A new hepatitis B elimination strategy for remote populations is needed

Alice Lee,[a] David Hilmers,[b] and Thomas Russell[c,*]

[a]Department of Gastroenterology and Liver Services, Concord Repatriation General Hospital, University of Sydney, Australia
[b]Department of Internal Medicine and Pediatrics, Center for Space Medicine, Baylor College of Medicine, Houston, TX, USA
[c]Department of Internal Medicine, Tungaru Central Hospital, Ministry of Health and Medical Services, Tarawa, Kiribati

The Lancet Regional Health - Western Pacific 2024;48: 101129

Published Online xxx https://doi.org/10.1016/j.lanwpc.2024.101129

In 2016, WHO declared that hepatitis B (HBV) is a global public health threat with case finding, treatment and elimination targets set to be achieved by 2030.[1] Progress towards elimination is slow with only a marginal increase in hepatitis B case-finding from 9% to 10.3% from 2015 to 2019 and treatment coverage from 8 to 22.7%.[2] One barrier to progress is the lack of screening and linkage to care in isolated populations where geographic, economic, political, or social conditions may result in limited access to the medical care necessary to prevent, detect, treat, and eliminate HBV. Without addressing these inequities in high prevalence areas such as those found in Pacific Island countries and territories (PICTs), elimination goals cannot be met. Despite the presence of several HBV treatment guidelines and ongoing efforts for simplification, most require laboratory testing that is unavailable in remote regions. Nevertheless, offering all hepatitis B patients antiviral therapy remains controversial. With the availability of low-cost antivirals with few side effects, a test and treat approach provides patients living in remote, high-prevalence, resource-poor regions access to life-saving drugs.

The country of Kiribati demonstrates the potential of a true test and treat strategy. Survey data demonstrates that HBV is hyperendemic (~15% prevalence), over 40% are coinfected with hepatitis D and is a major disease burden.[3–5] Its remote "outer" islands have only rudimentary health services (Supplementary 1, 2) with limited laboratory and imaging facilities and are separated by thousands of miles of ocean. Current WHO guidelines are too restrictive to permit treatment of many eligible patients (Supplementary Fig. S1). A new paradigm is needed that eliminates the reliance on costly infrastructure. In 2019, our group initiated hepatitis treatment in South Tarawa, home to 50% of the country's population.[5] In 2022, a "test and treat" program was introduced in the outer islands (Supplementary 3, 4). The algorithm relies on rapid HBsAg point of care (POC) tests to screen the entire population of an outer island, usually 7000 or less (Supplementary 5, 6).

To date, 11 outer islands with a total of 5497 individuals have been screened with 867 positive tests (15.8%) (Supplementary Table S1). Notably, persons 24 years or younger accounted for one-third of positives. Highest rates were seen in the 30–34 age group with a prevalence of almost 30%. Patients are started on treatment without biochemical testing after the initial diagnosis utilising a simplified algorithm (Supplementary Fig. S2). All positive females older than 15 years are offered tenofovir alafenamide (TAF), which can be safely given without routine creatinine monitoring. This age was chosen to include all potential mothers. Those younger than 15 years will be followed until they reach this milestone and then offered treatment. Positive males are offered TAF at age 18 (Supplementary Fig. S2).

To our knowledge our initiative is the first program designed specifically for less accessible locations in PICTs and one of the few reported globally. A conceptual test and treat strategy in Thailand is described by Posuwan and colleagues whereby universal screening by local caregivers is recommended; however, referral to a regional center was required prior to treatment initiation.[6] In South Africa, Mokaya et al., analysed three treatment strategies for the prevention of HBV maternal-to-child transmission using a decision-analytic model and concluded: "… screening pregnant women and providing tenofovir for all who test HBsAg + may be a cost-effective strategy for South Africa and other low/middle income settings.[7]" Our approach would go one step further by treating all HBsAg positive women of childbearing age whether they are pregnant or not. This would eliminate the possibility that seropositive women who present late in their pregnancy or do not present at all give birth without prophylaxis.

