

Battlefield against hepatitis B infection and HCC in Africa

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Summary

Despite effective and safe hepatitis B virus (HBV) vaccine and antiviral therapies, HBV-related hepatocellular carcinoma (HCC) remains a major cause of deaths in young adults in Africa. There are multiple barriers to control the burden of HBV infection and HCC. In comparison to other major infectious diseases, HBV infection and liver diseases have received remarkably little attention from the global health community. There is an urgent need to improve birth dose vaccine coverage and implementing screening and treatment interventions. This requires a dramatic simplification of the management of chronic hepatitis B in Africa, with access to reliable, robust and inexpensive diagnostic tools and strong support from the local governments and the international health community. This review analyses 1) the characteristics of HBV hepatitis and HCC epidemics in Africa and 2) the barriers and potential solutions to control it.

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Introduction

Hepatocellular carcinoma (HCC) is a leading cause of deaths in Africa and is mainly due to chronic infection with hepatitis B virus (HBV). However, little attention has been paid to this burden of disease over the last decades, and many barriers are contributing to the epidemic. This review analyses 1) the epidemiological characteristics of HCC and its main cause, chronic hepatitis B, in Africa and 2) the barriers and potential solutions to control this burden of diseases.

Viral hepatitis B and HCC epidemics in Africa

Epidemiology

According to the estimates of the global burden of disease study, deaths due to viral hepatitis increased by 63% from 0.89 million to 1.45 million between 1990 and 2013, and Africa is one of the regions with highest mortality rate [1]. Worldwide, HCC is the second most common cause of death from cancer, and was estimated to be responsible for about 750,000 deaths in 2012 [2]. HCC is a cancer of poor countries, which accounts for 80% of the global cases. Africa, especially West Africa, represents one of the most endemic regions in the world. HCC is the most common fatal malignancy in adult males on the continent, and the third most

common fatal malignancy in women [3,4]. The prognosis of HCC is very poor, especially in resource-limited countries (Fig. 1). The incidence of HCC matches precisely the fatality rate, as the majority of patients present at a late stage of the disease, when no therapeutic options exist. Very few data on survival of HCC patients living in Africa are available. These are derived from sparse cancer registry data collected by the International Agency for Research on Cancer (IARC). Although the data can be criticised for accuracy and completeness [5] it probably gives a reasonable perspective on HCC-related deaths. In contrast, there is virtually no system for collecting data on deaths attributable to decompensated cirrhosis. Although it is likely that the number of people dying from cirrhosis is the same order of magnitude as the number dying from HCC, this is not reflected in the global burden of disease study. In The Gambia, the Prevention of Liver Fibrosis and Cancer in Africa (PROLIFICA) programme [6] reported a very poor median survival of HCC patients, estimated at 91 days (4–789) (unpublished data). In patients with acute-on-chronic liver failure, a case-controlled study nested in the PROLIFICA programme found a high cumulative mortality rate at 28- and 90-day (70.0% and 92.9% respectively). Moreover, the vast majority of the patients were young men (median age 45 years [35–56]) [7]. In Europe, the median age at presentation with HCC is 65 years [8]; in contrast the median

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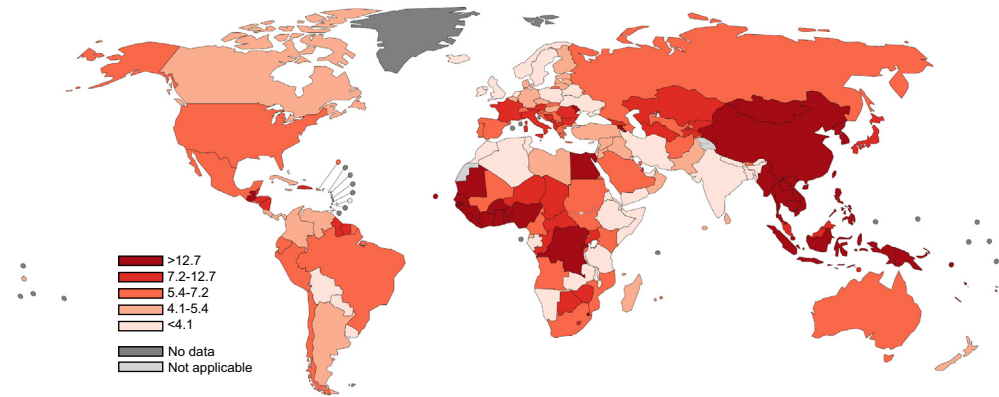


