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BACKGROUND

Stomach, or gastric, cancer incidence is second only to lung cancer worldwide, with an estimated 870,000 new cases and 650,000 deaths every year. The high-risk areas are East Asia, South America, and Eastern Europe. Data show that second-generation migrants from the high- to low-risk areas have lower incidence rates than their parents. Incidence rates are twice as high in males as in females. Thirty-eight percent of the world's stomach cancer cases occur in China, and it is the most frequent cancer in males in other parts of East Asia. Age-standardized incidence rates (ASRs) are the highest in the world in Japan (77.9 per 100,000 in men; 33.3 in women) *[1,2]*.

The major risk factors for stomach cancer are hypothesized to be nutritional, including inadequate intake of fresh fruits and vegetables, and high intake of salt, smoked fish, and meat. Refrigeration of food is considered protective. Vitamin C, contained in vegetables and fruits, may be protective for stomach cancer. Other possibly protective nutritional factors are whole-grain cereal, carotenoids, allium compounds (e.g., garlic), and green tea *[3]*. Smoking carries a slightly increased risk for stomach cancer *[4]*, and alcohol does not affect risk other than in the gastric cardia *[5]*. Smoking is quite common in countries of the Middle East Cancer Consortium (MECC) *[6-9]*.

Another important risk factor is *Helicobacter pylori* infection. Other gastric diseases, such as ulcer and atrophic gastritis, elevate gastric pH, thus causing anaerobic bacterial colonization in the stomach. *H. pylori* prevalence ranges from 25% in developed countries to 80%-90% in the developing countries *[10]*. It is now considered as the principal cause of chronic gastritis and peptic ulcer disease, and is a key risk factor for the development of gastric cancer *[11,12]*. The prevalence of *H. pylori* is thought to be high in MECC countries. In Israel, the prevalence has been reported to be 72% in a rural population and 65% in an urban population, which is higher than in the United States and Western Europe, but lower than in developing countries *[13]*. Another study has reported 33% positive for *H. pylori* in an elderly population in Israel *[14]*, and a case-control study in Israel found 63% positivity among the healthy controls *[15]*. In a population of Jordanian endoscopy patients, 82% prevalence was reported *[16]*, but there is no information for the general population.

RESULTS

Overall Incidence

Stomach cancer incidence in the MECC countries during the period 1996-2001 was low (Table 3.1), compared with the world ASR of 10.3 in females and 22.0 in males *[1]*. The incidence was highest in Israeli Jews (8.5), followed by Cypriots (4.9), Jordanians (4.8), and Israeli Arabs (4.6) (Table 3.1). Although a study from Jordan reports that the characteristics of gastric cancers diagnosed there resemble those in high-risk countries *[17]*, it nevertheless appears to be a low-incidence country. Egypt had the lowest incidence in the region, with 2.9. US SEER incidence was 5.3 for the same years (Table 3.1). These rates are 5 to 15 times lower than in Japan, where the overall rate is more than 50 *[1]*.

The Middle East has better access to fruits and vegetables throughout the year than in many places, and the nutritional practices have Mediterranean influences. This may result in the low incidence rates that were observed. On the other hand, *H. pylori* seroprevalence may be high in these countries, but this was not reflected in the observed cancer incidence.

Worldwide, the stomach cancer ASR in males is twice that in females *[1]*. Cyprus did not show this pattern; the male-to-female ratio was closer to 1 (1.44). Egypt's ratio was closer to the world pattern (1.64), while a ratio close to 2 was observed in Israeli Jews and Arabs, Jordanians, and in US SEER. A low male incidence rate was especially noticeable in Egypt and may be partially due to undiagnosed cases of stomach cancer, especially among the elderly.

The incidence rates of stomach cancer reported by GLOBOCAN *[2]* for countries in the Middle East (including some MECC populations) in 2002 are shown in Table 3.2. The Arab countries in the region had low rates, while Israel and Turkey had higher rates. In addition, all of the male-to-female rate ratios were lower than 2 for Cyprus and the Arab countries, while they were approximately 2 for Israel and Turkey. This may be partly due to ethnic differences and the more Western lifestyle in Israel and Turkey.

