Review

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Reducing the neglected burden of viral hepatitis in Africa: Strategies for a global approach

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Summary

The burden of liver disease may dramatically increase in the near future in Africa, where screening and access to care and treatment are hampered by inadequate disease surveillance, lack of high-quality tools to assess chronic liver disease, and underestimated needs for human and financial resources. Chronic hepatitis may be considered as silent and neglected killer, fuelled by many years of global inertia from stakeholders and policy makers alike. However, the global battle against viral hepatitis is facing a new era owing to the advent of highly effective drugs, innovative tools for screening and clinical follow-up, and recent signs that governments, advocacy groups and global health organizations are mobilizing to advocate universal access-to-treatment. This review details the barriers to prevention, screening and treatment of viral hepatitis on the African continent, focuses on the urgent need for operational and research programmes, and suggests integrated ways to tackle the global epidemic.

Keywords: Africa; Hepatitis B; Hepatitis C; Screening; Treatment.
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Abbreviations: AIDS, acquired immunodeficiency syndrome; ALT, alanine aminotransferase; ANRS, French Research Agency on HIV/AIDS and viral hepatitis; ART, antiretroviral treatment; AST, aspartate aminotransferase; DAA, direct-acting antiviral agent; GAVI, Global Alliance Vaccine & Immunization; GHIS, Gambian Hepatitis Intervention Study; GTZ/GIZ, Deutsche Gesellschaft für Technische Zusammenarbeit/Deutsche Gesellschaft für Internationale Zusammenarbeit; HBeAg, hepatitis B envelope antigen; HBsAg, hepatitis B surface antigen; HBV, hepatitis B virus; HCC, hepatocellular carcinoma; HIV, human immunodeficiency virus; HCV, hepatitis virus; MDM, Médecins du Monde; MSF, Médecins Sans Frontières; PCR, polymerase chain reaction; PEPFAR, President's Emergency Plan for AIDS Relief; POC, point-of-care; PROLIFICA, Prevention of Liver Fibrosis and Cancer in Africa; RNA, ribonucleic acid; SVR, sustained virological response; TDF, tenofovir disoproxil fumarate; WHO, World Health Organization; WHO-AFRO, World Health Organization-African Zone.

Introduction

Infection with chronic viral hepatitis affects 550 million people worldwide compared to 33 million with HIV. In total, 350 million are infected with hepatitis B virus (HBV), 185 million with hepatitis C virus (HCV) and 15 million with hepatitis delta virus [1,2]. Viral hepatitis causes substantial mortality, globally accounting for more than 1 million deaths each year. Chronic infection is the primary cause of hepatocellular carcinoma (HCC), which is one of the commonest cancers in developing countries and the third cause of cancer-related mortality worldwide [3]. The vast majority of individuals infected with viral hepatitis live in low to middle-income countries of Africa and Asia, where screening and access to care and treatment are not readily available. In Africa, about 100 million individuals are estimated to be infected with HBV or HCV, whereas resource-rich countries account for 23 million HBV or HCV-infected subjects [4]. Because of rather absent systematic screening policies and sub-optimal screening practices, it is commonly reported that more than 75% of infected individuals, living in Europe and the United States, are unaware of their HBV and HCV status [5,6]. Even though such data are unavailable in Africa, one might expect even higher figures considering the lack of emphasis on hepatitis screening and treatment, mainly due to severely constrained financial resources, the unavailability and inaccessibility of tests for hepatitis virus, as well as the insufficiency of well-trained health care workers.

The World Health Organization (WHO) is calling for improvement in interventions for the prevention, care, and control of viral hepatitis worldwide [7–10]. With the emergence of new, highly effective antivirals and a better implementation of HBV vaccine campaigns, viral hepatitis eradication can be rendered a feasible goal in Western countries [11–13]. However, a more global vision on viral hepatitis is needed and strategies for global eradication should be urgently extended to and implemented in endemic resource-limited countries. This review aims at highlighting the dramatic neglected burden of viral hepatitis in Africa, identifying the main barriers to screening, care and

treatment, and suggesting global strategies that can be adapted to the local setting.

