world over (14-18). Cancer

registries of some of the European countries have shown no rise in incidence (18). Reports from Asian countries, such as Singapore (13) and China (19) have shown a decline in incidence of SCC. No trends for AC were noticeable despite the low number of patients identified during the study period. This was irrespective of the site, age or gender; no trend towards an increase was noticeable. These observations

are not surprising since erosive reflux disease is rare in this part of the world (11,20,21) and obesity as a risk factor is not of major concern. The recent increase in number of esophageal AC in China (12) and Singapore (13) has shown a parallel rise in incidence of more severe forms of gastroesophageal reflux disease, though SCC continues to be the most common malignancy. The present study has shown AC to occur more frequently in patients below the age of 40, unlike reports from the West, where they occur predominantly in the elderly (14).

The present 16-year time trend has shown a reduction in the total number of esophageal SCC after 2000. A similar decline has been observed in Singapore (13) and China (19). Countries like New Zealand (15) Norway (22) and France (23) have shown no change in trends, while other countries in Europe have noted a decline (8). A study from South Carolina (24) reported previously that esophageal SCC was on the rise in women, whereas a rise amongst men was noted from Sweden (25).

The cause for this decline remains speculative, since data on time trends in risk factors for SCC such as smoking, betel-nut chewing, alcohol consumption, intake of salted tea, spicy food, sun dried vegetables and chillies are few and scanty.

The mean age of occurrence of esophageal carcinoma in correlation with the site or the gender did not show any significant change in the present study, an observation similar to Sharma et al (24) from South Carolina. In contrast, the study from China (12) showed that in the 1970's, patients in their 50s were at the highest risk for carcinoma of the esophagus, while in the 1980's it occurred a decade later. Comparing the age groups - less than versus more than or equal to 40 years, we observed that the proportion significantly declined for cancers of the middle third of the esophagus. This falls in line with the observation by Fernandes et al (13) that the age specific incidence has increased steeply from the age of 40 years in men and 50 years in women.

In high mortality areas of China, Iran and Africa, the incidence of esophageal tumors is approximately equal in men and women (26). By comparison, in low-incidence regions such as the United States and parts of Europe, there is a significant predilection for males (27). It was reported that the incidence rate in males is higher than that in females, and the ratio was 5-10:1. A study in China (12) reported the male to female ratio to be 5.5:1 and the difference was not significant over a 30 year period. During the period between 1968 and 2002 (13), it was observed in Singapore that the male:female ratio had changed significantly from 2.7:1 to 4.5:1 for all esophageal cancers. In the present study, the overall gender ratio was 2.16 for all esophageal cancers and no change in trends was observed across the four cohorts on site specific analysis.

Site specific changes of SCC have seldom been addressed in epidemiological studies. In New Zealand, about two thirds of the SCCs were evenly distributed in the lower two thirds of the esophagus. The Italian study did not note

any change in site distribution between 1986 and 1997 (17). The present study, however, has shown an increase in the number of cases involving the lower esophagus in the fourth cohort, making the latter the most common site for esophageal SCC.

In conclusion, squamous cell carcinoma continues to be the most common type of esophageal cancer in the Indian subcontinent. At the turn of the century, the lower esophagus appeared to have greater predilection for SCC *vis a vis* the middle third in the past. Adenocarcinoma continues to be uncommon.

Conflicts of interest

None declared.

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