Fig. 1. Estimated liver cancer mortality in men worldwide (2012). From GLOBOCAN 2012. The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Border lines are approximate or may not yet be fully agreed.

age in Sub-Saharan Africa is 45 years [9]. A consortium of collaborating centers on HCC in Africa has recently reported that 43% of HBV-related HCC developed in adults younger than 40 years, with a most frequent age range at HCC diagnosis at 32.5–37.5 years [10] (Fig. 2). By contrast, hepatitis C virus (HCV)-related HCC occurred later, mainly after 50 years, with a peak between 57.5–62.5 years (Fig. 2) [9,10]. In Africa, HCC is therefore a disease, which kills large numbers of young and middle aged men and women, and therefore deserves a robust public health response.

The aetiology of HCC in Africa has been partly documented [3,4,9,11]. Chronic hepatitis B is the main cause of HCC in the continent, but the proportion of cases attributable to HIV and/or hepatitis delta co-infections remain poorly analysed, although these viruses are highly endemic in the continent. Over 50–60% of the HCC cases in Sub-Saharan Africa arise in patients who are hepatitis

B surface antigen (HBsAg) positive [9,3,10], and it is likely that another 20–50% have previously had chronic HBV or occult HBV infection (HBsAg negative but detectable viraemia) [12,13]. The number of HCC cases attributable to occult hepatitis B is probably underestimated, and deserves to be better documented. Chronic HCV infection has also been identified as an important cause of HCC in North Africa (particularly Egypt) [14] and in Central Africa (Cameroon) [15]. Occult hepatitis B has also been identified as a cofactor of HCC in patients with chronic hepatitis C [16].

Although the distribution of viral hepatitis in Africa is heterogeneous, the continent as a whole represents one of the most HBV infection endemic parts of the world [17]. Of the 240 million people estimated to be chronically infected with HBV, 80 million reside in Sub-Saharan Africa. Prior to immunization programmes the prevalence of chronic infection in West Africa was around 15% in the adult population, and more than two thirds of children aged 12–19 years old had evidence of spontaneous clearance of the infection [18].

Good quality viral hepatitis sero-prevalence data are still lacking in Africa as the sero-surveys have been often conducted in selected populations (mainly blood donors, pregnant women or HIV-infected subjects). Within the PROLIFICA programme, a recent population-based study conducted in The Gambia and Senegal confirmed a high prevalence of HBsAg in both countries (over 8%) [19]. Relatively, a lower prevalence of HBsAg was reported in East Africa and in South Africa (6–8%) [17].

In Africa, HBV is mainly transmitted early in life. Although horizontal transmission represents the main mode of HBV transmission, perinatal transmission is thought to account for around 10% of chronic HBV infection [20]. Horizontal transmission occurs between the ages of 2 and 10 through mechanisms that remain poorly understood. It is likely that chil-

Key point

Hepatocellular carcinoma (HCC) is a major cause of premature death in Africa and is mainly attributable to chronic hepatitis B.

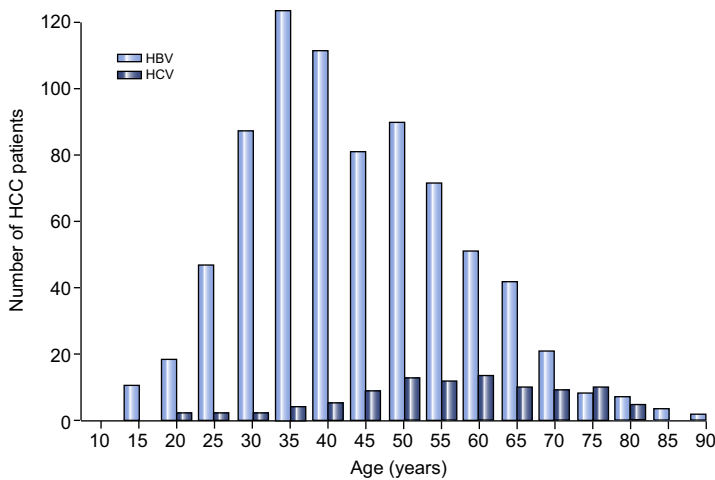


Fig. 2. Number of HCC cases per 5-year age range in Africa. Data from a consortium of collaborating Centers on HCC. Reprinted by permission from Macmillan Publishers Ltd: [Am J Gastroenterol.] [10], copyright (2015).

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