Key Points 1

- Viral hepatitis causes substantial mortality, globally accounting for more than 1 million deaths each year. The vast majority of individuals infected with viral hepatitis live in low to middle-income countries of Africa and Asia
- Access to screening, care and treatment in Africa is compromised by the lack of economic and human resources; prevention strategies, such as the HBV birth dose vaccine, although recommended by the World Health Organization (WHO), are not implemented on a large scale
- There was a global, national, and international inertia that has started to change with the publication of WHO guidelines for HCV care and management in resource-limited countries that will be shortly be followed by guidelines on HBV. Those are critical in shaping health policies at a national and regional level
- Strategies for a global approach include the implementation of operational and research programmes, the improvement of screening and diagnosis tools, broader access to treatment and the integration of prevention, screening and care for viral hepatitis in local health care systems

Viral hepatitis in Africa: A silent and neglected killer

Burden of liver disease

In Africa, HBV and HCV infections are highly endemic and responsible for 80% of cirrhosis and HCC cases, with HBV being the main cause of end-stage liver disease [3,14,15]. HCC has been reported as the most common cancer in males, the second commonest in females and affects young individuals often below 40 years of age with a rapid and fatal outcome (Fig. 1) [3]. HCV is steadily becoming the second cause for HCC, enhanced by the widespread exposure to aflatoxin, a carcinogenic mycotoxin that contaminates staple crops in many African countries [16]. Accurate data in Africa on the burden of cirrhosis related to viral hepatitis are hampered by the lack of high-quality tools to assess chronic liver disease, inadequate disease surveillance, and poor resources for proper data collection and management. Recent estimates show that, with 1.4 million attributed deaths in 2010, viral hepatitis poses a greater threat to mortality than tuberculosis or malaria worldwide (Fig. 2) [17]. Naturally, HIV/AIDS, tuberculosis and malaria will remain major causes of death in Africa. However, in the case of HIV, a significant increase in life expectancy will likely follow after the widespread use of antiretroviral therapy (ART). Deaths related to viral hepatitis mays subsequently increase, concomitant to the expected decrease in AIDS-related deaths, particularly in co-infected patients, as observed in Western countries [18,19]. As a consequence, the gain in life expectancy, as experienced by HIV-infected patients, may at the end be hampered by the burden of liver disease [20]. Other causes of liver-related deaths, such as lifestyle-related factors (alcohol, non-fatty liver disease) may also enhance this risk. Furthermore, the Global Burden of Disease Study 2010 separated morbidity and mortality due to cirrhosis from that of liver cancer, although both outcomes may be caused by chronic viral hepatitis [17]. As a result, cirrhosis and liver cancer were ranked at number 12 and 16, respectively. Yet, if mortality and morbidity from cirrhosis and liver cancer were grouped together, viral hepatitis would rank within the top ten causes of global mortality (Fig. 2), above that of tuberculosis and malaria, which could possibly give liver diseases greater attention to health policy makers [21].

According to WHO, HBV infection affects more than 5% of the local population in Sub-Saharan Africa and more than 8% in West Africa, reaching up to 15% in some areas [22]. The transmission of the virus occurs early in life and is associated with a low rate of spontaneous viral clearance and a high risk of chronic liver disease. It is estimated that 25% of young adults, infected during childhood, will die prematurely from HBV-related cirrhosis or HCC [23]. The prevalence of HCV infection varies geographically with estimates between 3% and 5.3% [24]. However, updated epidemiological data on the burden of HCV infection using more accurate methodology are missing particularly in Sub-Saharan Africa. Egypt bears the highest prevalence worldwide with a recent estimation of 14.7% in subjects aged 15 to 59 years [25]. This epidemic was the result of nosocomial transmission following mass treatment of schistosomiasis with the injectable drug antimony potassium tartrate during the 1960s. East and Central African countries, such as Burundi, Cameroon and Gabon, are also highly endemic for HCV with a prevalence in some areas reaching 11%, 13%, and 5% in the three respective countries [24]. In HIV-infected individuals or other specific populations, such as drug users, sex workers, men who have sex with men, prisoners or patients with multiple transfusions secondary to sickle cell disease, estimates can even reach up to 50% [26,27]. The distribution of HCV genotypes in Africa also varies by sub-regions and is characterized by a considerable HCV subtype diversity. In West Africa, genotypes 1, 2, and 3 are predominant, whereas in Central Africa genotype 4 is more frequent. Genotype 5 is more specifically observed in Southern Africa [28].

Issues in prevention

HBV immunisation has been available since 1982 and has been shown to be highly effective in reducing the prevalence of hepatitis B surface antigen (HBsAg) in children worldwide [29]. Accordingly, national immunisation programmes have led to a substantial decrease in the burden of chronic liver disease and HCC in young adults born after 1984 [30,31]. With the support of WHO and the Global Alliance for Vaccine and Immunization (GAVI), most African countries have elected to vaccinate all children against HBV through the WHO-sponsored expanded programme of immunisation. However, HBV vaccine coverage remains low or incomplete (around 79% of vaccine coverage for Africa as a whole [32]). Furthermore, current recommendations from WHO-AFRO state that birth dose HBV vaccination should be given to prevent maternal-to-child vertical transmission and early horizontal transmission, yet its implementation has been lacking thus far [33]. This issue is critical, as over 90% of children infected with HBV early in life will become chronic carriers of the virus, adding to their risk of cirrhosis and HCC. WHO estimates that very few countries have implemented an HBV birth dose