

## Ethnic and Geographical Distribution of Liver Cancer in Mexico. Review

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Received: April 24, 2023

Published: May 09, 2023

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### Abstract

Liver cancer is the fifth most common cancer in the world but it's increasing mortality led to be the second cause of cancer-related death. In 2021 we had in Mexico 41,890 deaths due to liver cirrhosis, 35.6% of them because of chronic alcoholic liver disease. and primary liver cancer represented the third cause of death in 2015. In the last 20 years liver cancer mortality increased about 50% years despite the recent advances in medical technology and new treatments available for hepatitis C-virus (HCV) and hepatocarcinoma. In our experience at three medical centers, two thirds of the patients with liver cancer were related to HCV and the mortality rate was higher in patients over 65 years and in males over 45 years.

According to Globocan 2022 report, the highest incidence in the world is in Southeast Asia and in the Americas the highest mortality is in Guatemala and El Salvador followed by Mexico and Costa Rica.

This review focuses on the geographical and ethnic distribution of liver cancer in Mexico as well as the mortality rate in the different regions of the country to identify possible risk factors affecting them and favor the development of liver cancer.

**Keywords:** Liver Cancer; Hepatocellular Carcinoma; Cirrhosis; Ethnic; Geographic

### Introduction

Liver cancer is the fifth most common cancer in the world but it's increasing mortality led to be the second cause of cancer-related death [1-3]. Hepatocellular carcinoma (HCC) represents almost 90% of all primary liver cancers and 80% arises in a cirrhotic liver [1,2]. Risk factors associated to HCC are very known such as viral hepatitis B and C, alcohol-related liver disease, obesity, non-alcoholic fatty liver disease (NAFLD) and aflatoxin exposure among others [2,3]. Other risk factors are related to geographical

distribution, genetic and environmental factors and limited health access in certain population [2].

The global HCC annual incidence rate is 9.3 (10<sup>5</sup>) and the major incidence and mortality are in Southeast Asia and Sub-Saharan Africa countries [2,3]. In Mexico in 2021 we had 41,890 deaths due to liver cirrhosis, 35.6% of them because of chronic alcoholic liver disease. and primary liver cancer represented the third cause of death in 2015 [4,5]. According to Globocan 2022 report in the

Americas the highest mortality was found in Guatemala and El Salvador followed by Mexico and Costa Rica [6].

In the last 20 years liver cancer mortality increased about 50% years despite the recent advances in medical technology and new treatments available for hepatitis C-virus (HCV) and hepatocellular carcinoma [4]. In 2000 the mortality rate was 4.16 per 100,000 and by 2015 mortality rate raised to 5.2 per 100,000. In our experience at three medical centers, two thirds of the patients with liver cancer were related to HCV and the mortality rate was higher in patients over 65 years and in males over 45 years [4,5].

### HCC epidemiology in Mexico

In Mexico incidence of HCC is steadily increasing and by 2020 represented the ninth cause of malignancy, in contrast HCC mortality rate is higher being the third cause of cancer-related death. There were no significant differences in gender mortality, accounting for 51.2% and 48.7% in females and males respectively [4]. In females liver cancer is the third cause of death only after breast and cervicouterine cancer, while in males is the fourth cause of death after prostate, lung and stomach [5]. HCC in pediatric population is very rare, usually found in older children (10-15 years) and rarely in younger than 5 years [7,8]. In our medical group we collected 7 patients between 2018 and 2021, the mean age was 13.6 (range 1 to 16) and surprisingly 28.5% of them were

1 year of age, and most of the patients showed HCC larger than 10 cm [8-10]. In Mexico it is reported that HCC in <18 years represent around 5% of all cases [4,5].

In general, most of the HCC arises in patients over 45 years and it is demonstrated that in elderly particularly women over 65 years HCC is the most prevalent malignancy with a rate of 14.0 per 100,000 [4,5,11].

