

# Changing Epidemiology of Esophageal Cancer in Fars Province, Iran

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## Abstract

**Background:** Esophageal carcinoma is one of the most lethal gastrointestinal (GI) malignant tumors worldwide. The disease is known to have a high incidence in northern Iran; however, its condition in the South is not much clear.

**Objective:** In this retrospective study we investigated the epidemiology and time trends of esophageal carcinoma in Fars Province, South of Iran.

**Methods:** In a retrospective study, we reviewed pathologic reports of all laboratories in Fars Province, South of Iran, from March 1997 to March 1999 to find cases of esophageal carcinoma. Annual and average incidence in different age groups were calculated for both sexes, based on four censuses results.

**Results:** Esophageal carcinoma was the third most common GI cancer in Fars, with an average incidence of 2.95 per 100,000 in the population older than 15 years. The incidence of esophageal carcinoma was found to drop by 64% during the study period. This was mainly due to the decreased incidence of squamous cell carcinoma. Females developed squamous cell carcinoma in relatively younger age as compared to males.

**Conclusion:** Our region in the South of Iran is one of the low incidence areas of esophageal carcinoma as compared to that of northern borders of the country and other parts of the world with some special features.

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**Keywords** • Esophagus • carcinoma • Iran • incidence

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## Introduction

**E**sophageal cancer is one of the most lethal malignancies of gastrointestinal (GI) tract with a one-year survival of around 25%.<sup>1</sup> The major reason for this high mortality is the late diagnosis, with the majority of patients already in stages III or IV when diagnosed. At present, implementation of screening programs in high incidence areas is important in reducing this high mortality. Nevertheless, it is important to know when and where these relatively expensive and time-consuming programs should be set up.<sup>1-3</sup> It is

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**Table 1:** incidence (95% C.I)\* and absolute frequency of squamous cell carcinoma and adenocarcinoma in different age groups in Fars province from 1977 to 1999.

Age groups (Yrs)	Squamous cell carcinoma		Adenocarcinoma	
	Frequency	Incidence	Frequency	Incidence
15-24	10	0.08 (0.00-1.33)	3	0.02 (0.00-1.33)
25-34	36	0.38 (0.1-2.5)	13	0.14 (0.00-1.9)
35-44	96	1.96 (0.6-6.7)	19	0.39 (0.00-4)
45-54	187	4.45 (1.8-10.9)	26	0.62 (0.1-5.1)
55-64	289	7.91 (3.8-16.3)	81	2.222 (0.05-8.1)
25-34	20	0.42 (0.00-4.2)	16	0.35 (0.00-4.3)
≥ 65	198	9.84 (4.1-23.5)	81	4.03 (0.1-14.8)
Total	816	2.18 (0.5-7.9)	223	0.59 (0.00-4.8)

\* Incidence per 100,000 population in each age group. Note: Age of 79 patients with squamous cell carcinoma and 23 with adenocarcinoma were not recorded.

believed that the incidence of esophageal carcinoma is high in Iran, especially in the northern parts.<sup>2,4-7</sup> Most of the published data on this issue originate from some old cross-sectional studies in which changes of the incidence over time are not acknowledged. Meanwhile, there is only little data on the incidence in other parts of the country, particularly the South.<sup>8-11</sup> In this retrospective study we tried to find trends in the epidemiology of esophageal carci-

noma in Fars Province, South of Iran.

### Materials and Methods

We reviewed pathology reports from all surgical-pathology laboratories in Fars Province, South of Iran, from March 1977 to March 1999. We took into consideration reports of both surgical and endo-

**Table 2:** Incidence (95% C.I)\* and Absolute frequency of squamous cell carcinoma in males and females of different age groups in Fars province from 1977 to 1999

Age group (Yrs)	Male		Female	
	Frequency	Incidence	Frequency	Incidence
15-24	7	0.1 (0.00-2.6)	3	0.05 (0.00-3)
25-34	20	0.42 (0.00-4.2)	16	0.35 (0.00-4.3)
35-44	36	1.50 (0.2-9.7)	60	2.40 (0.5-10.6)
45-54	93	4.22 (1.1-14.2)	94	4.70 (1.2-15.6)
55-64	186	9.32 (3.9-23)	103	6.22 (1.7-19.8)
≥65	137	13.86 (9.9-19.4)	61	5.96 (1.2-25.9)
Total	479	2.49 (0.5-13)	337	1.84 (0.2-11.8)

\* Incidence per 100,000 population in each age group of males or females. Note: Gender of 79 patients with SCC was not recorded.

