

World Journal of *Gastroenterology*

World J Gastroenterol 2021 September 28; 27(36): 5989-6160



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The WJG is now indexed in Current Contents®/Clinical Medicine, Science Citation Index Expanded (also known as SciSearch®), Journal Citation Reports®, Index Medicus, MEDLINE, PubMed, PubMed Central, and Scopus. The 2021 edition of Journal Citation Report® cites the 2020 impact factor (IF) for WJG as 5.742; Journal Citation Indicator: 0.79; IF without journal self cites: 5.590; 5-year IF: 5.044; Ranking: 28 among 92 journals in gastroenterology and hepatology; and Quartile category: Q2. The WJG's CiteScore for 2020 is 6.9 and Scopus CiteScore rank 2020: Gastroenterology is 19/136.

RESPONSIBLE EDITORS FOR THIS ISSUE

Production Editor: Jia-Hui Li; Production Department Director: Yu-Jie Ma; Editorial Office Director: Ze-Mao Gong.

NAME OF JOURNAL

World Journal of Gastroenterology

ISSN

ISSN 1007-9327 (print) ISSN 2219-2840 (online)

LAUNCH DATE

October 1, 1995

FREQUENCY

Weekly

EDITORS-IN-CHIEF

Andrzej S Tarnawski, Subrata Ghosh

EDITORIAL BOARD MEMBERS

<http://www.wjgnet.com/1007-9327/editorialboard.htm>

PUBLICATION DATE

September 28, 2021

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INSTRUCTIONS TO AUTHORS

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<https://www.wjgnet.com/bpg/gerinfo/240>

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<https://www.wjgnet.com/bpg/GerInfo/288>

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<https://www.wjgnet.com/bpg/gerinfo/208>

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<https://www.wjgnet.com/bpg/gerinfo/242>

STEPS FOR SUBMITTING MANUSCRIPTS

<https://www.wjgnet.com/bpg/GerInfo/239>

ONLINE SUBMISSION

<https://www.f6publishing.com>

Hepatitis B virus infection and hepatocellular carcinoma in sub-Saharan Africa: Implications for elimination of viral hepatitis by 2030?

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Author contributions: Amponsah-Dacosta E defined the topic, performed the literature search, screened, and reviewed the literature, and wrote the manuscript.

Supported by The Harry Crossley Postdoctoral Research Fellowship 2021.

Conflict-of-interest statement: The author has no conflict of interest to disclose.

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Manuscript source: Invited manuscript

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Abstract

Elimination of viral hepatitis in sub-Saharan Africa by 2030 is an ambitious feat. However, as stated by the World Health Organization, there are unprecedented opportunities to act and make significant contributions to the elimination target. With 60 million people chronically infected with hepatitis B virus (HBV) of whom 38800 are at risk of developing highly fatal hepatocellular carcinoma (HCC) every year, sub-Saharan Africa faces one of the greatest battles towards elimination of viral hepatitis. There is a need to examine progress in controlling the disproportionate burden of HBV-associated HCC in sub-Saharan Africa within the context of this elimination target. By scaling-up coverage of hepatitis B birth dose and early childhood vaccination, we can significantly reduce new cases of HCC by as much as 50% within the next three to five decades. Given the substantial reservoir of chronic HBV carriers however, projections show that HCC incidence and mortality rates in sub-Saharan Africa will double by 2040. This warrants urgent public health attention. The trends in the burden of HCC over the next two decades, will be determined to a large extent by progress in achieving early diagnosis and appropriate linkage to care for high-risk chronic HBV infected persons.

Key Words: Hepatitis B virus; Viral hepatitis, Hepatocellular Carcinoma; Elimination; Human Immunodeficiency Virus; Sub-Saharan Africa

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Core Tip: Chronic hepatitis B virus (HBV) infection is the primary risk factor for

Specialty type: Gastroenterology and hepatology

Country/Territory of origin: South Africa

Peer-review report's scientific quality classification

Grade A (Excellent): 0

Grade B (Very good): B

Grade C (Good): 0

Grade D (Fair): 0

Grade E (Poor): 0

Received: February 28, 2021

Peer-review started: February 28, 2021

First decision: May 1, 2021

Revised: May 10, 2021

Accepted: August 13, 2021

Article in press: August 13, 2021

Published online: September 28, 2021

P-Reviewer: Peng S

S-Editor: Wang JL

L-Editor: Webster JR

P-Editor: Li JH



hepatocellular carcinoma (HCC) in sub-Saharan Africa. In 2020, HBV-associated HCC accounted for approximately 36700 deaths. By 2040, it is projected that approximately 72200 people will die each year from this disease without an intensive public health response. The high mortality-to-incidence ratio associated with HCC in sub-Saharan Africa suggests significant inequities in access to appropriate health care. This review examines the evidence on the extent of the disease burden in sub-Saharan Africa and advocates for prioritizing HCC control as part of ongoing viral hepatitis elimination strategies within this region.

