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Original Article

Mortality trends for liver cancer in Mexico from 2000 to 2006

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Abstract

Hepatocellular carcinoma (HCC) is the most common primary liver cancer, with an estimated incidence of half a million new cases per year around the world. Furthermore, HCC is the third greatest cause of cancer-related death in the world, and most of these deaths are registered in developing countries. Recently it has been suggested that Hispanics in the United States have high rates of HCC, but no information regarding this is available in Mexico. The aim of this study was to investigate recent trends (2000–2006) in HCC mortality rates in Mexico. *Methods*. Data on national mortality (death certificates) reported for the years 2000–2006 by the Health Ministry of Mexico were analyzed (www.salud.gob.mx). HCC as a cause of death was analyzed. Mortality rates were calculated for all population ages. Causes of death related to HCC were selected in accordance with the International Classification of Diseases, 10th Revision, Liver Cancer (C22.0, C22.7, C22.9). *Results*. We found that age-adjusted mortality rates were remarkably higher in men than in women in the period 2000–2006. In addition, we found an increase in the general mortality rates of HCC from 4.1 per 100,000 in 2000 to 4.7 per 100,000 in 2006. *Conclusions.* The results of this study suggest an increase in the mortality rate for HCC in the period 2000–2006. HCC will become a significant cause of morbidity and mortality in the near future.

Key words: Hepatocellular carcinoma, Hepatitis C, Alcohol, NASH, Mexico.

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Hepatocellular carcinoma (HCC) is the most common primary liver cancer, with an estimated incidence of half a million new cases per year around the world.[1] Estimates from the year 2000, based on combined analysis of the reports of population based cancer registries[2,3] and the World Health Organization (WHO) mortality databank,[4] indicate that 564,000 new cases of liver cancer occurred worldwide, including 398,364 cases in men and 165,972 in women. This tumor accounted for 5.6% of all human cancers (7.5% among men and 3.5% among women). In addition, several studies have indicated that 1–4% of all cirrhotic patients per year will develop HCC,[5] with differences in rate according to the leading cause of the cirrhosis *(Table I)*.[6–10]

Liver cirrhosis has a critical impact on public health in Mexico, representing the third greatest cause of death in the general population, and predicted trends for the next five decades are not promising *(Figure 1)*.[11,12] Recently we found alcohol consumption and HCV infection to be the main causes of liver cirrhosis in Mexico (39.5 and 36.6%, respectively; $p = 0.113$), followed by cryptogenic cirrhosis.[13] The aim of this study was to investigate trends in the mortality rate of HCC in Mexico in the period 2000–2006.

Methods

Deaths from hepatocellular carcinoma were selected from the mortality databases published by the Ministry of Health of Mexico. Codes C22.0–C22.9 of the 10th International Classification of Diseases were considered. Data from the years 2000 to 2006 were available. In order to determine mortality rates, the population at risk was based on the official statistics of the Mexican Government (Consejo Nacional de Población y Vivienda). The analyses of trends were focused to describe the general trends for mortality from hepatocellular carcinoma in the period 2000–2006. Particular emphasis was placed on comparing trends between gender and age groups of 0–14, 15–59 and 60 or more years.

Results

Mortality from hepatocellular carcinoma in Mexico showed an increasing trend in the period 2000–2006. The specific-cause mortality rate showed a significant

Table I. Annual incidence of hepatocellular carcinoma related to the etiology of liver cirrhosis.

Author, year	No. patients	Etiology of liver cirrhosis	Mean follow-up*	HCC annual incidence**
Fattovich et al., 1997	361	HCV	60	1.4%
Chiaramonte et al., 1999	166	HCV	64.5	3.8%
Fattovich et al., 2002	136	HCV	66	2.5%
Solá et al., 2006	200	HCV	39	5.5%
	177	Alcoholic	39	1.7%
Fattovich et al., 2002	161	HBV	66	2.2%
Chiaramonte et al., 1999	66	HBV	64.5	1.7%
	27	HBV/HCV	64.5	7.6%
Ratziu et al., 2002	22	Cryptogenic, obesity-related	18	0.8%