**Table 3:** Incidence (95% C.I)\* and absolute frequency of adenocarcinoma in males and females of different age groups in Fars province from 1977 to 1999.

Age group (Yrs)	Male		Female	
	Frequency	Incidence	Frequency	Incidence
15-24	3	0.04 (0.00-2.6)	-	-
25-34	11	0.23 (0.00-3.8)	2	0.04 (0.00-3.8)
35-44	13	0.54 (0.00-7.5)	6	0.24 (0.00-7.2)
45-54	19	0.86 (0.1-9)	7	0.35 (0.00-9)
55-64	68	3.41 (0.8-14.1)	13	0.78 (0.00-10.9)
≥65	65	6.57 (4.10.7)	16	1.56 (0.00-19.4)
Total	179	0.93 (0.01-1.03)	44	0.24 (0.00-0.98)

\* Incidence per 100,000 population in each age group of males or females. Note: Gender of 23 patients with AC was not recorded.

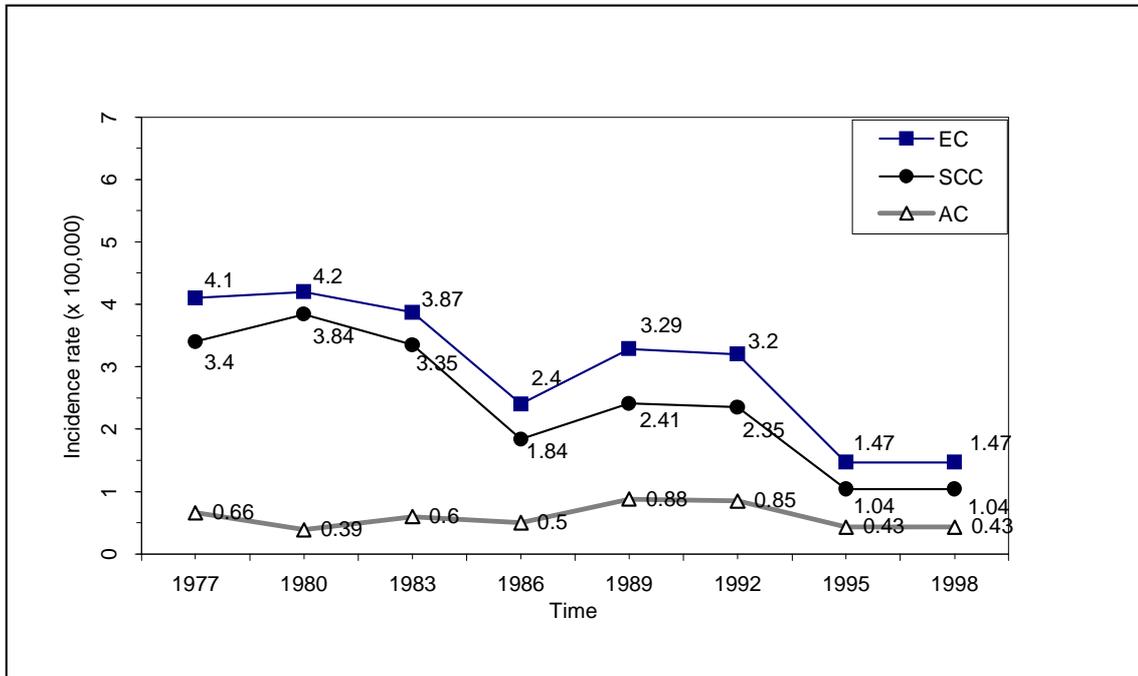


Figure.1: Incidence rate (CI%95) of esophageal cancer from 1977 to 1999 in Fars Province . Iran