Age

The incidence of stomach cancer rises from age 50 years and is highest in the 70-and-older group. The highest incidence in that group was in Israeli Jews (121.2 in males; 60.5 in females), and the lowest was in Egyptians (17.5 in males; 5.4 in females) (Table 3.1). The high incidence in older Israeli Jews, many of whom originated from Europe, could be related to the deprived environmental and nutritional conditions they suffered during the Second World War. This is supported by data showing that Israeli Jews born in Europe have a higher stomach cancer incidence than Israeli Jews born elsewhere *[18]*. The low rates in Egypt in this oldest age group, among both males and females, strongly suggests that older cases have not been diagnosed, perhaps due to elderly patients' underuse of health care services.

Table 3.1. Stomach 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	198	112	86	3,605	2,169	1,436	177	108	69	206	126	80	687	434	253	9,235	5,541	3,694
Age Groups (Distribution)																		
<50 y	16.2%	16.1%	16.3%	7.9%	7.1%	9.1%	30.5%	28.7%	33.3%	34.0%	31.0%	38.8%	29.5%	26.5%	34.8%	10.8%	10.8%	10.7%
50-69 y	37.9%	36.6%	39.5%	33.7%	35.9%	30.3%	39.0%	42.6%	33.3%	54.9%	55.6%	53.8%	47.5%	48.6%	45.5%	33.3%	36.7%	28.0%
70+ y	46.0%	47.3%	44.2%	58.4%	56.9%	60.7%	30.5%	28.7%	33.3%	11.2%	13.5%	*7.5%*	23.0%	24.9%	19.8%	56.0%	52.5%	61.2%
Age Groups (Rates)‡																		
Total rate	4.9	5.9	4.1	8.5	11.7	6.0	4.6	6.0	3.4	2.9	3.6	2.2	4.8	6.0	3.5	5.3	7.4	3.6
<50 y	1.2	1.4	1.1	1.2	1.3	1.0	1.1	1.2	1.0	0.9	1.0	0.8	1.3	1.4	1.1	0.9	1.0	0.7
50-69 y	14.4	16.4	12.7	26.0	36.3	17.1	13.2	18.5	8.4	10.8	13.3	8.3	15.0	18.5	11.2	16.1	22.5	10.4
70+ y	40.2	54.6	29.0	85.9	121.2	60.5	40.1	52.3	30.7	11.1	17.5	*5.4*	33.5	48.3	20.1	51.8	75.0	36.1

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.

Histology

According to Table 3.3, the majority of stomach cancers in the MECC and US SEER registries were adenocarcinomas. The proportion of adenocarcinomas was highest in Cyprus (78.1%) and lowest in Egypt (43.9%). According to US SEER data, adenocarcinomas comprised 50.1% of the total cases. The second most common histologic type in all MECC populations was signet ring cell carcinoma. This pattern was the same in the SEER results.

Basis of Diagnosis

The percentage of stomach cancer cases that were microscopically confirmed ranged from 80% to 99% (Table 3.3). Stomach cancer is among those cancers that are more difficult to detect, and is mostly diagnosed at a later stage, often with metastasis to other sites. Therefore, the high levels of microscopic confirmation reported in Cyprus (99.0%) and Jordan (98.8%) suggest either undercoverage of cases by the registries or underdiagnosis by the health care systems. Note that the high proportion (96.8%) of microscopically confirmed cases in the United States might be expected for a country with a highly equipped health care service, but lower proportions would be expected for Cyprus and Jordan. Conversely, in Egypt, only 79.6% of cases were reported as microscopically confirmed, and this may raise questions about the validity of the remaining diagnoses. These observations argue for caution in the interpretation of the trends discussed in this chapter.

Table 3.2. Stomach Cancer: Age-Standardized Incidence Rates,* by Sex, in Middle Eastern Countries − 1998-2002

Country	Male	Female
Cyprus	6.8	4.3
Iraq	4.5	3.8
Israel	12.5	6.9
Jordan	6.6	4.0
Kuwait	4.8	3.0
Lebanon	7.0	4.6
Syrian Arab Republic	7.2	5.5
Turkey	12.2	6.4

*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.

