

Hepatitis B in Sub-Saharan Africa

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Abstract

Hepatitis B virus (HBV) infection causes a spectrum of acute and chronic liver disease, ranging from inactive chronic carrier status to progressive chronic hepatitis, leading to end-stage cirrhosis and primary liver cancer. In sub-Saharan Africa, over 8% of the population has chronic HBV carriage with a high risk for progressive liver disease. HBV-related hepatocellular carcinoma is the most common cancer among men and third most common among women. HBV therefore represents a critical threat to health in the African continent.

Overview

In this article, we outline the state of HBV prevalence, screening and management in sub-Saharan Africa (SSA). We highlight the urgent need for greater international support to improve local infrastructure for effective prevention and clinical management strategies for HBV infection.

Hepatitis B virus (HBV) infection causes a spectrum of acute and chronic liver disease, ranging from inactive chronic carrier status to progressive chronic hepatitis, leading to end-stage cirrhosis and liver cancer [1EASL 2012]. Over one third of the world's population has been, or is currently infected with, HBV and 350-400 million people remain chronic HBV surface antigen (HBsAg) carriers [1]. There are over 500-750,000 reported deaths annually due to HBV-related cirrhosis and primary liver cancer worldwide. However, this figure underestimates the true HBV mortality rate due to inadequate disease and cancer surveillance in many resource-poor countries where HBV is endemic [2].

Within SSA, HBV infection is endemic and the HBV-related disease burden is high. The lifetime risk of HBV infection is over 60% and more than 8% of the population remain chronic HBV carriers who are at risk of progressive liver disease and hepatocellular carcinoma (HCC). HCC is a highly aggressive cancer with limited treatment options, particularly in resource-poor settings

[3]. SSA has one of the highest HBV-related liver cancer rates in the world [4], with HBV-related liver cancer the most common cancer among males and third most common cancer among females [5, 6]. Furthermore, the average age of HCC development in Africa is considerably younger than in other parts of the world (mean age 33 years compared with 50 years in Asia and 60 years in Western Europe [9], meaning HBV-related HCC affects patients in their working and reproductive years [10]. HBV therefore represents a critical threat to health in the African continent.

Treatment

Early detection and treatment of HBV infection reduces HCC incidence and mortality (primary prevention) [11, 12]. Furthermore, HCC survival is improved by early detection of potentially treatable HCC by screening of at-risk patients (secondary prevention)[13]. However, access to medical care and the cost of screening, diagnosis and treatment of viral hepatitis and HCC are major limiting factors in hepatitis and liver cancer management in SSA. Routine HBV screening and surveillance programs for the general population are virtually non-existent in SSA and most nations lack the laboratory and medical infrastructure to implement such screening. A minority of countries in SSA offers free HBV screening of pregnant mothers, healthcare workers and HIV-infected individuals. However, there is a lack of infrastructure to support channeling of screened patients into long-term treatment programs [14].

Safe and effective treatments for HBV exist, but treatment access is severely limited in SSA. The recent WHO Global Policy Report on the Prevention and Control of Viral Hepatitis reported that only 16.7% of WHO-AFRO countries have publicly funded HBV treatment available, despite highly effective nucleoside analogues, such as tenofovir being available in most countries in SSA at generic price for the treatment of HIV [14]. This staggering lack of accessibility to affordable, effective HBV treatments needs addressing urgently if any gains

are to be made in controlling the costly disease burden of HBV-related liver disease and HCC.

Control

Vaccination is the cornerstone of HBV prevention and is most effective when given within 24 hours of birth [15, 16]. Multiple studies from SSA have demonstrated that HBV vaccination of infants is both feasible and highly effective for preventing chronic HBV carriage and HCC [17, 18, 19]. Despite WHO guidelines recommending that HBV vaccination should be given within 24 hours of birth, the vaccine schedule of 6, 10 and 14 weeks has been adopted in most African countries to allow the use of combination vaccines and to minimise costs and logistic expenses by streamlining vaccination schedules [20]. However, HBV vaccination coverage remains highly variable in SSA and there are little data on infant HBV vaccination coverage in South Sudan [21, 14].

Control of HBV prevalence is a major goal for the World Health Organization (WHO) worldwide, with a key focus on HBV prevention in African countries. In 2010, the World Health Assembly (WHA) passed a resolution calling for public health intervention to prevent and control viral hepatitis. There is also a forthcoming WHA resolution requesting the Global Health Fund to provide antiviral medications for HBV mono-infected patients. HBV treatment that is accessible and affordable to all is a pressing requirement in SSA and greater support from the international medical community is critical to engender support from the pharmaceutical industry for equitable drug availability. Greater support for medical service infrastructure and staff education is paramount to assist countries in SSA to develop and sustain essential HBV research platforms and public health intervention campaigns. African and international medical associations for liver disease and infectious diseases, community hepatitis groups and healthcare workers need to band together to forge a path for the education and promotion of viral hepatitis among all levels of the African community. The crucial importance of viral hepatitis research, treatment and prevention campaigns is more likely to be heard by pharmaceutical industry and government policy makers when delivered by a strong united voice.

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to diagnose, treat and follow-up a cohort of hepatitis B-positive patients in The Gambia, Senegal and Nigeria (EC FP7, P34114; www.prolifica.eu).