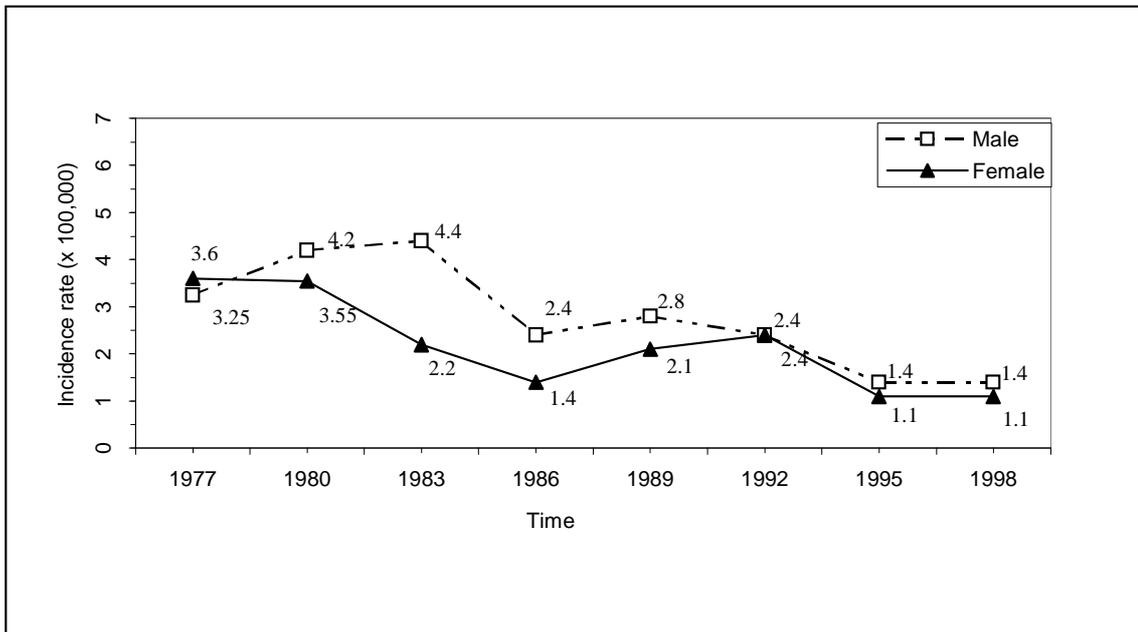


Figure 2: Incidence rate (CI%95) of squamous cell carcinoma according to sex from 1977 to 1999 in the Fars province, Iran.

**Table 4:** Relative Risk (95% C.I) of squamous cell carcinoma and adenocarcinoma in different age groups among males compared to females in Fars province from 1977 to 1999.

Age groups (Yrs)	Squamous cell carcinoma	Adenocarcinoma
15-24	2 (0.52-7.73)	
25-34	1.2 (0.62-2.32)	5.75 (1.29-24.76)
35-44	0.63 (0.41-0.94)	2.25 (0.86-5.94)
45-54	0.90 (0.67-1.2)	2.46 (1.04-5.86)
55-64	1.5 (1.18-1.91)	4.37 (2.4-7.86)
≥65	2.32 (1.72-3.14)	4.21 (2.43-7.27)
total	1.36 (1.18-1.56)	4 (2.79-5.39)

Scopic specimens. If there were more than one report for a patient, we considered the first and discarded the rest. Since the incidence of the disease in young people is almost zero, the annual incidence was calculated for every 100,000 individuals older than 15 years. The mean annual incidence for each age group in the study period was also calculated for both males and females.

**Results**

During the study period, more than 500,000 surgical pathology reports were recorded. Altogether, there were 5,421 GI cancers comprising 2,326 (43%) gastric cancers, 1,398 (26%) colonic cancers, 1,161 (21%) esophageal carcinomas, and 536 (10%) small bowel cancers. Of esophageal malignancies, 895 (78.4%) were squamous cell and 246 (21.6%) were adenocarcinomas. The remainder of 20 (1.7%) consisted of 13 undetermined esophageal carcinomas; two cases of epidermoid carcinoma, one carcinoid tumor, one case of mucocellular carcinoma and three metastatic tumors to the esophagus. The data of these 20 patients were not used in the study. Annual incidence of esophageal carcinoma over the past 22 years is shown in figure 1. In the period of 1977-1979, the annual incidence was 4.09 per 100,000 population aged more than 15 years. There was 64% decrease in annual incidence over the study period, falling to an annual incidence rate of 1.47 per 100,000 population > 15 years in 1998. For squamous cell carcinoma, this incidence had decreased from 3.43 to 1.04 over the same time span. The figure for adenocarcinoma was somewhat different. There was a rise in incidence from 0.66 on 1977 up to 0.88 on 1991. The incidence then decreased to 0.43 at 1999.

Overall, the means of annual incidence of esophageal carcinoma, squamous cell carcinoma and adenocarcinoma during the study period were 2.95, 2.31, and 0.64 per 100,000 population, respectively. Annual incidence of squamous cell carcinoma and adenocarcinoma in males and females and among different age groups are shown in figures 2 and 3 and tables 1-3. The male to female ratio for squamous cell carcinoma was 1.45 and 4.23 for adenocarcinoma. Overall, male to female ratio for all esophageal carcinomas over the period was 1.78 (p<0.001). The relative risk for squamous cell carcinoma and adenocarcinoma in males compared to females in different age groups are shown in table 4.