SUMMARY AND CONCLUSIONS

Among the MECC countries, stomach cancer presents as a larger problem in Israel, especially for Israeli Jews. Rates are especially low in Egypt, and quite low in Jordan and Cyprus, but the low rates may be partly due to underdiagnosis. The lower socioeconomic groups who are more prone to stomach cancer due to lifestyle and environment may have less access to health care services, and thus might be missed in the registration systems because they remain undiagnosed or are not hospitalized. Equal access to health care will eventually lead to improved reliability in registration records.

Although H. pylori infection is common in developing countries in the Middle East, this is not reflected in the relatively low stomach cancer ASRs in these countries. Studies on the effect of H. pylori infection in this region and possible interactions with nutritional behaviors may give further insight into the etiology of stomach cancer in Middle Eastern populations.

Table 3.3. Stomach Cancer: Number of Cases and Proportions of Microscopic Confirmation and Histologic Type, 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	196	110	86	3,241	1,964	1,277	165	103	62	164	102	62	679	429	250	8,936	5,419	3,517
Microscopically confirmed	99.0%	98.2%	100.0%	89.9%	90.5%	88.9%	93.2%	95.4%	89.9%	79.6%	81.0%	77.5%	98.8%	98.8%	98.8%	96.8%	97.8%	95.2%
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%
Neoplasm, NOS§	*0.0%*	*0.0%*	*0.0%*	0.7%	*0.4%*	*1.1%*	*0.0%*	*0.0%*	*0.0%*	*4.3%*	*3.9%*	*4.8%*	*1.3%*	*1.2%*	*1.6%*	0.6%	0.5%	0.8%
Carcinoma, NOS§	*0.0%*	*0.0%*	*0.0%*	4.1%	4.3%	3.9%	-	*0.0%*	-	-	-	*0.0%*	7.4%	7.2%	7.6%	2.3%	1.9%	2.8%
Carcinoma undifferentiated, NOS§	*0.0%*	*0.0%*	*0.0%*	*0.5%*	*0.4%*	*0.6%*	-	-	*0.0%*	*4.9%*	*3.9%*	*6.5%*	*0.6%*	*0.9%*	*0.0%*	0.2%	*0.3%*	*0.1%*
Carcinoma anaplastic, NOS§	*0.0%*	*0.0%*	*0.0%*	0.9%	0.9%	*0.9%*	-	*0.0%*	-	*9.1%*	*8.8%*	*9.7%*	*0.0%*	*0.0%*	*0.0%*	*0.1%*	-	*0.1%*
Adenocarcinoma	78.1%	77.3%	79.1%	54.9%	57.6%	50.7%	44.2%	44.7%	43.5%	43.9%	50.0%	33.9%	67.3%	71.6%	60.0%	50.1%	55.1%	42.5%
Intestinal adenocarcinoma	*5.6%*	*7.3%*	*3.5%*	7.4%	7.7%	7.0%	*6.1%*	*6.8%*	*4.8%*	*0.0%*	*0.0%*	*0.0%*	*0.9%*	*0.7%*	*1.2%*	9.1%	9.7%	8.2%
Diffuse carcinoma	*5.1%*	*5.5%*	*4.7%*	0.9%	0.9%	*0.9%*	*1.8%*	-	-	*0.0%*	*0.0%*	*0.0%*	*1.5%*	*1.2%*	*2.0%*	3.6%	3.2%	4.4%
Carcinoid tumor	-	*0.0%*	-	1.5%	0.8%	2.4%	*6.1%*	*4.9%*	*8.1%*	-	-	*0.0%*	*2.2%*	*1.4%*	*3.6%*	2.6%	1.6%	4.2%
Mucinous adenocarcinoma	-	*0.0%*	-	2.3%	2.3%	2.2%	*3.6%*	*3.9%*	-	*6.1%*	*6.9%*	*4.8%*	*1.5%*	*1.6%*	*1.2%*	1.5%	1.5%	1.5%
Mucin-producing adenocarcinoma	-	-	*0.0%*	2.1%	1.8%	2.6%	*1.8%*	*2.9%*	*0.0%*	*0.0%*	*0.0%*	*0.0%*	-	-	*0.0%*	1.4%	1.4%	1.3%
Signet ring cell carcinoma	*6.6%*	*5.5%*	*8.1%*	21.0%	18.6%	24.5%	27.9%	28.2%	27.4%	21.3%	17.6%	27.4%	13.5%	10.5%	18.8%	18.0%	15.1%	22.5%
Leiomyosarcoma	-	-	*0.0%*	*0.3%*	*0.3%*	*0.4%*	*0.0%*	*0.0%*	*0.0%*	*3.0%*	-	*6.5%*	*0.9%*	*0.9%*	-	0.5%	0.4%	0.5%
Gastrointestinal stromal sarcoma	-	*0.0%*	-	*0.2%*	*0.3%*	-	-	-	*0.0%*	*1.8%*	-	-	*0.4%*	-	-	2.6%	2.1%	3.4%

