

Personal view

Hepatitis B in Rwanda: Closing the gaps to end an epidemic

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Introduction

Hepatitis B virus (HBV) is a global scourge, affecting over two billion people worldwide, with 350 million active infections (Franco et al., 2012). While present all over the world, it disproportionately affects Africa; 60% of Africans are exposed across their lifetime, and 8% have active infection at any point in time (Howell, Lemoine, & Thursz, 2014). Despite the adoption of the World Health Assembly resolution 63.18 in 2010, which acknowledged HBV as a key global public health problem (*Viral hepatitis: WHA 63.18*, 2010), care of HBV patients remains fragmented across sub-Saharan Africa (SSA).

This article reviews the progress made in Rwanda within the wider health system context, and lays out key strategic foci for further action. We believe that the example of Rwanda is instructive, both because of the progress already made, and owing to the fact that the remaining gaps in the care are likely to be similar or greater across the Sub-Saharan region.

The Rwandan Healthcare Context

Rwanda has been a highly successful and prominent example of health system transformation over the last fifteen years, following the 1994 genocide. Major drops in childhood mortality and infectious diseases (Binagwaho et al., 2014), vastly improved insurance coverage and major international partnerships around clinical care and education have led Rwanda from a position where it was the furthest country in Sub-Saharan Africa (SSA) from meeting its millennium development goals, to its current reputation as the fastest-improving health system in Africa (Farmer et al., 2013).

In particular, a commitment to health access equity and system strengthening, combined with strong public health measures, have been instrumental in Rwanda's success. Vaccination has been a key strategic priority; vaccination rates against 9 key childhood illnesses, including hepatitis

B, have been universally implemented, with population coverage of greater than 90% (Rwanda Demographic and Health Survey 2010). The dramatic upsurge in HBV vaccination following this introduction will be expected to pay health dividends over many decades, with reductions in chronic HBV infections, cirrhosis and hepatocellular carcinoma.

Rwanda also has a rate of HBV that is intermediate by global standards but which would be considered low for the region; about 1.6% of blood donor units are HBV positive each year (almost certainly a moderate underestimate of true prevalence due to HBV negative repeat donors), while 2.9% of health care workers (HCWs) were positive in a recent screening study (Kateera et al., 2015; *Rwandan Biomedical Center Annual Report 2011-12*, 2013). This translates to at least 200,000 Rwandans living with hepatitis B, and about 50,000 of these (i.e. 25%) are likely to die from cirrhosis or hepatocellular carcinoma due to the infection (Franco et al., 2012).

Gaps in HBV Care

Key gaps remain in the care of HBV in Rwanda. Ongoing vertical (mother-to-child) transmission is the Achilles' heel of the Rwandan effort to contain and ultimately eradicate hepatitis B, but health care worker HBV infection, and availability of testing and treatment are also significant areas of concern.

Vertical transmission prevention and neonatal vaccination

As much as 50% of hepatitis B transmission is estimated to be vertical (Howell et al., 2014). However, detection of antenatal HBV is a particular problem in Rwanda, as, despite national guidelines recommending pregnant women as a key target group for screening, antenatal screening of infected mothers has unfortunately not yet been fully implemented ("National Guidelines for Prevention and Management of HIV, STIs & Other Blood Borne Infections," 2013). This in turn limits the effectiveness of

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neonatal HBV vaccination, which is routinely given at 6 weeks of age unless the mother is known to be HBV positive, in which case it needs to be given within 24 hours of birth, and combined with hepatitis B immunoglobulin, if maximal protection for the infant is to be achieved (Howell et al., 2014).

There is currently no HBV vertical transmission prevention program that is integrated in the health care system, in contrast with the HIV prevention-of-mother-to-child-transmission program, and this is a key strategic priority if HBV vertical transmission is to be tackled successfully. Such a program should involve screening of all pregnant mothers, provision of hepatitis B immunoglobulin and changes to the vaccination system to provide immediate vaccination *at birth* of all infants born to hepatitis B positive mothers.

HCW HBV infection

A key Rwandan achievement in HBV over the last few years has been the provision of HBV vaccination to all public system health care providers. However, private sector HCWs and ancillary staff working within health contexts (e.g. cleaners) have not yet been fully covered. While medical student HBV vaccination is now occurring routinely, newly recruited medical, nursing and laboratory staff are not always screened and immunised prior to starting clinical work. A policy and monitoring system needs to be developed which requires proof of HBV immunity status at recruitment.