* Months, ** Data were recalculated from the original paper. Abbreviations: HCC, hepatocellular carcinoma; HCV, hepatitis C virus; HBV, hepatitis B virus
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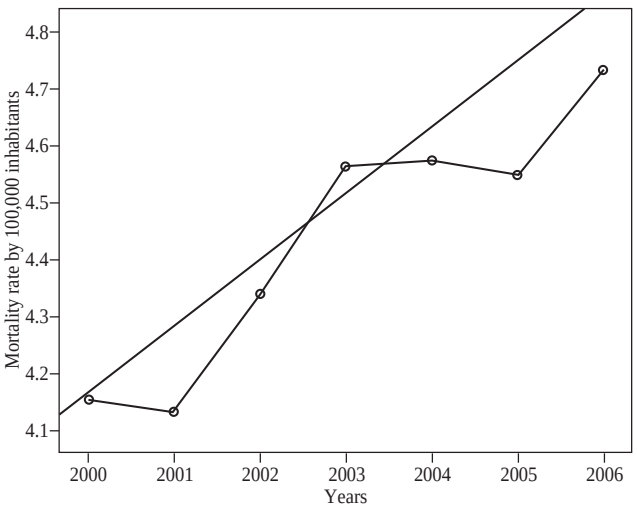

Figure 1. The specific-cause mortality rate showed a significant change of 14%, corresponding to an increase in rate from 4.16 per 100,000 inhabitants in the year 2000 to a rate of 4.74 per 100,000 inhabitants in the year 2006. Pearson's correlation coefficient = 0.94, p = 0.001

change of 14%, corresponding to an increase in rate from 4.16 per 100,000 inhabitants in the year 2000 to a rate of 4.74 per 100,000 inhabitants in the year 2006 (*Figure 1*; Pearson's correlation coefficient = 0.94, $p = 0.001$).

The increasing trend in mortality rates according to gender also shows a clear difference, with higher rates in males. However, in terms of percentage change, women had a 15.5% rise in mortality rate from the year 2000 (3.81 per 100,000 women) to the year 2006 (4.40 per 100,000 women), in comparison with the men whom had a change of 12.4% (4.5 per 100,000 men in 2000 *vs* 5.06 per 100,000 men in 2006; *Figure 2*).

Higher mortality rates were observed in the population 60 or more years of age. The 0–14 and 15–59 year age groups had rates lower than two per 100,000 inhabitants, while the greater than 60 years age group had rates around 45 per 100,000 inhabitants *(Figure 3)*.

Discussion

We found that in Mexico, mortality from HCC showed an increasing trend in the period 2000–2006. This increase in mortality rate is similar to that found in the United States (4.7 per 100,000 persons in 2001).[14] Furthermore, El-Serag et al.[15] analyzed the database of the National Cancer Institute of the United States to calculate race-specific mortality for HCC. They found a 31% increase in the incidence of HCC in Hispanic men and a 63% increase in Hispanic women in the period of 2000–2002 compared with that of 1992–1995. Hispanic women had the fastest increase in HCC incidence compared with other groups. Interestingly, rates for native-born Hispanic men were found to be twice as high as those for immigrant Hispanic men.

International trends in mortality have also been evaluated in 22 populations for the period 1979–1998. Among men, increases in mortality from liver cancer have been reported in the United States, Japan, Australia, Scotland, France, and Italy, whereas decreasing trends have been reported in the United Kingdom.[16] Trends among women were similar.

Interestingly, a recent study[17] that analyzed the trends in mortality from HCC in 23 European countries over the period 1980–2004 using data from the World Health Organization found that in males, overall mortality from HCC increased in Austria, Germany, Switzerland, and some other western European countries, while it significantly decreased over recent years in France and Italy, which had large upward trends until the mid-1990's. Also in that study, the investigators found that in most countries, trends for those aged 45–59 years were consistent with overall trends, whereas they were more favorable for those aged 20–44 years of both sexes. In contrast, in our study, higher mortality rates according with age were observed in the population of aged 60 or more years. The 0–14 and 15–59 years age groups had rates lower than two per 100,000 inhabitants, while the group aged 60 or more years had rates around 45 per 100,000 inhabitants. These