Citation: Amponsah-Dacosta E. Hepatitis B virus infection and hepatocellular carcinoma in sub-Saharan Africa: Implications for elimination of viral hepatitis by 2030? *World J Gastroenterol* 2021; 27(36): 6025-6038

URL: <https://www.wjgnet.com/1007-9327/full/v27/i36/6025.htm>

DOI: <https://dx.doi.org/10.3748/wjg.v27.i36.6025>

INTRODUCTION

Despite the availability of a safe and effective prophylactic vaccine since 1982, chronic hepatitis B which is a serious liver disease caused by hepatitis B virus (HBV), remains a major global public health threat. Estimates from the World Health Organization's (WHO) current Global Hepatitis Report suggest that in 2015, 3.5% (257 million persons) of the world's population were living with chronic hepatitis B, with the Western Pacific and sub-Saharan African regions bearing the brunt (68%) of the disease burden (WHO, 2017). In addition to this, 887000 deaths due to HBV-associated hepatic sequelae such as acute hepatitis, liver cirrhosis and liver cancer or hepatocellular carcinoma (HCC), were recorded worldwide[1].

With an estimated 830180 associated deaths recorded in 2020, liver cancer remains a leading cause of cancer-related death worldwide, third only to lung (1.8 million deaths) and colorectal (935153 deaths) cancers[2]. Globally, incidence rates of liver cancer have remained high, with 905677 newly diagnosed cases in 2020 [compared to 748000 (5.9% of all cancers) new cases in 2008, for example[3]], representing 4.7% of all cancer cases recorded in that year alone[2]. The most common type of malignant transformation in the liver is HCC (75%-85%), followed by intrahepatic cholangiocarcinoma (10%-15%), with other rare types accounting for the remainder of all primary liver cancers. The geographic distribution of the incidence of HCC tends to mirror that of its major risk factors, chronic hepatitis B and hepatitis C virus (HCV) infection, which account for approximately 56% and 20% of all HCC cases, respectively[2,4-6]. This implies that the highest incidence rates [age-standardized incidence rate (ASIR) > 20 cases per 100000 persons per year] of HCC are recorded in hepatitis B endemic countries including those in sub-Saharan Africa, while non-endemic regions like Europe and North America report relatively lower incidence rates (ASIR < 10 cases per 100000 persons per year)[2,7-9]. A further cause for concern in most resource limited countries within regions like sub-Saharan Africa where HCC screening and diagnostic services, and medical interventions are often inadequate, is the poor survival and extremely high mortality rates associated with HCC. Approximately 93% of patients die within a year of the onset of symptoms[7,9-11]. Evidently, elimination of viral hepatitis caused by HBV and HCV presents the best opportunity to reduce the incidence of HCC, especially in regions like sub-Saharan Africa, where the disease burden and need for intervention are oftentimes the greatest.

Recognizing the devastating impact of viral hepatitis on global health, the WHO in May 2016 adopted a Global Health Sector Strategy on Viral Hepatitis aimed at achieving a 90% reduction in new cases and a 65% reduction in mortality due to HBV and HCV infection, towards an ambitious target of eliminating viral hepatitis by 2030 [12]. To eliminate chronic hepatitis B, the health service targets to be attained by 2030 include; 90% coverage of routine childhood hepatitis B vaccination, a reduction in mother-to-child transmission (MTCT) of HBV such as through > 90% coverage of hepatitis B birth dose vaccination, 100% of all blood donations screened for HBV, 90% of all HBV infections diagnosed, and 80% of eligible persons with chronic hepatitis B linked to appropriate treatment and care[12]. While largely in the planning phase of executing this global strategy, a recent WHO report suggests that overall, member

states are making progress in developing national viral hepatitis management guidelines and strategic plans towards attaining the elimination targets, although availability of dedicated funding to support implementation appears to be an important challenge in some countries[13].

To contribute to the knowledgebase on the scope of the burden of chronic hepatitis B in sub-Saharan Africa, the status and public health response to HBV-associated HCC in sub-Saharan Africa are reviewed. Opportunities and challenges towards achieving the 2030 viral hepatitis elimination target – at least where chronic hepatitis B and HCC are concerned – are also identified, with the intent of arguing for continued financial and technical investments to support ongoing health sector strategies and interventions within sub-Saharan Africa.

GLOBAL BURDEN OF CHRONIC HEPATITIS B

The seroprevalence of chronic hepatitis B which is based on the detection of the hepatitis B surface antigen (HBsAg) within the general population, is highly variable worldwide. This variability is demonstrated by substantial regional and inter-country disparities in the burden of the disease. Available estimates[14] suggest that HBsAg prevalence rates in the Americas, for example, range from < 2% in countries like the United States of America, Mexico, and Guatemala, to 13.55% (95%CI: 9.00-19.89) in Haiti. In the South East Asian region, HBsAg prevalence rates range from 0.82% (95%CI: 0.80-0.84) in Nepal to as high as 6.42% (95%CI: 6.37-6.47) in Thailand. Overall, countries within the Eastern Mediterranean and European regions mostly have lower-intermediate endemicity levels (HBsAg prevalence ranging from 2% to 4.99%) while the Western Pacific can be classified as a high-intermediate endemic region with most countries recording HBsAg prevalence rates > 5%. Within the African region, the lowest HBsAg prevalence rates are reported in countries like Seychelles [0.48% (95%CI: 0.12-1.90)], Eritrea [2.49% (95%CI: 2.32-2.67)], and Algeria [2.89% (95%CI: 2.50-3.33)], while Mauritania [16.16% (95%CI: 14.92-17.49)], Liberia [17.55% (95%CI: 15.70-19.55)], Swaziland [19% (95%CI: 17.65-20.43)], and South Sudan [22.38% (95%CI: 20.10-24.83)] have recorded some of the highest prevalence estimates[14].