The mean age of esophageal carcinoma, squamous cell carcinoma, and adenocarcinoma in males and females are shown in table 5. The mean age of patients with squamous cell carcinoma and adenocarcinoma in the second half of the study period was 4 years more than that in the first half (p<0.004). This rise in mean age of patients was correct for both males and females and it was even more pronounced in females (p<0.003).

The most common symptoms in this retrospective study were dysphagia (84.8%), weight loss (9.9%), epigastric pain (4.1%), vomiting (3.5%) and anorexia (2.3%). Other symptoms including, upper GI bleeding, heartburn, and hoarseness was observed in 4.4% of patients.

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**Discussion**

We found esophageal carcinoma to be the third most common GI tumor, lagging only behind gastric and colon cancer. Compared to earlier reports from this center, claiming esophageal carcinoma as the 2<sup>nd</sup> most common GI tumor in the region, our findings reflects a change in incidence rates of tumors, with an increase in the cancer of colon and a decrease in

**Table5:** Mean age ±SD in esophageal carcinoma, squamous cell carcinoma and adenocarcinoma in males and females in Fars province from 1977 to 1999.

Gender	Esophageal carcinoma	Squamous cell carcinoma	Adenocarcinoma
Male (Mean age ±SD)	57.2 ±11.83	56.3 ±11.55	58.1 ±12.53
Female (Mean age ±SD)	55.2 ±11.71	52.5 ±11.6	57.9 ±12.12
Total	56.2 ±11.9	54.4 ±11.72	58 ±12.43

esophageal carcinoma.<sup>9,10</sup> Our results show that currently, the incidence of esophageal carcinoma in Fars Province is low, compared to reports from northern parts of Iran where esophageal carcinoma is the most common form of GI tumor or those of western countries where the incidence has been reported as 2-8 per 100,000 population.<sup>4-6,12-14</sup>

Adenocarcinoma showed a dramatic upsurge from less than 7% (according to a previous report from this center) to 21.6% in this series.<sup>11</sup> In the second half of the study period, squamous cell carcinoma being still the most common type of cancer of esophagus, dropped to 31.5% in incidence rate in distinction to a 29% rise in adenocarcinoma. This finding is also in agreement with recent reports from western countries as adenocarcinoma is currently the most prevalent type of the esophageal tumor.<sup>12-16</sup> Increased incidence of gastro-esophageal reflux disease, smoking and obesity perhaps, have been incriminated as etiologic factors for this change.<sup>13,17</sup>

As in case of incidence, different reports indicate also a geographical variation of male to female ratio of esophageal carcinoma in Iran.<sup>9,10,18</sup>

In our series, the ratios for esophageal carcinoma, squamous cell carcinoma and adenocarcinoma were 1.78, 1.45, and 4.23, respectively. This denotes a male predominance in all types of esophageal carcinoma, especially adenocarcinoma and is in keeping with reports from other low incidence areas. Nonetheless, it is in contrast to reports from

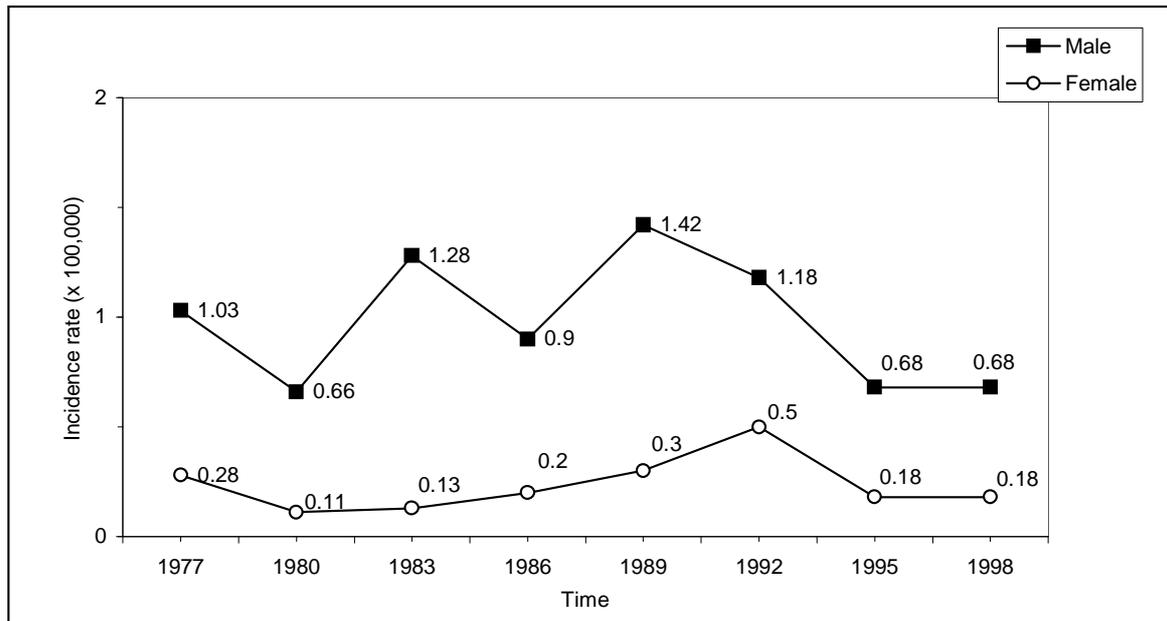
high-incidence areas, where male to female ratio is close to one.<sup>7,14</sup>