In Mexico general mortality rate secondary to HCC is 5.2 per 100,000. Veracruz is the region with the highest rate of 10.0, followed by Yucatan 7.2 and Campeche 7.0, interestingly all of these states are geographical located in the Gulf of Mexico [4,5]. Other states with mortality rate between 2 and 6 per 100,000 are Oaxaca 6.6, Mexico City 6.5, Tamaulipas 6.4 and Chiapas 6.4 (Figure 1). Ethnicity may play a role in the epidemiology of HCC [12], in Mexico more studies are needed to have a valid conclusion, in the meantime it is well known that black and Hispanic patients have shorter median survival than whites [1,2]. Mexico has great ethnicity disparity, so it is very difficult to recognize if some specific ethnicities are at increased risk for developing HCC and higher mortality rate. In the Gulf of Mexico where the higher mortality rate was found, besides white Hispanics or mestizos, two predominant native ethnicities live there: Nahuatl and Maya [4].

**Figure 1:** Geographical distribution of HCC mortality rate per 100,000 persons in Mexico.

### Risk factors for HCC

Global risk factors for HCC are very well known, approximately 80% of HCC occurs in cirrhotic patients while the estimated risk for developing HCC in cirrhotic is 1 to 8% per year. The annual risk for developing HCC is higher in viral hepatitis-B (VHB) and viral hepatitis-C (VHC) in about 3 to 8% and 3 to 5% respectively, while alcohol-related liver disease is 1 to 3% and for NAFLD the risk is 1.5%. Other risk factors include aflatoxin exposure, hemochromatosis and obesity, tobacco consumption and autoimmune liver cirrhosis [1-3].

In Mexico the two main risk factors for developing HCC are HCV and alcohol related cirrhosis [13-16], there are some studies where alcohol-related cirrhosis is the main cause [16,17] but in others like in our group VHC-cirrhosis is responsible for 66% of HCC cases, in fact in our liver transplantation series 66.6% of liver transplants due to HCC were VHC cirrhosis [8,10].

The relationship between alcohol consumption and the development of HCC has been widely studied, sometimes with unconvincing data, but recent meta-analysis estimated a 16% and 22% increased risk of liver cancer between 3 and 6 drinks per day consumers [18,19]. Alcohol-related liver disease rate is increasing over the last 30 years and there is strong evidence showing high prevalence and mortality due to cirrhosis including alcohol as one of the most common causes [19,20]. Mexico is the Latin American country with the highest liver cirrhosis adjusted to age mortality rate (38.3 per 100,000 person-years). In 2016 globally alcohol consumption was 6.4 liters per person (APC), being Europe the highest with 9.8 L, but interestingly Latin America was the second highest with 8.4 L and Mexico's average APC was 6.5L [19].

Obesity represents a worldwide pandemic and its relationship to NAFLD is very well known [21]. In Mexico, between 2010-2018 the obesity prevalence increased 42.2% as well as morbid obesity which did in 96.5% this data resulted in an overweight prevalence of 39.1%, obesity 36.1% and abdominal adiposity 81.6% [22]. It seems that there is no significant differences between geographic regions or socioeconomic level, but adults over 40-50 years and women had the highest prevalence, whether this meant to be an additional risk for developing HCC is not known so far [20].

### Conclusion

Mexico is one of the Latin American countries with the highest mortality rate due to hepatocellular carcinoma, in the last 20 years mortality increased about 50%. Most of the recognized risk factors such as VHC cirrhosis, alcohol intake, NAFLD are similar to what is reported globally. Other risk factors that are increasing comparing to other countries are NAFLD and obesity. In the last 10 years obesity and morbid obesity rate increased 42.2% and 96.5% respectively, meaning that Mexico is the country with the second highest obesity rate in the world only after the United States.

Mexico is a country with great ethnic and racial multi variety. Around 15% of the population is from the 68 native indigenous communities, white Hispanics and mestizos are the main population. HCC is more prevalent in the Gulf of Mexico and in the southeast, although it seems that socioeconomics is not a strong risk factor for mortality, traditionally these regions have less access to health services compared to the rest of the country. In the other hand in this same region Nahuatl and Maya people density are prevalent.

More epidemiological studies and genetic testing is needed to precisely know about ethnicity and racial risk factors for the development of HCC in Mexico.

### Availability of Data and Materials

Not applicable.

### Financial Support and Sponsorship

None.

### Conflicts of Interest

All authors declared that there are no conflicts of interest.

### Ethical Approval and Consent to Participate

Not applicable.

### Consent for Publication

Not applicable.

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