EPIDEMIOLOGICAL SHIFT IN THE BURDEN OF CHRONIC HEPATITIS B IN SUB-SAHARAN AFRICA

Historically, sub-Saharan Africa has been classified as hyper-endemic for chronic hepatitis B based on the detection of HBsAg among $\geq 8\%$ of the general population. Table 1 shows the variable prevalence of HBsAg among populations in some sub-Saharan African countries prior to introduction of universal hepatitis B vaccination and how this has changed over time post-vaccine introduction[15-47]. At the peak of the hepatitis B epidemic in sub-Saharan Africa, the disease burden was characterized by a preponderance of horizontal transmission of HBV among young children (between 1-4 years of age), 30%-50% of whom would go on to develop chronic hepatitis B, and later progress to potentially fatal sequelae (mainly liver cirrhosis and HCC) within 30-50 years after infection[15,29,48]. This contrasts with HBV infection acquired during adulthood which carries a considerably lower risk (< 5%) of progression to chronic disease as observed in non-endemic regions of the world.

Currently, the prevalence of HBsAg in sub-Saharan Africa is reported to be 6.1%, equating to 60 million people living with chronic hepatitis B, of which approximately 4.8 million are children < 5 years of age[1]. The decline in the prevalence of HBsAg within the population can be largely attributed to the success of universal childhood hepatitis B vaccination programmes implemented in sub-Saharan Africa since the early 1990s[49]. In most sub-Saharan African countries, the first dose of the hepatitis B vaccine is administered at 6 weeks of age, with the remainder of the regimen completed within the 1st year of life in an effort to interrupt transmission and prevent incident HBV infection in early childhood. Coverage of the third dose of the hepatitis B vaccine in the region is currently estimated at 73%[50]. Countries like The Gambia and South Africa with longstanding hepatitis B vaccination programmes have achieved marked declines in incident infections over time, especially among children < 5 years of age (Table 1).

Despite this success, we are still decades away from realizing the full benefits of universal childhood hepatitis B vaccination programmes in sub-Saharan Africa, given

Table 1 Prevalence of hepatitis B surface antigen among pre- vs post-hepatitis B vaccine introduction populations in some sub-Saharan African countries

Country	Year of hepatitis B vaccine introduction ¹	Prevalence of HBsAg (%)		
		Pre-vaccine introduction	Post-vaccine introduction	
			< 15-yr-olds	≥ 15-yr-olds
Burundi	2004	11.0[15]	2.6[16]	1.0-4.6[17]
Democratic Republic of Congo	2007	> 20.7[18]	2.2[19]	3.7[19]
Ethiopia	2007	11.0[20]	4.4[21]	7.4[22]
Gambia	1990	20.0[23]	0.4[24]	10.0[25]
Kenya	2002	11.4[26]	0.9[16]	3.4[27]
Mali	2003	> 8.7[28]	4.9[16]	8.5[16]
Mozambique	2001	14.6[29]	3.7[16]	4.5[30]
Namibia	2009	14.0[31]	2.7[32]	1.8[33]
Nigeria	2004	13.3[34]	11.5[35]	8.2[36]
Rwanda	2002	Approximately 5.0[37]	1.7[16]	2.2[38]
Senegal	2004	11.8[39]	1.6[40]	> 11.0[41]
South Africa	1995	9.6[15]	0.4[42]	4.0[43]
Uganda	2002	10.3[44]	0.6[45]	4.1[45]
Zimbabwe	2000	15.4[46]	4.4[16]	3.3[47]

¹The year the hepatitis B vaccine was introduced into national Expanded Programme on Immunization. HBsAg: Hepatitis B surface antigen.

