



Epidemiology note

Gastric cancer in Mexico

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Most cancer epidemiology statistics in Mexico are extracted from the *Histopathologic Register of Neoplasia in Mexico*, which is the most complete register and the only one with national coverage [1]. This tumor register is based on the information generated by 930 pathologists and hematologists from 671 private and public hospitals in the country.

Based on this register, gastric cancer (GC) is the most frequent gastrointestinal malignant neoplasm in Mexico [1], and it is the second cause of cancer-related mortality after lung cancer [1,2]. In contrast to the declining incidence and mortality associated with this tumor in most countries, GC mortality in Mexico has been reported to be steady during the past three decades (Fig. 1) [2]. The reason for this could be increasing efficiency in clinical diagnosis and in the reporting of new cases.

Wide variations in GC incidence have been reported worldwide, and Mexico is considered a low-risk area. The crude GC-associated mortality rate is 5.1 per 100000 inhabitants [2]. However, a GC cluster has been reported in the highlands of Chiapas, in a mountainous region close to the Guatemalan border [3]. So, important differences in the country have been found, which possibly reflect differences in diet habits and in social and economic factors. Chiapas has the highest GC-associated mortality rate (6.4×10^4) in the country; in Mexico City, the risk is medium (4.5×10^4), and in Mexico State it is low (2.5×10^4).

Dietary factors related to GC have not been studied extensively in Mexico. However, specific features of the lifestyle that could be related to GC have been identified. Chili pepper is a traditional product in the Mexican diet, and some studies suggest that the hot-tasting component of Chili pepper, capsaicin, may be carcinogenic.

A case-control study performed in Mexico City suggests that Chili pepper consumers were at a higher risk of GC than nonconsumers. There was a highly significant trend of increasing risk with increasing self-rated level of consumption. Multivariable adjustment increased the magnitude of the Chili pepper-gastric cancer association. Chili pepper consumption may be a strong risk factor for gastric cancer, but further studies are needed to prove causality [4].

Saturated fat and cholesterol consumption have been identified as a major risk factor for intestinal-type GC in Mexico [5]. A reduction in the risk of developing GC has been associated with the intake of polyunsaturated fat, fiber, and vitamin E; this effect was independent of the histological type of the tumor (intestinal or diffuse) [5]. These findings are consistent with many studies around the world that indicate important roles for salt, processed meat, and fruit and vegetable consumption in GC risk.

Gastric infection by *Helicobacter pylori* is present in 80% of the adult population in Mexico and is acquired

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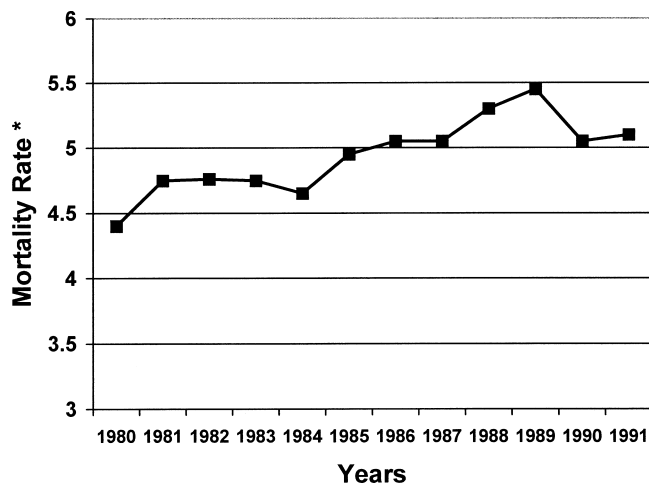


Fig. 1. Time trend for gastric cancer-associated mortality rates in Mexico from 1980 to 1991. *Asterisk*, mortality rates per 100000 inhabitants

in the early years of life [6]. Worldwide seroepidemiological studies on the association of *CagA*⁺ antibody prevalence and GC have yielded conflicting results. In Mexico, gastric infection with *H. pylori* and *CagA*⁺ seropositivity have been reported to be significantly associated with an increased risk of mortality due to GC [6].

In the southern state of Chiapas, with the highest incidence of GC reported in Mexico, an 85.7% prevalence of *H. pylori* infection has been found [7]. This study revealed a strong association between *H. pylori* infection, determined by biopsy, with gastric atrophy, intestinal metaplasia, dysplasia, and GC [7].

Gastric Epstein-Barr virus (EBV) infection has also been implicated in the genesis of gastric carcinoma. In a Mexican study, EBV-encoded small non-polyadenylated RNA (EBER) in-situ hybridization was performed on paraffin-embedded tissue sections of gastric tumors. Eleven (8.15%) of 135 Mexican patients with GC were EBER-1-positive, and 5 had lymphoepithelioma-like carcinomas [8].

No specific Laurén histological type of GC predominates in Mexico. In a study of 220 cases of GC, intestinal type was found in 44.5% and diffuse type in 43.3%; the remaining 12.3% corresponded to mixed type and indeterminate tumors [9], even when intestinal type predominated in high-risk areas such as Chiapas [3]. In another study, a predominance of diffuse type was observed in the young age group, and the global intestinal/diffuse ratio was 1:2, with a trend to increase with age [10]. The distribution of these histological types did not vary significantly according to socioeconomic status [9].