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.

‡The histologic types are included if they are higher than 1% in total in any of the MECC registries; percentages should sum over a column to 100% (with some rounding). Where a percentage has been suppressed because it is based on only 1 or 2 cases, the remaining percentages may not sum to 100%.

§NOS indicates "not otherwise specified."

REFERENCES

[1] Parkin DM, Pisani P, Ferlay J. Estimates of the worldwide incidence of 25 major cancers in 1990. Int J Cancer 1999;80:827-41.

[2] 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.

[3] World Cancer Research Fund and American Institute for Cancer Research. Food nutrition and the prevention of cancer: a global perspective. Washington (DC): World Cancer Research Fund; 1997.

[4] Koizumi Y, Tsubono Y, Nakaya N, Kuriyama S, Shibuya D, Matsuoka H, et al. Cigarette smoking and the risk of gastric cancer: a pooled analysis of two prospective studies in Japan. Int J Cancer 2004;112:1049-55.

[5] Stewart BW, Kleihues P, editors. World cancer report. Lyon (France): International Agency for Research on Cancer; 2003.

[6] Ministry of Health. National survey of tobacco, MOH. (Jordan): Ministry of Health; 1999.

[7] Ministry of Health. First Israeli National Health and Nutrition Survey-MABAT, 1999-2001. (Israel): Ministry of Health; 2000.

[8] Countrywide Integrated Non Communicable Disease Intervention (CINDI) and Conjunto de Acciones para la Reduccion Multifactorial de las Enfermedades No Transmisibles (CARMEN). Survey on tobacco prevention. Cyprus (Italy): World Health Organization; 1998.

[9] Ministry of Health. National survey of tobacco, MOH. (Egypt): Ministry of Health; 1998.

[10] Paunder RE. The prevention of H. pylori in different countries. Aliment Pharmacol Ther 1995;9:33-40.

[11] Logan RP, Walker MM. Epidemiology and diagnosis of H. pylori infection. Br Med J 2001;323:920-2.

[12] Parsonnet J, Friedman GD, Vandersteen DP, Chang Y, Vogelman JH, Orentreich N, et al. Helicobacter pylori infection and the risk of gastric carcinoma. N Engl J Med 1991;325:1127-31.

[13] Gilboa S, Gabay G, Zamir D, Zeev A, Novis B. Helicobacter pylori infection in rural settlements (Kibbutzim) in Israel. Int J Epidemiol 1995;24:232-7.

[14] Niv Y, Niv G, Koren R. 13C-urea breath test for diagnosis of Helicobacter pylori infection in the elderly. Dig Dis Sci 2004;49:1840-4.

[15] Fireman Z, Trost L, Kopelman Y, Segal A, Sternberg A. Helicobacter pylori: seroprevalence and colorectal cancer. Isr Med Assoc J 2000;2:6-9.

[16] Bani-Hani KE, Hammouri SM. Prevalence of Helicobacter pylori in Northern Jordan. Endoscopy based study. Saudi Med J 2001;22:843-7.

[17] Bani-Hani KE, Yaghan RJ, Heis HA, Shatnawi NJ, Matalka II, Bani-Hani AM, et al. Gastric malignancies in Northern Jordan with special emphasis on descriptive epidemiology. World J Gastroenterol 2004;10:2174-8.

[18] Health.Gov (Israel). Stomach 2001. 2001. Available at: http://www.health.gov.il/download/sartan/2001/Stomach2.xls. [Last Accessed: 1/06].