

GÜL ERGÖR

BACKGROUND

Cancer of the esophagus is the eighth most common cancer worldwide [1], with more than 400,000 cases per year. Incidence is highest in western and south central Asia. The geographical differences in incidence that are observed are more extreme than for any other cancer. A high-risk area known as the “esophageal cancer belt” ranges from northern Iran all the way to north central China [2].

The 2 main types of esophageal cancer are squamous cell carcinoma and adenocarcinoma. Squamous cell carcinoma is seen predominantly in developing countries and is associated with tobacco and alcohol consumption as well as with hot beverage consumption and malnutrition. Low intakes of fruits and vegetables are also risk factors for squamous cell cancers. Adenocarcinoma is mostly found in developed countries, and is mostly related to obesity and chronic gastroesophageal reflux. This reflux causes a clinical condition called Barrett’s esophagus, which is considered a premalignant lesion [3].

Many risk factors play a role in the etiology of esophageal cancer, although these vary with geographic region. For example, betel chewing and oral consumption of opium are factors primarily found in Southeast Asia and the Caspian Sea area [2]. The factor for which there is the most convincing evidence is alcohol consumption, and this risk is even greater among drinkers who also smoke. The alcohol relationship is not specific to a type of drink, but to the level of consumption.

McCredie et al. reported that migrants from the Middle East to Australia had a lower cancer incidence than other Australians for many sites, including the esophagus [4]. A characteristic of this

disease is that it shows marked differences between ethnic groups in the same country or same geographical areas. For example, Scotland has very high rates compared with England and Ireland [5]. In a recent study by de Martel et al., high prevalence of *Helicobacter pylori* was reported as a protective factor for esophageal adenocarcinoma (OR = 0.37; 95% CI, 0.16-0.88) [6].

RESULTS

Overall Incidence

Table 2.1 displays the age-standardized incidence rates in the MECC countries and US SEER. The incidence of esophageal cancer in the MECC countries during this period (1996-2001) was among the lowest in the world. The rates worldwide were 11.5 in males and 4.7 in females [7]. In MECC countries, the highest rate was in Israeli Jews (1.5), and the lowest was in Israeli Arabs and Cypriots (0.6). Egyptians (1.4) showed a rate similar to that of Israeli Jews, while Jordanians had a slightly lower rate (1.1). In comparison, US SEER rates for the same years were more than twice as high (3.0). Because the MECC countries are outside the esophageal cancer belt, lower rates than in this high-risk region are expected.

The low rates of esophageal cancer in the MECC countries might also be explained by the relatively low levels of alcohol consumption in Arab countries with a Muslim majority. Alcohol consumption by Israeli Jews is lower than in most Western countries, but higher than consumption by Israeli Arabs. According to Neumark et al., the prevalence of any non-ritual alcohol consumption by males over a 1-month period was 67% in Israeli Jews and 46% in Israeli Arabs. The differences were even more marked in females: 33% in Israeli Jews and 7% in Israeli Arabs [8]. Data from the

same study showed that Ashkenazi Israeli Jews had higher drinking patterns than Sephardi Israeli Jews (68% and 59%, respectively) [9].

In contrast to alcohol, in almost all of the MECC countries there is a high prevalence of smoking, which would tend to increase esophageal cancer rates. Smoking prevalence in Israel was 39% in males during 1999-2001, according to the First Israeli National Health and Nutrition Survey [10]. Similarly, smoking is very common in the other MECC countries. The low esophageal cancer rates suggest under-diagnosis of esophageal cancers in all the countries in the region.

As indicated above, world esophageal cancer rates were 2 to 3 times higher in males (11.5) than in females (4.7). Sex ratios for Middle Eastern populations can be judged from data taken from GLOBOCAN, which are presented in Table 2.2. The ratios are

similar to those seen in the MECC data. Most ratios in the MECC data were around 2, except in Israeli Arabs, where the male rate was 3 times the female rate, and in Cyprus, where the male rate was 5 times the female rate (Table 2.1). However, due to the very small numbers, these differences in ratios should be interpreted with caution. The sex ratio in the United States was more than 4 (Table 2.1), which may be explained by the fact that the majority of these cancers were adenomatous, originating from Barrett’s esophagus, which is 7 times more commonly seen in males [2].

Age

Esophageal cancer incidence increases with age in all countries. In the MECC populations and in SEER, the age-specific rates were very low below 50 years of age (Table 2.1). Between ages 50-69 years, the rates were 5.0 in Egyptians, 4.5 in Israeli Jews, 3.4 in

Table 2.1. Esophageal Cancer: Number of Cases, Age Distribution, and Age-Standardized Incidence Rates, by Age and Sex, in Cyprus, Israel (Jews and Arabs), Egypt, Jordan, and US SEER – 1996-2001*