The proportion of distal and proximal tumors in the tumor register of the National Cancer Institute has been

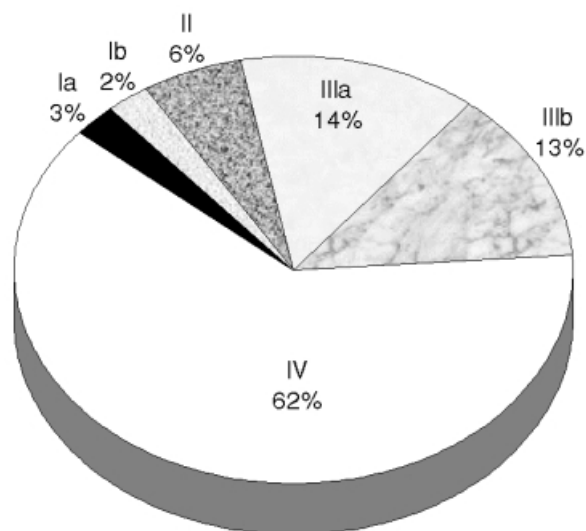


Fig. 2. Relative frequency of TNM stages ($n = 793$ patients treated at the National Cancer Institute Hospital in Mexico City; modified from Oñate-Ocaña et al.¹² [Rev Gastroenterol Mex 1999;64:114–21.]; with permission)

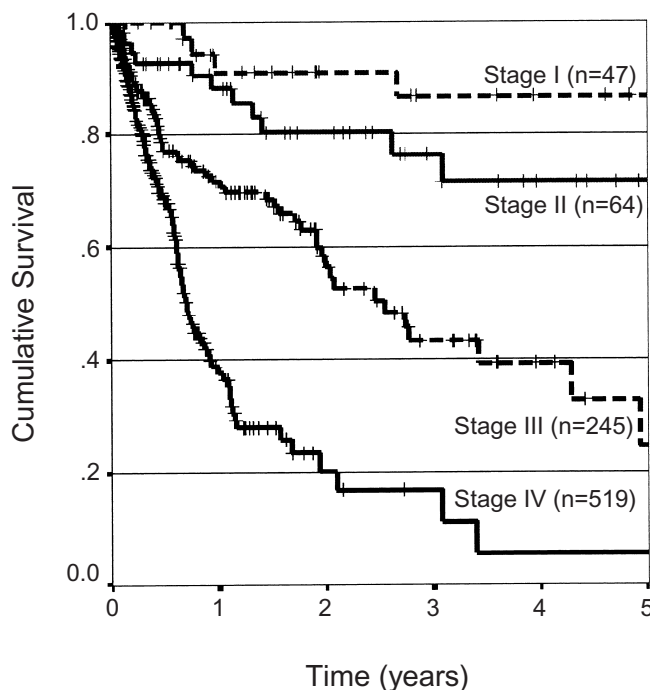


Fig. 3. Survival curves by TNM stage ($n = 875$ patients with gastric carcinoma treated at the National Cancer Institute Hospital in Mexico City from January 1987 to June 2000)

fairly constant in the past 14 years. Excluding tumors invading the whole stomach, 465 patients (66.5%) had distal tumors and 234 (33.5%) had proximal tumors.

In Mexico, early GC is found with very low frequency. In a retrospective cohort study of 834 patients

with GC treated at the National Cancer Institute in Mexico City, only 21 presented with early GC [11]. This represents 2.3% of all stages. None presented with lymph node metastases at the time of surgical resection, and 2 patients presented with recurrence. The 5-year survival rate of this small cohort was 84%. An explanation for this extremely low proportion is selection bias. Our institute is a third-level referral hospital that specializes in unresectable cases, so the stage distribution is marked by a high proportion of far-advanced cases [12]. The relative frequency of TNM stages is depicted in Fig. 2, and survival curves by TNM stage are shown in Fig. 3.

Subtotal or total gastrectomy with D1 lymph node dissection (LND), following Western standards, is the preferred resection procedure for gastric cancer in most hospitals in Mexico. However, Japanese-style D2 LND has been used since 1985 at the National Cancer Institute in Mexico City, with promising results. In a retrospective study, D2 LND-associated surgical morbidity was similar to that of D1 LND, and a survival benefit for patients treated with D2 LND was found by multivariate analysis with adjustment for the major prognostic and confounding factors [13]. Possibly, in terms of ethnic aspects, Mexican patients are more comparable to Japanese than to North Americans or Europeans.

Adjuvant chemotherapy is not used routinely in Mexico after complete (R0) surgical resection. When it is used, the preferred combination chemotherapy is fluorouracil, doxorubicin and methotrexate (FAMtx) or cisplatin, leucovorin and fluorouracil (PLF) and it is administered as palliative treatment in patients with far-advanced disease.

Recently, we used the P-ELF combination (cisplatin, etoposide, leucovorin, 5-fluorouracil) as neoadjuvant chemotherapy in patients with unresectable GC. This combination chemotherapy permitted 17.5% resectability after 2.9 courses of treatment per patient [14].

In conclusion, GC is an important health problem in Mexico. In the coming decades, education programs and clinical research must be directed toward methods for diagnosing GC at early stages, because this is the only significant way to reduce mortality.

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