the protracted natural history of chronic hepatitis B, and the long interval between early childhood infection and development of chronic sequelae[51,52]. As such, high prevalence rates of HBsAg persist among a reservoir of adult populations, including women of childbearing age, most of whom were born before the introduction of the hepatitis B vaccine or were not fully vaccinated in infancy (Table 1). This continues to feed the epidemic in sub-Saharan Africa, contributing to the 87890 HBV-associated deaths (approximately 10% of the global total) recorded each year[1]. What further compounds the situation in sub-Saharan Africa is the disproportionate burden of human immunodeficiency virus (HIV) co-infection (69% of all HBV-HIV co-infected persons reside in sub-Saharan Africa) which is associated with a more severe prognosis than that observed in HBV mono-infected individuals[53-55]. Emerging evidence also suggests that perinatal transmission or MTCT of HBV, which was previously presumed to be insignificant in the epidemiology of chronic hepatitis B in sub-Saharan Africa, actually contributes to 367250 incident HBV infections (twice the number of paediatric HIV infections) among neonates annually[56]. In fact, the risk of HBV MTCT increases by up to 2.5-fold among the substantial population of HBV-HIV co-infected pregnant women in sub-Saharan Africa, compared to their HBV mono-infected counterparts[57-60]. This is concerning, given that perinatally acquired HBV infections carry a 90% risk of progression to chronic hepatitis B. This implies that hepatitis B vaccination from 6 weeks of age may be inadequate in preventing incident HBV infections among neonates, especially where the burden of maternal HBV-HIV co-infection is high and prevention of HBV MTCT (PMTCT) strategies are sub-optimal, as is the case in most sub-Saharan African countries. This is a stark contrast to HIV MTCT in sub-Saharan Africa which is on course for elimination due to rapid expansion of antenatal screening and access to timely HIV antiretroviral therapy[61]. The marked decline in HIV MTCT has led to a growing population of HIV-exposed uninfected children in sub-Saharan Africa. Of the 14.8 million HIV-exposed uninfected children in the world, 90% live in sub-Saharan Africa[62]. Although inconclusive, there is some evidence to suggest that HIV-exposed uninfected children may have a modified immune response to hepatitis B vaccination and may also be at increased risk for HBV infection, presenting an additional complexity to elimination strategies in sub-Saharan Africa[58,63-66].

EPIDEMIOLOGICAL TRENDS IN HBV-ASSOCIATED HCC IN SUB-SAHARAN AFRICA

Of the 60 million people currently living with chronic hepatitis B in sub-Saharan Africa, 38800 are at risk of developing HCC every year, characterized by an aggressive clinical course[2,67,68]. In addition, approximately 93% (36700) of persons with HCC will die within a year of their diagnosis without appropriate and timely medical intervention[2,11,67]. Most of these HCC cases (and deaths) will occur among a predominantly male population (sex ratio of 2:1) with age at diagnosis ranging between 38-67 years (compared to 50-70 years in resource rich countries), who are in their prime reproductive and working years, draining productive capacity, and placing a further burden on already strained economic, societal, and health, systems in sub-Saharan Africa[9,11,69-71]. While cases of paediatric HCC are diagnosed more frequently in some sub-Saharan African countries than those in Europe and North America for example, they remain uncommon when compared to the HCC incidence among adult populations[72-75]. Within the next two decades, HCC incidence and mortality rates in sub-Saharan Africa are predicted to double (Figure 1[67,76,77]) unless addressed through reforms in regional and national health policy and practice, including intensifying prevention, diagnostic and treatment strategies, in a whole system approach.

A comparison of the 2020 estimates of age-standardized liver cancer (mainly HCC) incidence and mortality (ASMR) rates in sub-Saharan Africa *vs* other regions of the world is shown in Figure 2[2,67,78]. With ASIRs of 8.1 and 4.2, and ASMRs of 7.8 and 4.0 per 100000 persons per year among men and women, respectively, HCC is a common cause of cancer-related morbidity and mortality in sub-Saharan Africa. There are substantial regional variations in HCC incidence and mortality rates across sub-Saharan Africa. Among males for example, the highest HCC ASIRs (> 12.9 per 100000 persons per year) and ASMRs (> 12.6 per 100000 persons per year) are recorded in West African countries, while East African countries generally appear to experience a lower burden (ASIRs < 5.1 and ASMRs < 4.9 per 100000 persons per year) of the disease (Figures 3 and 4)[2,67,78]. It should be noted however, that the true burden of HCC in sub-Saharan Africa is grossly underestimated by as much as 40%, given that cases are often underreported due to challenges in effectively diagnosing the disease, while the quality and coverage of data in population-based cancer registries are suboptimal[9,11,79].

The overall HCC mortality-to-incidence ratio (MIR = 0.95) in sub-Saharan Africa is comparable to that in the Western Pacific and South-East Asian regions (MIR = 0.95) but higher than that in Northern America (MIR = 0.82)[80]. This high MIR reflects disparities in outcomes of HCC in sub-Saharan Africa compared to resource-rich regions, owing to limited availability and accessibility of diagnostic and treatment services[81,82]. These disparities go beyond the clinical context and are rooted in socio-economic inequities. A recent South African study[82] investigating trends in liver cancer-associated mortality found key socio-economic and sex disparities. The average MIR for black South African men and women was 4.0 and 3.3 respectively, compared to 2.2 and 1.8 among their white counterparts. This underscores the inequities in HCC prognosis experienced by socio-economically disadvantaged populations[82]. Evidently, addressing the disproportionate burden of HCC in sub-Saharan Africa will require careful consideration of socio-economic and demographic inequities prevalent within its population.