References

1. EASL (European Association for the Study of the Liver) clinical practice guidelines: Management of chronic hepatitis B virus infection. *J Hepatol.* 2012;57(1):167-85.
2. WHO 2002. Hepatitis B. WHO [online], http://www.who.int/csr/disease/hepatitis/HepatitisB_whoocdsrlyo2002_2.pdf accessed 21st April 2014).
3. EASL-EORTC (European Association for the Study of the Liver. European Organisation for Research and Treatment of Cancer) clinical practice guidelines: Management of hepatocellular carcinoma. *J Hepatol.* 2012a;56(4):908-43.
4. Parkin DM, Bray F, Ferlay J, Pisani P. Global cancer statistics, 2002. *CA Cancer J Clin.* 2005;55(2):74-108.
5. Parkin DM, Sitas F, Chirenje M, Stein L, Abratt R, Wabinga H. Part I: Cancer in Indigenous Africans--burden, distribution, and trends. *Lancet Oncol.* 2008;9(7):683-92.
6. Kirk GD, Lesi OA, Mendy M, Akano AO, Sam O, Goedert JJ, et al. The Gambia Liver Cancer Study: Infection with hepatitis B and C and the risk of hepatocellular carcinoma in West Africa. *Hepatology.* 2004;39(1):211-9.
7. Colombo M, de Franchis R, Del Ninno E, Sangiovanni A, De Fazio C, Tommasini M, et al. Hepatocellular carcinoma in Italian patients with cirrhosis. *New England Journal of Medicine.* 1991;325(10):675-80.
8. Tsukuma H, Hiyama T, Tanaka S, Nakao M, Yabuuchi T, Kitamura T, et al. Risk factors for hepatocellular carcinoma among patients with chronic liver disease. *New England Journal of Medicine.* 1993;328(25):1797-801.
9. Prates MD, Torres FO. A cancer survey in Lourenco Marques, Portuguese East Africa. *Journal of the National Cancer Institute.* 1965;35(5):729-57.
10. EASL-EORTC clinical practice guidelines: Management of hepatocellular carcinoma. *Journal of Hepatology.* 2012b;56(4):908-43.
11. Robotin MC, Kansil MQ, George J, Howard K, Tipper S, Levy M, et al. Using a population-based approach to prevent hepatocellular cancer in New South Wales, Australia: effects on health services utilisation. *BMC health services research.* 2010;10:215.
12. Liaw YF, Sung JJ, Chow WC, Farrell G, Lee CZ, Yuen H, et al. Lamivudine for patients with chronic hepatitis B and advanced liver disease. *New England Journal of Medicine.* 2004;351(15):1521-31.
13. Lopez PM, Villanueva A, Llovet JM. Systematic review: evidence-based management of hepatocellular carcinoma--an updated analysis of randomized

controlled trials. *Alimentary pharmacology & therapeutics*. 2006;23(11):1535-47.

14. WHO 2014 Global policy report on the prevention and control of viral hepatitis in WHO Member States http://www.who.int/csr/disease/hepatitis/global_report/en/; accessed 21st April 2014
15. Poovorawan Y, Chongsrisawat V, Theamboonlers A, Srinivasa K, Hutagalung Y, Bock HL, et al. Long-term benefit of hepatitis B vaccination among children in Thailand with transient hepatitis B virus infection who were born to hepatitis B surface antigen-positive mothers. *J Infect Dis*. 2009;200(1):33-8.
16. Poovorawan Y, Chongsrisawat V, Theamboonlers A, Leroux-Roels G, Kuriyakose S, Leyssen M, et al. Evidence of protection against clinical and chronic hepatitis B infection 20 years after infant vaccination in a high endemicity region. *J Viral Hepat*. 2011;18(5):369-75.
17. Mendy M, Peterson I, Hossin S, Peto T, Jobarteh ML, Jeng-Barry A, et al. Observational study of vaccine efficacy 24 years after the start of hepatitis B vaccination in two Gambian villages: no need for a booster dose. *PLoS One*. 2013;8(3):e58029.
18. Montesano R. Hepatitis B immunization and hepatocellular carcinoma: The Gambia Hepatitis Intervention Study. *J Med Virol*. 2002;67(3):444-6.
19. Chiang CJ, Yang YW, You SL, Lai MS, Chen CJ. Thirty-year outcomes of the national hepatitis B immunization program in Taiwan. *Journal of the American Medical Association*. 2013;310(9):974-6.
20. Ekra D, Herlinger KH, Konate S, Leblond A, Fretz C, Cilote V, et al. A non-randomized vaccine effectiveness trial of accelerated infant hepatitis B immunization schedules with a first dose at birth or age 6 weeks in Cote d'Ivoire. *Vaccine*. 2008;26(22):2753-61.
21. Howell J, Lemoine M, Thursz M. Prevention of materno-foetal transmission of hepatitis B in sub-Saharan Africa: the evidence, current practice and future challenges. *J Viral Hepat*. 2014;21(6):381-96.

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NEOPLASM OF THE COLON: A CLINICAL QUIZ

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A 34-year old male presented with a 3-months history of anorexia, weight loss and rectal bleeding. There was a strong family history of several members with colorectal cancer. Examination was unremarkable except for generalized muscle wasting. Investigations revealed anaemia and a positive faecal blood test. Colonoscopy showed an ulceroproliferative growth involving the proximal descending colon causing significant luminal narrowing. Biopsy was consistent with adenocarcinoma colon. At endoscopy distal colon also revealed the appearance as in Figure 1.



Figure 1. Endoscopy of distal colon

Questions

- Q1. What is the endoscopy finding in Figure 1?
- Q2. What is the most probable diagnosis?
- Q3. What is the genetic abnormality involved?
- Q4. What are the variants?
- Q5. Name the associated extra-gastrointestinal neoplasms.
- Q6. What is the treatment?