

# Epidemiology of Hepatocellular Carcinoma



Kelly J. Lafaro, MD, MPH<sup>a</sup>, Aram N. Demirjian, MD<sup>b</sup>,  
Timothy M. Pawlik, MD, MPH, PhD<sup>c,\*</sup>

## KEYWORDS

- Hepatocellular carcinoma • Chronic liver disease • Cirrhosis • Hepatitis B
- Hepatitis C • Incidence • Risk factors • Aflatoxin

## KEY POINTS

- HCC is a common malignancy worldwide with nearly equal numbers of new cases and cancer-related death each year.
- Most HCCs arise in the background of chronic liver disease caused by hepatitis B virus, hepatitis C virus, and chronic excessive alcohol intake.
- A detailed understanding of these risk factors and how they lead to cancer development is necessary to improve the screening, prevention, early identification and management of HCC.

## INTRODUCTION

Primary liver cancer is the fifth most common cancer worldwide and the second leading cause of cancer mortality. In 2008, there were 749,000 new cases and 695,000 deaths from liver cancer, which increased to an estimated 782,000 new cases in 2012.<sup>1</sup> Hepatocellular carcinoma (HCC) is the most common histologic type of primary liver cancer, and it accounts for between 85% and 90% of these malignancies. HCC arises from hepatocytes that comprise the parenchymal cells of the liver. The overall prognosis of patients with liver cancer is poor (ratio of mortality to incidence 0.95), and thus, a detailed understanding of this disease and its risk factors is crucial for screening at-risk individuals, early recognition, and timely diagnosis, and therefore,

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Funding sources: none (Dr T.M. Pawlik, Dr K.J. Lafaro); Speaker's Bureau – Bayer, Speaker's Bureau – Aptalis (Dr A.N. Demirjian).

Conflicts of interest: none.

<sup>a</sup> Department of Surgery, Johns Hopkins Hospital, The Johns Hopkins University School of Medicine, 600 North Wolfe Street, Blalock 688, Baltimore, MD 21287, USA; <sup>b</sup> Department of Surgery, University of California-Irvine, 333 City Boulevard West, Suite 1205, Orange, CA 92868, USA; <sup>c</sup> Division of Surgical Oncology, Department of Surgery, Johns Hopkins Hospital, 600 North Wolfe Street, Blalock 688, Baltimore, MD 21287, USA

\* Corresponding author.

E-mail address: [tpawlik1@jhmi.edu](mailto:tpawlik1@jhmi.edu)

Surg Oncol Clin N Am 24 (2015) 1–17  
<http://dx.doi.org/10.1016/j.soc.2014.09.001>

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it is hoped, more effective and successful intervention.<sup>1</sup> Most HCCs arise in the background of chronic liver disease, and these underlying causes are characterized by marked variations in geography, gender, and other well-documented risk factors, some of which have become potentially preventable in recent years.

## INCIDENCE

The incidence of HCC is not evenly distributed throughout the globe. A great preponderance of cases occur in sub-Saharan Africa and Eastern Asia (>80%), and China is believed to account for approximately 50% of all cases of HCC worldwide. Conversely, North and South America, as well as Europe, have a comparatively low incidence of HCC. These marked differences can be attributed to several specific factors.

### *Asia*

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More than half of HCCs occur in China alone, where in 2008, the age-standardized incidence rate was 37.4 per 100,000 individuals for males and 13.7 per 100,000 individuals for females.<sup>1</sup> The incidence of HCC in Mongolia and Korea are also high, with 99 and 49 cases per 100,000 persons, respectively.<sup>1</sup> The high incidence of HCC in these areas is related to the high hepatitis B virus (HBV) infection rates in Asia, and especially in China, where HBV has traditionally been acquired via vertical transmission from mother to child.<sup>2,3</sup> Widespread HBV vaccination programs introduced in the 1980s have brought hope that reduction of the HBV burden might be achieved, thereby decreasing the HCC rates in these endemic areas. In a recent 20-year follow-up study<sup>4</sup> after the introduction of the vaccine in Taiwan, hepatitis B surface antigen (HBsAg) seropositivity rates decreased from 10% to 17% to 0.7% to 1.7%. These studies in Taiwan also showed a decrease in the incidence of HCC among children aged 6 to 19 years (from 0.51 to 0.15/100,000 person-years in children aged 6–9 years, from 0.6 to 0.19/100,000 person-years in children aged 10–14 years, and from 0.52 to 0.16/100,000 person-years in children aged 15–19 years).<sup>4</sup>

Japan also has a high incidence of HCC with a case index of approximately 40 per 100,000 population. Unlike other Asian countries where HBV predominates, hepatitis C virus (HCV) is the dominant hepatitis virus in Japan, accounting for 80% of HCC cases.<sup>5</sup> The prevalence of HCV in Japan after World War II secondary to intravenous (IV) drug use, as well as contaminated blood transfusions, which led to quickly increasing rates of infection in the 1970s.<sup>5,6</sup> It is estimated that the peak in HCV-related HCC rates will occur in approximately 2015. The HCC incidence associated with HCV in Japan is 2-fold higher than that in Europe or the United States, with 5-year cumulative incidences of 30% and 17%, respectively.<sup>7</sup> This incidence may be attributed to the increased incidence of HCV genotype 1b in Japan, which has been shown to have decreased response to antiviral therapy compared with genotype 1a, which is prevalent in the United States and Europe.<sup>8</sup>

### *Africa*

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The first case of HCC in Africa was reported in 1879.<sup>9</sup> Although the true incidence of HCC in Africa is likely underestimated, because of lack of screening and access to medical care in rural areas, it is a major cause of death in the black African population. Within Africa, Mozambique has the highest incidence of recorded HCC, with an age-standardized incidence of 41.2/100,000 persons each year. Most of these cases are

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