	Cyprus 1998-2001			Israel (Jews) 1996-2001			Israel (Arabs) 1996-2001			Egypt 1999-2001			Jordan 1996-2001			US SEER† 1999-2001		
	Total	Male	Female	Total	Male	Female	Total	Male	Female	Total	Male	Female	Total	Male	Female	Total	Male	Female
Total cases	23	19	4	665	390	275	20	14	6	94	58	36	144	99	45	4,826	3,616	1,210
Age Groups (Distribution)																		
<50 y	-	-	0.0%	5.6%	6.9%	3.6%	15.0%	-	-	26.6%	27.6%	25.0%	18.1%	18.2%	17.8%	7.6%	8.2%	5.6%
50-69 y	43.5%	42.1%	-	32.2%	36.9%	25.5%	35.0%	50.0%	0.0%	55.3%	56.9%	52.8%	48.6%	48.5%	48.9%	44.6%	48.1%	33.9%
70+ y	47.8%	47.4%	-	62.3%	56.2%	70.9%	50.0%	35.7%	83.3%	18.1%	15.5%	22.2%	33.3%	33.3%	33.3%	47.9%	43.7%	60.5%
Age Groups (Rates)‡																		
Total rate	0.6	1.0	0.2	1.5	2.1	1.0	0.6	0.9	0.3	1.4	1.7	1.0	1.1	1.5	0.7	3.0	5.1	1.2
<50 y	-	-	0.0	0.1	0.2	0.1	0.1	-	-	0.3	0.4	0.2	0.2	0.2	0.1	0.3	0.5	0.1
50-69 y	2.0	3.3	-	4.5	6.6	2.7	1.3	2.8	0.0	5.0	6.6	3.6	3.4	4.4	2.2	11.2	19.1	4.1
70+ y	4.6	8.8	-	16.6	21.2	13.3	7.7	8.9	6.8	8.2	8.9	7.6	9.8	14.4	5.7	24.5	42.0	12.2

*The symbols "-" = 1-2 cases; and "[numeral]" (italic) = 0 or 3-15 cases.

†SEER 13 Registries, Public Use Data Set, from data submitted November 2004.

‡Rates are per 100,000 and are age-standardized to the World Standard Million.

Table 2.2. Esophageal Cancer: Age-Standardized Incidence Rates,* by Sex, in Middle Eastern Countries – 1998-2002

Country	Male	Female
Cyprus	1.7	0.3
Iraq	1.2	0.9
Israel	2.3	1.1
Jordan	1.4	0.7
Kuwait	1.7	1.8
Lebanon	1.4	0.7
Syrian Arab Republic	1.4	0.9
Turkey	2.1	1.5

*Rates are per 100,000 and are age-standardized to the World Standard Million.

Source: Ferlay J, Bray F, Pisani P, Parkin DM. GLOBOCAN 2002: cancer incidence, mortality and prevalence worldwide. IARC cancer base no. 5, version 2.0. Lyon (France): IARC Press; 2004.

Jordanians, 2.0 in Cypriots, and 1.3 in Israeli Arabs. The highest rates in the MECC populations were in the 70-and-older group, ranging from 4.6 in Cypriots to 16.6 in Israeli Jews. The age-specific rates also varied by sex.

Histology

Squamous cell carcinoma was the most common type of esophageal cancer in each of the MECC populations (Table 2.3). However, it is important to note that the ratio of squamous cell carcinoma to adenocarcinoma (the other main type of esophageal cancer) was far higher in females than in males. Overall, approximately half of the esophageal cancers were of the squamous cell type in Cyprus and Israel. In Egypt and Jordan, the proportions reached above 60%, which is typical for developing countries. In the United States, the proportion of adenocarcinomas was higher than for squamous cell carcinomas, as in other Western countries (Table 2.3).

Subsites

The MECC registries record the localization of tumors within the esophagus; however, the majority of the esophageal cancers were recorded as occurring at an unspecified site in 4 of the populations: Cypriots (56.5%), Israeli Jews (60.8%), Israeli Arabs (60.0%), and Jordanians (72.2%) (Table 2.4). Only in Egypt were a majority recorded for a specified site. The most common specific site of localization in the MECC countries was in the “abdominal and one-third distal” part of the esophagus, which was recorded far more frequently than were cancers localized in the upper one-third and middle one-third of the esophagus.

Basis of Diagnosis

The proportion of microscopically confirmed esophageal cancer cases varied from 85.4% to 100% in the MECC countries (Table 2.3). US SEER results had a very high (96.1%) microscopic confirmation, which could be explained by the country’s highly technology-dependent health care system. This high rate is less expected in MECC countries, where patients may generally receive less aggressive management of their disease.

In Cyprus, all cases were microscopically confirmed. This may indicate that some cases were missing, because one would expect that there would be patients treated palliatively whose cancers were not microscopically confirmed. Evidently, if there were such patients, they were not notified to the registry. Likewise, the very high proportion of microscopically confirmed cases among Israeli Arabs and Jordanians suggests that some clinically diagnosed cases were missed.