PREDOMINANCE OF HBV-ASSOCIATED HEPATOCARCINOGENESIS IN SUB-SAHARAN AFRICA

The association of chronic hepatitis B with the development of most cases of HCC [attributable fraction, AF = 50% (95%CI: 39-60)] occurring among sub-Saharan African populations is well established in the literature[5,6,83,84]. The remainder of HCC cases are typically associated with HCV infection [AF = 21% (95%CI: 13-32)] and exposure to the dietary carcinogen, aflatoxin B1, although metabolic syndrome is emerging as an important risk factor in sub-Saharan Africa[6,85-88]. In comparison, the major risk factors for HCC development in low incidence regions of the world (North America, and Western, Central, and Eastern Europe) include host and environmental factors such as genetic predisposition to primary liver cancer, chronic alcohol intake, obesity, hemochromatosis, and exposure to nitrosamines, followed by HCV infection[71,89-

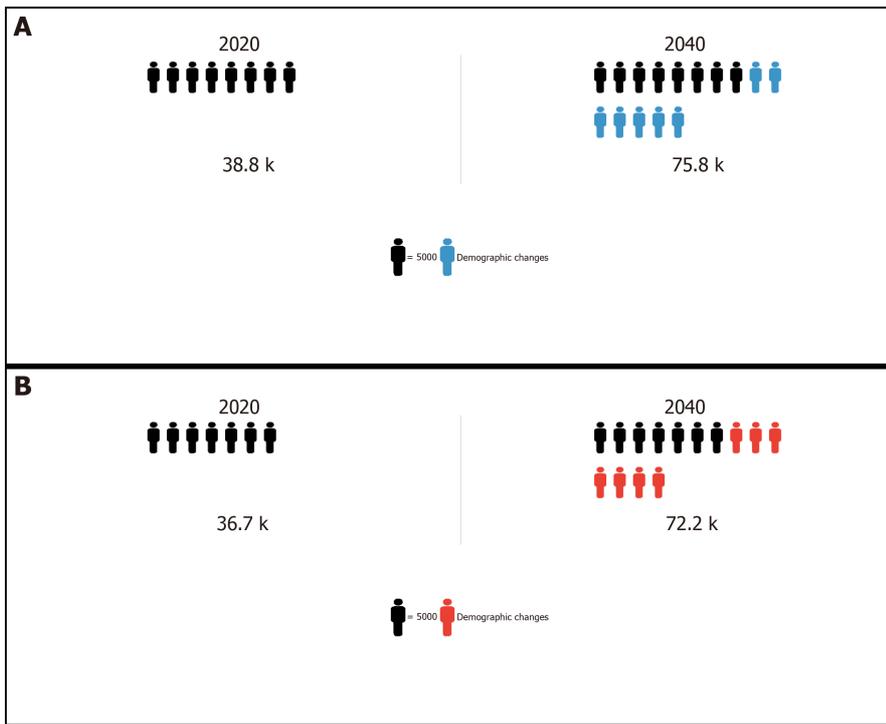


Figure 1 Projected increase in estimated number of cases and deaths due to cancers of the liver and intrahepatic bile ducts within sub-Saharan Africa from 2020 to 2040[67,76,77]. GLOBOCAN 2020 (<https://gco.iarc.fr/>). A: Estimated number of cases from 2020 to 2040, both sexes, age (0-85+); B: Estimated number of deaths from 2020 to 2040, both sexes, age (0-85+).

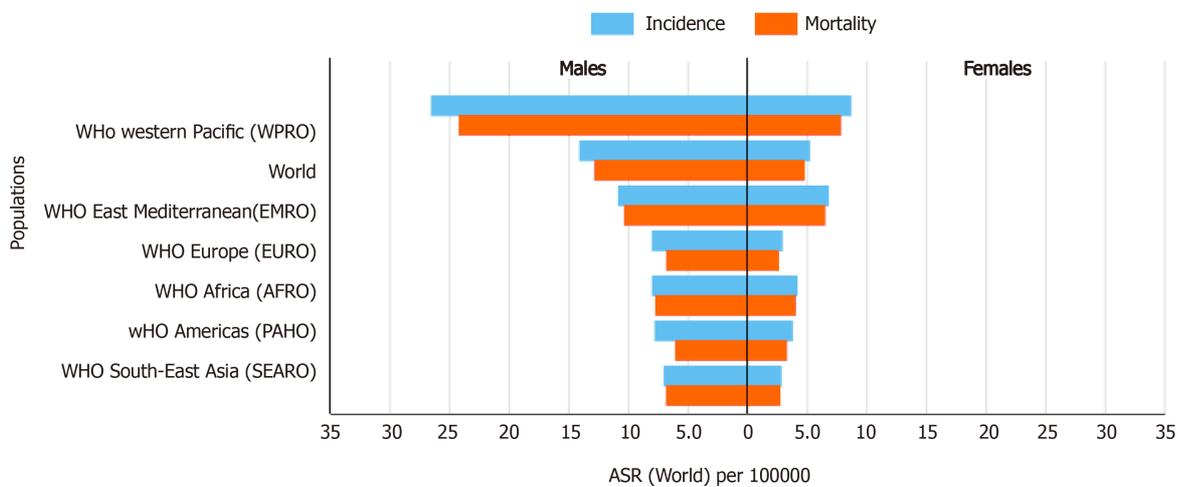


Figure 2 Estimated age-standardized liver cancer incidence and mortality rates per 100000 persons per year shown worldwide in 2020[2, 67,78]. GLOBOCAN 2020 (<https://gco.iarc.fr/>). WHO: World Health Organization; ASR: Liver cancer age standardized incidence rate.