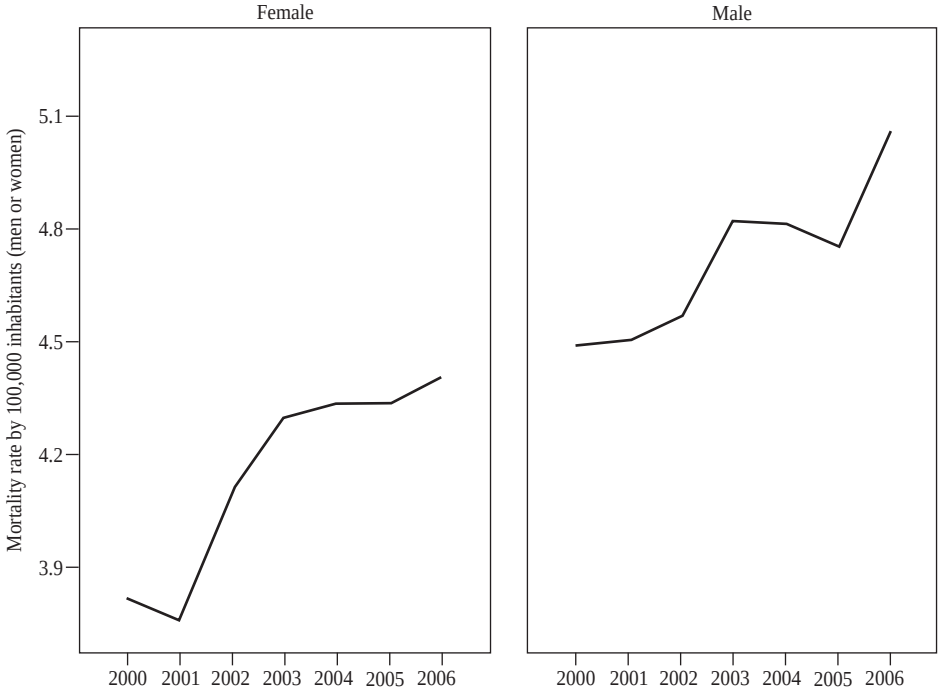

Figure 2. In terms of percentage change, women had a 15.5% rise in mortality rate from the year 2000 (3.81 per 100,000 women) to the year 2006 (4.40 per 100,000 women), in comparison with the men whom had a change of 12.4% (4.5 per 100,000 men in 2000 *vs* 5.06 per 100,000 men in 2006.

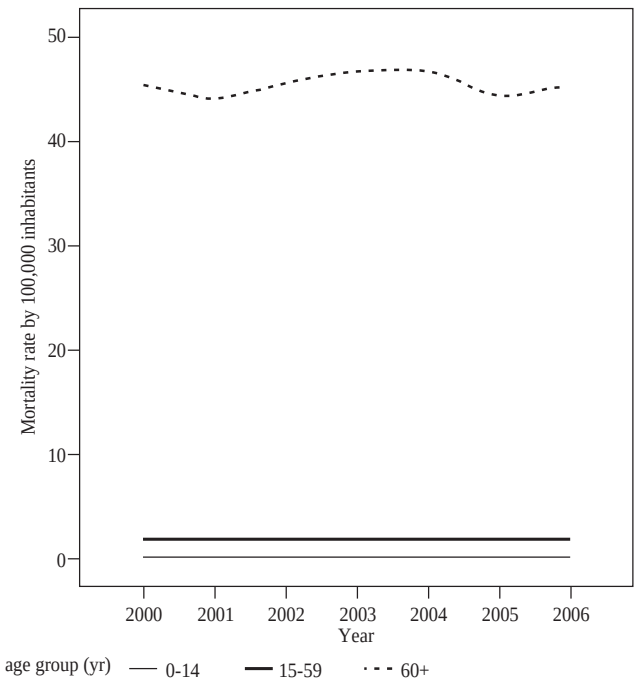

Figure 3. Higher mortality rates were observed in the population 60 or more years of age. The 0–14 and 15–59 year age groups had rates lower than two per 100,000 inhabitants, while the greater than 60 years age group had rates around 45 per 100,000 inhabitants.

differences in mortality trends in young and middle-aged populations observed between European countries and Mexico may be related to the time of diagnosis or HCC surveillance programs available in Europe.

In the United States, the three main risk factors associated with HCC are infection with hepatitis C virus (HCV), infection with hepatitis B virus (HBV), and alcoholic cirrhosis.[18] However, in Mexico, the main risk factors are HCV and alcohol.[18] Furthermore, cryptogenic cirrhosis has been estimated to account for 5 to 30% of patients with end-stage liver disease.[19]

Finally, an association between diabetes and liver disease has been suggested. In fact, Hassan et al.[20] reported a case-control study of 115 HCC patients and 230 non-liver-cancer patients in which the odds ratio for diabetes was 4.3 (95% CI: 1.9–9.9). If this information is confirmed in well-designed cohort studies, diabetes, which is highly prevalent in Mexico,[21] may be shown to be another important risk factor for HCC in the Mexican population.

In conclusion, the results of this study suggest an increase in HCC mortality rates in the period 2000–2006. HCC will become a significant cause of morbidity and mortality in the near future. Efforts to collect representative etiologic data on new HCC cases are needed to enable better characterization of trends and to guide the planning and evaluation of prevention programs.