SUMMARY AND CONCLUSIONS

The low incidence rates reported for esophageal cancer are most probably due to low consumption of alcohol in the Middle East compared with other parts of the world. However, the possibility of under-diagnosis is also a partial explanation. In some countries,

male/female ratios were very high; this might be a result of gender-related problems of access to health care due to traditional or organizational factors, though it could also be due to fluctuations in small numbers. Discrepancies between Israeli Jews and Arabs might be partly due to ethnic distinctions, but differences in alcohol consumption and smoking are the most likely contributing causes.

Table 2.3. Esophageal Cancer: Number of Cases and Proportions of Histologic Type and Microscopic Confirmation, by Sex, in Cyprus, Israel (Jews and Arabs), Egypt, Jordan, and US SEER – 1996-2001*

	Cyprus 1998-2001			Israel (Jews) 1996-2001			Israel (Arabs) 1996-2001			Egypt 1999-2001			Jordan 1996-2001			US SEER† 1999-2001		
	Total	Male	Female	Total	Male	Female	Total	Male	Female	Total	Male	Female	Total	Male	Female	Total	Male	Female
Total cases microscopically confirmed	23	19	4	568	338	230	19	14	5	83	54	29	141	96	45	4640	3499	1141
Microscopically confirmed	100.0%	100.0%	100.0%	85.4%	86.7%	83.6%	95.0%	100.0%	83.3%	88.3%	93.1%	80.5%	97.9%	97.0%	100.0%	96.1%	97.0%	94.3%
Distribution of Microscopically Confirmed Cases																		
Histologic distribution‡	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%
Carcinoma	100.0%	100.0%	100.0%	98.1%	97.0%	99.6%	94.7%	92.9%	100.0%	100.0%	100.0%	100.0%	97.2%	97.9%	95.6%	98.9%	98.9%	98.8%
Squamous cell carcinoma	56.5%	52.6%	75.0%	50.5%	39.6%	66.5%	52.6%	50.0%	60.0%	67.5%	61.1%	79.3%	62.4%	56.3%	75.6%	41.5%	35.7%	59.4%
Adenocarcinoma	43.5%	47.4%	-	39.1%	48.5%	25.2%	42.1%	42.9%	-	20.5%	25.9%	10.3%	29.8%	37.5%	13.3%	50.5%	57.1%	30.4%
Other specified carcinoma	0.0%	0.0%	0.0%	3.0%	3.8%	1.7%	0.0%	0.0%	0.0%	-	-	0.0%	0.0%	0.0%	0.0%	1.9%	1.8%	2.5%
Unspecified carcinoma	0.0%	0.0%	0.0%	5.5%	5.0%	6.1%	0.0%	0.0%	0.0%	9.6%	9.3%	10.3%	5.0%	4.2%	6.7%	4.9%	4.3%	6.5%
Sarcoma	0.0%	0.0%	0.0%	0.5%	0.9%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.2%	0.2%	-
Other histologies	0.0%	0.0%	0.0%	0.5%	-	-	-	-	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.4%	0.4%	0.4%
Unspecified cancer	0.0%	0.0%	0.0%	0.9%	1.5%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	2.8%	-	-	0.6%	0.5%	0.8%

*The symbols "-" = 1-2 cases; and "[numeral]" (italic) = 0 or 3-15 cases.

†SEER 13 Registries, Public Use Data Set, from data submitted November 2004.

‡Percentages should sum over a column to 100% (with some rounding). However, where a percentage has been suppressed because it is based on only 1 or 2 cases, the remaining percentages will not sum to 100%.

Table 2.4. Esophageal Cancer: Number of Cases and Proportions of Subsites, by Sex, in Cyprus, Israel (Jews and Arabs), Egypt, Jordan, and US SEER – 1996-2001

	Cyprus 1998-2001			Israel (Jews) 1996-2001			Israel (Arabs) 1996-2001			Egypt 1999-2001			Jordan 1996-2001			US SEER* 1999-2001		
	Total	Male	Female	Total	Male	Female	Total	Male	Female	Total	Male	Female	Total	Male	Female	Total	Male	Female
Total cases	23	19	4	665	390	275	20	14	6	94	58	36	144	99	45	4,826	3,616	1,210
Total percentage†	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%
Abdominal and distal 1/3	26.1%	31.6%	0.0%	25.9%	29.2%	21.1%	25.0%	28.6%	-	48.9%	60.3%	30.6%	18.1%	16.2%	22.2%	53.6%	58.2%	40.0%
Other subsites	17.4%	-	-	13.4%	9.7%	18.5%	15.0%	21.4%	0.0%	20.2%	15.5%	27.8%	9.7%	8.1%	13.3%	36.3%	32.6%	47.5%
NOS‡	56.5%	57.9%	-	60.8%	61.0%	60.4%	60.0%	50.0%	83.3%	30.9%	24.1%	41.7%	72.2%	75.8%	64.4%	10.1%	9.3%	12.5%

*SEER 13 Registries, Public Use Data Set, from data submitted November 2004.

†Percentages should sum over a column to 100% (with some rounding). However, where a percentage has been suppressed because it is based on only 1 or 2 cases, the remaining percentages will not sum to 100%.

‡NOS indicates "not otherwise specified."

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