91]. It is worth noting however, that the potential for interaction among these different risk factors, leading to synergistic or additive effects in the development of HCC in both endemic and non-endemic regions of the world cannot be undervalued.

The mechanism underlying HBV-associated hepatocarcinogenesis is multifactorial, involving various direct and indirect viral mechanisms required to stimulate the host oncogenic pathway and achieve hepatocyte transformation[92,93]. These mechanisms, which may act synergistically, include integration of the viral DNA into host genome, persistent and enhanced HBV replication, as well as infection with specific HBV genotypes and HBV genetic variants. Important HBV-specific risk factors involved in the development of HCC have been identified in previous studies conducted in sub-Saharan Africa. In a recent case control study, Atsama Amougou *et al*[94] demonstrated the role of circulating quasi-genotypes and viral genetic variations in HBV-

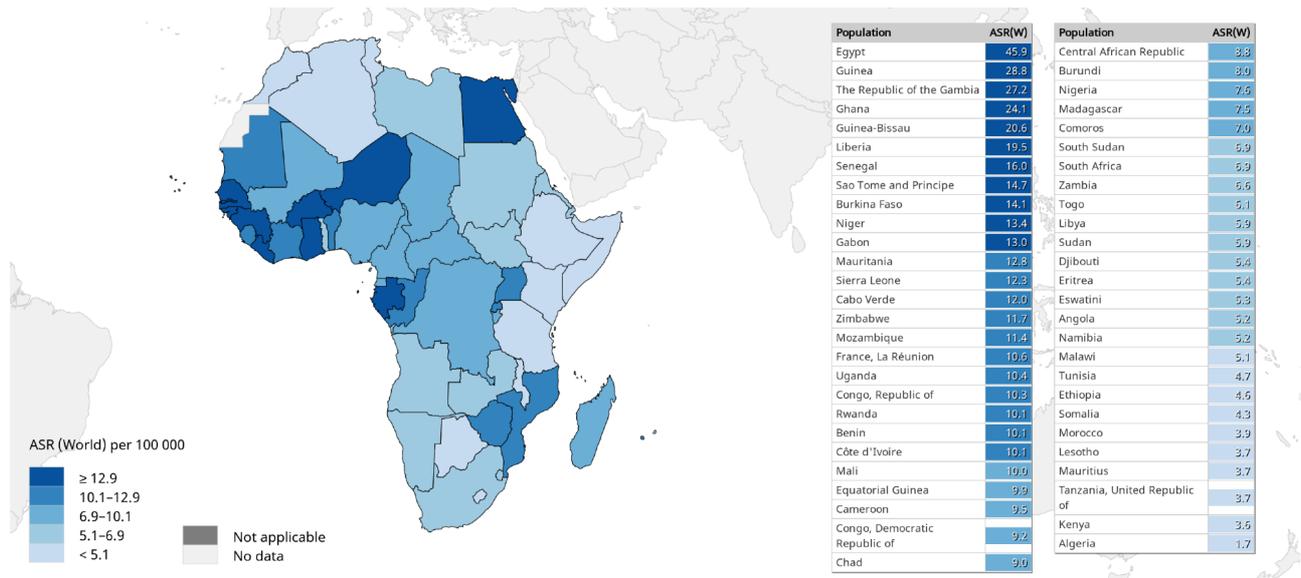


Figure 3 Estimated age-standardized liver cancer incidence rates per 100000 persons per year in males in Africa (2020)[2,67,78]. GLOBOCAN 2020 (<https://gco.iarc.fr/>). The designations employed and the presentation of the material in this publication do not imply the expression of any opinion whatsoever on the part of the World Health Organization/International Agency for Research on Cancer concerning the legal status of any country, territory, city, or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted or dashed lines on maps represent approximate borderlines for which there may not yet be full agreement.