A second issue is that some HCWs have been vaccinated for HBV without first being tested for hepatitis B surface antigen (HBsAg) positivity. This can provide false reassurance as HCWs may then believe they are protected, when in fact they are both at risk of HBV complications themselves, and also potentially infective to those who come into contact with them.

Availability of HBV testing and treatment

While testing is obviously vital to timely case identification for a largely silent disease like HBV, the availability of serological tests for HBV remains patchy in the Rwandan healthcare context. Some secondary and tertiary health care facilities have only intermittent reagent availability, and the testing platforms used vary between institutions, which fragments the supply chain for the critical reagents needed. Lessons here can be learned from the national transfusion service (CRTS) where similar tests are used daily to screen donated blood for HBV, often at sites co-located with these hospitals; the issue here is a logistic one and with sufficient attention to detail is clearly resolvable. There is a great need to decide which tests should be recommended to all health facilities, and

to arrange buying in bulk to ensure quality and reduce cost. No screening recommendations can be successfully implemented without wide spread availability of HBV serologic test results, and clinicians comfortable in interpreting them.

For those who are already infected with HBV, selecting cases for treatment and monitoring treatment success poses fresh challenges. HBV viral load testing, which is needed for treatment decisions, can now be done in the country, but few public hospitals can do the test and the high cost makes it inaccessible to many who need it most. Western HBV treatment algorithms are often very complex, and lead to many patients receiving long-term treatment without any clear endpoint. Policy leaders in Rwanda need to make a decision about whether this model of care best suits our resources at present, or whether more selective criteria should be delineated; the authors favour an approach where those whose prognosis can be significantly improved with time bounded therapy (patients entering an immunotolerant phase) and those at greatest risk of complications (patients with cirrhosis or advanced fibrosis, acute severe hepatitis B) receive priority for treatment. Clearly this should not preclude others receiving treatment if they so wish. The availability of subsidised drugs, particularly sole-agent tenofovir which has proven remarkable long-term effectiveness and low rates of resistance, needs to be improved for HBV patients.

Few doctors and nurses in Rwanda currently have the knowledge and clinical expertise required to manage HBV patients. There is a need for training and clinical experience in the use of HBV diagnostic tests and treatments. Care for HBV infected patients is now only available in referral hospitals, but clearly needs to be expanded to include provincial and district hospitals, and antenatal diagnosis for pregnant women needs to reach right to the health centre level.

Inspiration from the HIV story

HBV has never garnered the attention brought to bear on HIV, despite the ongoing global HBV epidemic. As a silent killer, often with a very long latency phase before clinical symptoms appear, and subject to sexual and bloodborne transmission, where treatment can result in altered prognosis but not cure, there are many parallels between the two epidemics. Although HIV has attracted far more resources than viral hepatitis to this point, much of the hard-won experience of fighting the HIV epidemic in Rwanda can be applied to treatment and control of hepatitis B.

Fighting the HIV epidemic has led to wider health system strengthening (Binagwaho et al., 2014; Farmer et al., 2013), with a particular emphasis on training of health care workers, raising awareness, infection control measures and universal availability of testing and treatment. All of this occurs in a decentralised care system with an evolution towards task shifting to more peripheral sites, under central supervision. The fight against HBV infection should take advantage of this and follow the same principles. Indeed, it may be possible to develop “HIV care centres” into “HIV and viral hepatitis care centres” with very little additional expenditure, once public awareness, appropriate additional testing and treatment resources, and sufficient public and HCW sensitisation has taken place.

HIV posed one of the gravest threats to health care in the region yet seen; the Rwandan experience in fighting the epidemic demonstrates what is also possible in combating HBV. HBV may pose less extreme challenges than HIV, especially due to the availability of a HBV vaccine. As a community, we have walked this road before with HIV, and can anticipate similar or greater success on our journey to HBV control in Rwanda.

Proposed solutions

The World Health Organization (WHO) has proposed a four-axis strategy for combating viral hepatitis, and we have adapted this framework in considering how the above gaps might be closed (“Global policy report on the prevention and control of viral hepatitis in WHO member states,” 2013).