References

1. El-Serag HB. Epidemiology of hepatocellular carcinoma. *Clin Liver Dis* 2001; 5: 87-107, vi.
2. Parkin DM, Bray F, Ferlay J, Pisani P. Global cancer statistics 2002. *CA Cancer J Clin* 2005; 55: 74-108.
3. Levi F. Cancer incidence in five continents, Vol. VI. *Eur J Cancer* 1994; 29A: 2315–2319.
4. Parkin DM, Bray F, Ferlay J, Pisani P. Global cancer statistics, 2002. *CA Cancer J Clin* 2005; 55: 74-108.

5. Bailey MA, Brunt EM. Hepatocellular carcinoma: predisposing conditions and precursor lesions. *Gastroenterol Clin North Am* 2002; 31: 641-62.
6. Fattovich G, Giustina G, Degos F, Tremolada F, Diodati G, Almasio P, Nevens F, et al. Morbidity and mortality in compensated cirrhosis type C: a retrospective follow-up study of 384 patients. *Gastroenterology* 1997; 112: 463-72.
7. Chiaramonte M, Stroffolini T, Vian A, Stazi MA, Floreani A, Lorenzoni U, Lobello S, et al. Rate of incidence of hepatocellular carcinoma in patients with compensated viral cirrhosis. *Cancer* 1999; 85: 2132-7.
8. Fattovich G, Pantalena M, Zagni I, Realdi G, Schalm SW, Christensen E. Effect of hepatitis B and C virus infections on the natural history of compensated cirrhosis: a cohort study of 297 patients. *Am J Gastroenterol* 2002; 97: 2886-95.
9. Ratziu V, Bonyhay L, Di Martino V, Charlotte F, Cavallaro L, Sayegh-Tainturier MH, Giral P, et al. Survival, liver failure, and hepatocellular carcinoma in obesity-related cryptogenic cirrhosis. *Hepatology* 2002; 35: 1485-93.
10. Sola R, Álvarez MA, Balleste B, Montoliu S, Rivera M, Miquel M, Cirera I, et al. Probability of liver cancer and survival in HCV-related or alcoholic-decompensated cirrhosis. A study of 377 patients. *Liver Int* 2006; 26: 62-72.
11. National System of Health Information. [Bases de datos en formato de cubo dinámico]. *http://sinais.salud.gob.mx/*.
12. Méndez-Sánchez N, Villa AR, Chavez-Tapia NC, Ponciano-Rodriguez G, Almeda-Valdes P, Gonzalez D, Uribe M. Trends in liver disease prevalence in Mexico from 2005 to 2050 through mortality data. *Ann Hepatol* 2005; 4: 52-5.
13. Méndez-Sánchez N, Aguilar-Ramirez JR, Reyes A, Dehesa M, Juorez A, Castaneda B, Sanchez-Avila F, et al. Etiology of liver cirrhosis in Mexico. *Ann Hepatol* 2004; 3: 30-3.
14. El-Serag HB. Hepatocellular carcinoma: recent trends in the United States. *Gastroenterology* 2004; 127(5 Suppl 1): S27-34.
15. El-Serag HB, Lau M, Eschbach K, Davila J, Goodwin J. Epidemiology of hepatocellular carcinoma in Hispanics in the United States. *Arch Intern Med* 2007; 167: 1983-9.
16. Khan SA, Taylor-Robinson SD, Toledano MB, Beck A, Elliott P, Thomas HC. Changing international trends in mortality rates for liver, biliary and pancreatic tumours. *J Hepatol* 2002; 37: 806–813.
17. Bosetti C, Levi F, Boffetta P, Lucchini F, Negri E, La Vecchia C. Trends in mortality from hepatocellular carcinoma in Europe, 1980-2004. *Hepatology* 2008; 48: 137-45.
18. El–Serag HB. Hepatocellular Carcinoma: Recent trends in the United States. *Gastroenterology* 2004; 127: S27–S34.
19. Méndez-Sánchez N, Sánchez-Castillo CP, Villa AR, Madrigal H, Merino B, García E, López P, Pichardo-Ontiveros E, Uribe M. The relationship of overweight and obesity to high mortality rates from liver cirrhosis in Mexico. *Ann Hepatol* 2004; 3: 66-71.
20. Hassan MM, Hwang LY, Hatten CJ, Swaim M, Li D, Abbruzzese JL, Beasley P, Patt YZ. Risk factors for hepatocellular carcinoma: synergism of alcohol with viral hepatitis and diabetes mellitus. *Hepatology* 2002; 36: 1206–1213.
21. *Encuesta Nacional de Salud y Nutrición 2006*. Cuernavaca, México: Instituto Nacional de Salud Pública, 2006.