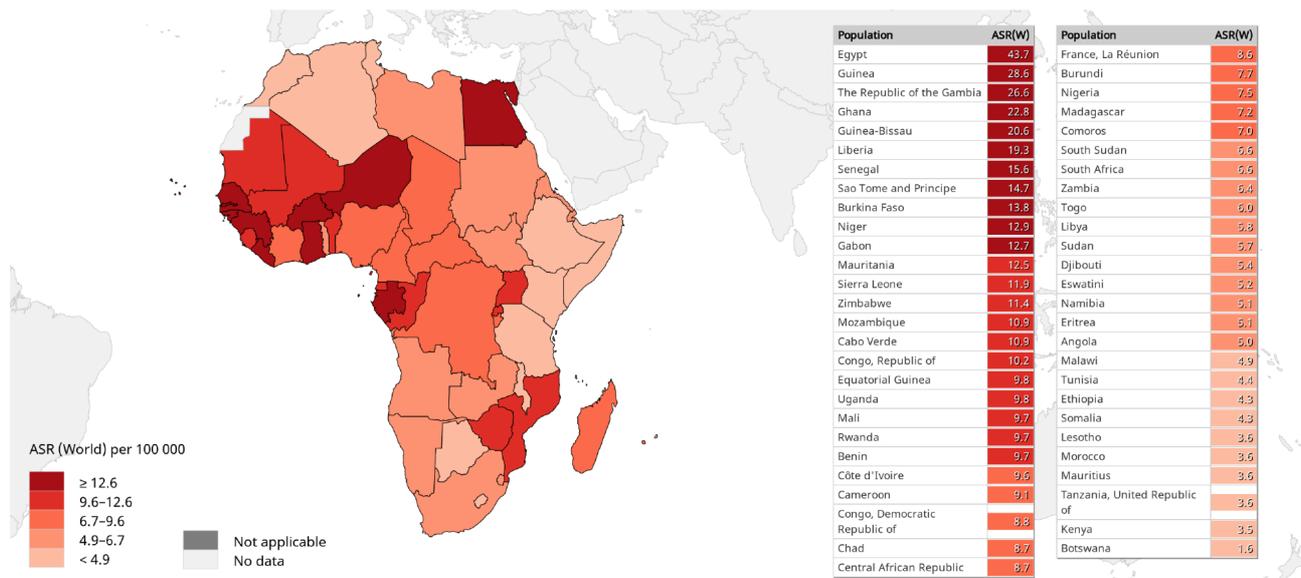


Figure 4 Estimated age-standardized liver cancer mortality rates per 100000 persons per year in males in Africa (2020)[2,67,78]. GLOBOCAN 2020 (<https://gco.iarc.fr/>). The designations employed and the presentation of the material in this publication do not imply the expression of any opinion whatsoever on the part of the World Health Organization/International Agency for Research on Cancer concerning the legal status of any country, territory, city, or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted or dashed lines on maps represent approximate borderlines for which there may not yet be full agreement.

associated hepatocarcinogenesis among Cameroonian HCC patients. A previous study [95] conducted in South Africa found an increasing risk of HCC with increasing HBV viremia, showing an increasing trend in odds ratio (OR) from ≥ 2000 IU/mL (OR = 8.55, 95% CI: 3.00 ± 24.54) to ≥ 200000 IU/mL (OR 16.93, 95% CI: 8.65 ± 33.13). While this finding is consistent with that from another study conducted in The Gambia, there is evidence to suggest that low-level viremia may also be a significant risk factor for HCC[96]. The South African study further demonstrated a 4-fold increase in the risk of developing HCC among participants with occult HBV infection (HBsAg negative but HBV DNA positive infections) compared to controls[95]. Interestingly, a previous longitudinal study conducted in The Gambia which followed chronic carriers of HBV

over a median duration of 28.4 years (interquartile range = 17.7-32.7) found that maternal HBsAg positivity - as a proxy of MTCT of HBV - was statistically significantly ($P < 0.001$) associated with a higher incidence of HCC [crude incidence rates of 89.2 (95%CI: 22.3-356.8) vs 0 (unadjusted) per 100 000 persons per year, among those born to HBsAg positive vs HBsAg negative mothers][70]. Based on these findings, the authors recommend further investigation into the feasibility of scaling-up implementation of hepatitis B birth dose vaccination and other PMTCT strategies within sub-Saharan Africa in order to interrupt incident HBV infections among neonates[70]. Of the 111 countries which report having introduced a hepatitis B birth dose as part of national routine immunization programmes, only 11 (Algeria, Botswana, Cabo Verde, Côte d'Ivoire, The Gambia, Mauritania, Namibia, Nigeria, Sao Tome and Principe, Senegal, and Zambia) are in Africa[50]. While the global coverage of the birth dose is reported to be suboptimal (43%), that in the sub-Saharan African region is even more dismal at an estimated 6%[50]. When considered together with the reported low coverage of maternal screening for HBV infection and linkage to antiviral prophylaxis, current PMTCT strategies are inadequate to significantly reduce perinatal transmission and avert neonatal HBV infections within the region[97,98].

CHALLENGES AFFECTING MANAGEMENT OF HBV-ASSOCIATED HCC IN SUB-SAHARAN AFRICA

Management of chronic hepatitis B involves suppressing HBV viremia and minimizing the risk of progression to liver cirrhosis, chronic liver failure and HCC, using oral nucleotide/nucleoside analogues like tenofovir disoproxil fumarate (TDF) and entecavir. Treatment with nucleotide/nucleoside analogues is indicated in chronic carriers with elevated HBV viremia, elevated liver enzymes, and evidence of liver fibrosis and cirrhosis. Appropriate linkage to care requires the identification of chronically infected individuals who are eligible for treatment through HBV screening programmes[99]. It is estimated that < 1% of chronic HBV infected individuals in sub-Saharan Africa are currently being diagnosed[100]. In addition, there are major gaps in determining treatment eligibility. Significant limitations have been identified when applying internationally recommended treatment eligibility criteria in the sub-Saharan African context. Only 10%-15% of persons with liver cirrhosis are detected for linkage to appropriate treatment[99-102].