Awareness-raising, Partnerships and Resource Mobilization

HBV has too long been a neglected disease in Africa and Asia, routinely thrown into the “too-hard basket.” Access to testing and treatment facilities reflects this reality; over 100,000 Rwandans are receiving HIV treatment, but less than 100 are on HBV treatment, despite seroprevalences that are likely similar at 2-3% (*Rwandan Biomedical Center Annual Report 2011-12*, 2013). International financial support through the Global Fund to fight AIDS, Tuberculosis and Malaria is routinely used to pay for HIV treatment; yet the same medications (lamivudine and tenofovir) remain out of reach of HBV patients, unless they are co-infected with HIV. This double standard, decreed by international funders focussed on HIV, needs to cease if HBV patients are to receive the care they deserve.

A concerted campaign needs to be undertaken by the Rwandan health care community, insurers and social, political and religious leaders, together with our international allies, to change this mindset, and overcome the access

and resource allocation issues that plague this disease. As a first step, the Rwanda Biomedical Centre has formed a Viral Hepatitis Working Group, comprising clinicians, public health experts and health care funders, to review policy and advocate change. World Hepatitis Day (July 28th each year) forms an international opportunity to bring public and media attention to bear on these diseases, and the disparities faced by HBV patients and those who care for them.

Evidence-based Policy and Data for Action

While data exists from the Rwandan blood bank and several small studies documenting HBV seroprevalence in various populations, we do not know currently in Rwanda if vertical transmission is the most important driver of the epidemic or if horizontal transmission still forms a significant component. Eventually, with the success of the national childhood HBV vaccination program, it can be anticipated that vertical transmission will be the predominant driver of new chronic infections, as (older, unvaccinated) adults have a much lower propensity to chronic infection following exposure than children.

We need to close this knowledge gap, with carefully conducted representative studies amongst the general population and perinatal women, and also to drive the policy focus of our efforts into the peripartum period. Again the parallels with the HIV epidemic are clear, and the experiences of the Prevention of Mother-to-Child Transmission (PMTCT) program for HIV can aid our HBV program design.

Prevention of Transmission

A HBV program aimed at the prevention of vertical transmission should be a central strategic focus of attempts to control hepatitis B in any high-prevalence country. Unfortunately, the current standard practice of giving combined childhood vaccinations at six weeks of age, while cost effective and simple, cannot prevent vertical transmission (Howell et al., 2014). We need to identify pregnant women with HBV antepartum, vaccinate all their exposed infants at birth, and work to ensure availability of hepatitis B immunoglobulin at all birthing centres.

Horizontal transmission prevention should be done through increasing the number of vaccinated young people. While the group 0-13 years is adequately covered by prior neonatal vaccination, those 14-30 year old, who are also at increased risk, are not. Careful thought and health economic analysis needs to be applied to this problem, once the necessary data on horizontal and vertical transmission is available, to determine the best use of our limited resources in controlling this epidemic.

Screening, Care and Treatment.

Pregnant women, sex workers, men who have sex with men, health care workers, relatives and those who live with HBV seropositive people are the obvious high-risk, high-reward groups that our screening program should first attempt to target. As socio-political institutions have accepted HIV testing as part of pre-nuptial processes, HBV should be added, taking advantage of the existing and well-functioning machine. Screening of relatives of a positive patient should be routine, as the high infectivity of HBV makes horizontal transmission a major threat.

Screening should be followed by treatment of the positive cases when indicated. Deciding who to treat is a complex issue, but, as discussed above, treatment should focus upon those with the most to gain from treatment (young adults entering an immunocompetent phase) and those with the most to lose from delays in treatment (those with advanced fibrosis and cirrhosis). Such an approach could not prevent every case of hepatocellular carcinoma in Rwanda, but can provide a cost-effective and appropriately targeted response to the HBV epidemic.

Conclusion

Rwanda has made great strides in public health policy and delivery in the last two decades, and the stories of HIV prevalence reduction and childhood vaccine delivery are two of its most prized successes. While the drive for vaccination has brought some success to the efforts to control HBV, much more needs to be done if the burden of this insidious virus upon the Rwandan community is to be halted. A multi-pronged approach, focussing upon case detection and vertical transmission prevention, then using advocacy and the example of HIV to leverage greater access to treatment, provides a real hope that this burden can be greatly reduced in the coming years and decades.

Disclosure

Although Drs Walker and Musabeyezu serve on the Rwanda Viral Hepatitis Working Group, this article represents their personal views and not those of any particular body or institution.

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