The age range (for both sexes) of people mostly afflicted by esophageal carcinoma is also no exception to the rule of geographical variation; compare ranges of 50-54 and 60-65 years reported from two northern cities which highly contrasts the figure of 34-55 years previously reported from our center.<sup>5,7,9-11</sup>

We found that increased age was a major risk factor for esophageal carcinoma, as all types of esophageal carcinomas were most commonly seen among 65 years and older.

Further analysis of our results showed that the most common age of presentation for squamous cell carcinoma in males was 65 years or older, whereas in females it was between 55 and 64. In the 35-45 year age group, more females developed squamous cell carcinoma than males. In this age group male to female ratio dropped to less than one. In other words, more than half of the women who developed squamous cell carcinoma did so before the age of 55 years. Gallus *et al.* reported that heavy smoking and heavy alcohol consumption were the main risk factors while fruit and vegetable intake, oral contraceptive pills (OCP) or hormone replacement therapy had protective effects.<sup>19</sup> Heavy smoking or drinking are uncommon among women in our country; however, decreased fruit and vegetable intake and underuse of OCP might be contributing factors.

In a report, Mahboubi has pointed to the role of



**Figure 3:** Incidence rate (CI%95) of esophageal adenocarcinoma according to gender from 1977 to 1999 in the Fars province, Iran, in logarithmic scale.

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more severe malnutrition among females, and also exposure to the smoke during cooking among rural population, and postulated the possible role of certain foods consumed by women during pregnancy.<sup>4</sup> In another report, Kmet *et al.* asserted that the number of pregnancy and/or lactation during major parts of female reproductive life in this part of the world, might be of some relevant etiologic importance.<sup>5</sup>

In our study, regardless of sex, adenocarcinoma had its highest incidence over the age of 65 years, with male to female ratio of more than one in all age groups. This finding is in agreement with reports from other regions.<sup>12,13</sup> Considering the two half periods of this study, one would notice that the mean ages of clinical presentation in patients with either adenocarcinoma (58.0 yrs), squamous cell carcinoma (54.4 yrs) in particular, and that for esophageal carcinoma (56.0 yrs), at large, has increased over time. These mean ages, however, are still lower than figures reported from western countries.<sup>12,13</sup>

In this study, men were affected by squamous cell carcinoma (RR=1.36), and by adenocarcinoma (RR=4.0) much more frequently than women. This trend, however, fluctuated over time so that it had an increase during the first nine years followed by a decrease over the second nine years with a small increase thereafter. Overall, we can assert that over the 22 years studied, the male/female ratio has decreased for esophageal carcinoma.

Admittedly, there are some shortcomings in the current study; all the reports studied did not belong to the residents of Fars Province. Therefore, we accept that the calculated incidence rates might not be quite precise. However, considering our daily practice regarding the number and distribution of referred patients, we believe that the amount of error in our observation is negligible.

### Conclusion

In conclusion, during the past 22 years in Fars Province, South of Iran, the incidence of esophageal carcinoma, squamous cell carcinoma and adenocarcinoma has decreased, with more pronounced changes in squamous cell carcinoma. Overall, the incidence of esophageal carcinoma was much lower than earlier reports from this Province and women developed esophageal carcinoma at younger ages than men.

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