Low uptake of HBV screening and treatment services in sub-Saharan Africa has been attributed to the lack of publicly funded, national HBV screening and treatment programmes. This leaves the responsibility for seeking an HBV test to the patient, which is highly detrimental when considered in the context of limited public awareness of the virus, and the asymptomatic nature of the infection until onset of late-stage sequelae[103]. As currently available nucleotide/nucleoside analogues cannot eradicate intrahepatic HBV DNA, treatment is typically lifelong, and this amounts to a significant cost[100,102]. A recent WHO report indicates that by 2019, < 8 of the 47 member states within the WHO African region (WHO AFRO) had established subsidized HBV treatment programmes[16]. This suggests that a substantial proportion of chronic HBV carriers continue to incur undue financial burden as a consequence of paying out-of-pocket for the treatment they need, while others may be unable to afford it altogether. In Ghana, the annual cost of TDF is estimated at \$670 which, when considered against an average annual income of \$1778, is a major constraint to accessing lifesaving treatment[104]. It should not come as a surprise then that most patients in sub-Saharan Africa present to health care facilities with established liver cirrhosis or symptomatic advanced-stage HCC, at which point the prognosis is grim and therapeutic options are limited to palliative care.

TOWARDS ELIMINATION OF CHRONIC HEPATITIS B AND CONTROL OF HCC IN SUB-SAHARAN AFRICA

Future trends in the burden of HCC in sub-Saharan Africa will be determined by our progress in preventing new HBV infections, screening and treating existing chronic hepatitis B cases, as well as detecting and appropriately managing HCC. As part of a scorecard to monitor progress towards elimination of viral hepatitis within WHO AFRO in 2019, six core indicators were listed; (1) development of national hepatitis policies in the form of a national strategic plan for viral hepatitis; (2) implementation

of hepatitis B birth dose vaccination; (3) achieving > 90% national coverage of the third dose of the hepatitis B vaccine; (4) being on track for the HBV and HCV 2020 testing target; (5) implementation of a national hepatitis treatment programme; and (6) commemoration of World Hepatitis Day in 2018. Overall, most sub-Saharan African countries were found lagging in almost all indicators[16].

Within the next decade, there is a need to scale-up primary prevention of incident HBV infections in sub-Saharan Africa. Despite adopting resolutions to improve hepatitis B birth dose and routine childhood vaccination in WHO AFRO by 2020, implementation and coverage of the birth dose remains unacceptably low, while coverage of routine childhood vaccination remains well below the global average of 84%[49,105,106]. Recognizing the significant threat of HBV MTCT to public health in sub-Saharan Africa, there have been renewed calls to expand access to the hepatitis B birth dose and leverage HIV PMTCT infrastructure in screening pregnant women and providing timely prophylaxis[56,98,107]. The future research agenda in sub-Saharan Africa should include investigating the need for tailored hepatitis B vaccination strategies for unique populations like HIV-exposed uninfected children.

As national governments grapple with the feasibility of implementing subsidized hepatitis surveillance and treatment programmes, the success of the HIV test and treat model in sub-Saharan Africa has been recognized as an opportunity to expand screening and antiviral treatment for chronic hepatitis B in the interim. To ensure a comprehensive package of care, there is a need to prioritize integration of cost-effective point-of-care screening tests with good diagnostic accuracy, guided by appropriate treatment eligibility criteria[49,108].

Within the past decade, there have been significant advances in the development of new diagnostic and therapeutic approaches for HCC, with prospects for further innovation in the field[109,110]. These advances present unique opportunities to improve surveillance and management of HCC. Biannual surveillance among high-risk chronic carriers of HBV using both liver ultrasonography and serum α -fetoprotein concentrations, is commonly used for early detection of progression to HCC. Curative treatment approaches for early-stage HCC include surgical resection, tumour ablation, or liver transplantation. For advanced-stage HCC, combination treatment using atezolizumab and bevacizumab over sorafenib alone, have shown promising long-term outcomes in phase III clinical trials[110]. Other immunotherapeutic agents for the treatment of late-stage HCC have also been recently explored[109]. While all these advancements present much needed opportunities to improve the quality of life of patients with HCC, the cost and feasibility of implementation within the sub-Saharan African public health context are always important considerations.

CONCLUSION

Ultimately, sub-Saharan Africa faces one of the toughest battles against chronic hepatitis B and HCC. Despite this, there are opportunities to achieve significant reductions in incident HBV infections and alter future trends in the burden of HCC. This calls for strong political will, regional coordination, and effective partnerships with donor agencies and non-governmental organizations in order to mobilize financial investments and technical support. Finally, the role of advocacy and awareness campaigns like World Hepatitis Day in enabling public ownership and demand for accessible, equitable, and quality health services cannot be undervalued.

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