A test and treat strategy can hasten HBV elimination in remote populations. Horizontal transmission is reduced through lowering viral load in those who are positive. Vertical transmission prevention is enhanced by ensuring that all HBsAg-positive females of childbearing age are treated during their pregnancy, a very effective intervention when coupled with birth dose HBV vaccination.[8] A simplistic algorithm such as this can be sustained by healthcare workers with a modicum of training, offer improved access to treatment and

*Corresponding author. 10 Rue Thomy Celieres, Noumea 98800, New Caledonia.
E-mail addresses: kirirussell@gmail.com (T. Russell), aliceulee@gmail.com (A. Lee), dhilmers@bcm.edu (D. Hilmers).

Challenges	Implications	Solutions
Adherence	Ineffective treatment; flares	Education; local champions
Stock out of medications	Patients without access to medications	Better estimates of future needs; order meds further in advance
Paucity of health care workers	Loss of expertise	More generous salaries
Funding	Lack of resources	Grant applications to multiple partners
Geographic separation	Difficulty reaching remote islands	Training HCW's to be self-sufficient
Record keeping	Inability to track patients	New Electronic Medical Records system (Tamanu)

Table 1: **Challenges, implications, and solutions.**

enhance adherence in remote communities (Supplementary Fig. S2). The strategy is likely to be controversial with notable challenges (Table 1), but the debate on its potential benefit can only be theoretical until it is implemented and studied. The simple truth is that HBV elimination using current guidelines is not achievable in remote locations such as the outer islands of Kiribati, and a new paradigm is needed. Despite its limitations, the strategy appears to be the most practical and cost-effective (Supplementary 7) solution to meeting elimination goals in resource-limited regions.

Contributors

AL conceptualised the study, analysed and interpreted the results, refined the original draft and provided overall supervision of the manuscript development. DH conceptualised the study, analysed and interpreted the results, and provided critical review and revision of the article. TR initiated the original draft, collected data and contributed to the final edits of the manuscript.

Data sharing statement

For data protection purposes, the data used in this manuscript will require the necessary permissions to be obtained directly from the Ministry of Health and Medical Services of Kiribati upon reasonable request.

Declaration of interests

The authors declare no conflict of interests.

Acknowledgements

We thank the National Hepatitis Program staff and allied healthcare workers in the outer islands for their contributions and dedication.

Funding: No funding was received for preparing this manuscript.

Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.lanwpc.2024.101129.

References

1 *Combatting hepatitis B and C to reach elimination by 2030.* Geneva, Switzerland: WHO Advocacy Brief; 2016.
2 Cui F, Blach S, Manzengo Mingiedi C, et al. Global reporting of progress towards elimination of hepatitis B and hepatitis C. *Lancet Gastroenterol Hepatol.* 2023;8(4):332–342. https://doi.org/10.1016/S2468-1253(22)00386-7. Epub 2023 Feb 8. PMID: 36764320.
3 World Health Organization Western Pacific Region. *Hepatitis B control country profile 2015;* 2016. http://www.wpro.who.int/immunization/documents/hepb_control_country_profile_2015/en/.
4 Jackson K, Tekoaua R, Holgate T, et al. Hepatitis B and D in the pacific islands of Kiribati. *J Clin Virol.* 2020;129:104527. https://doi.org/10.1016/j.jcv.2020.104527. Epub 2020 Jun 29. PMID: 32645613.
5 Lee AU, Jackson K, Tekoaua R, Lee C, Huntley MS, Hilmers DC. A programme to treat chronic hepatitis B in Kiribati: progress and challenges. *Western Pac Surveill Response J.* 2020;11(3):21–25. https://doi.org/10.5365/wpsar.2019.10.4.003. PMID: 33936856; PMCID: PMC8053900.
6 Posuwan N, Wanlapakorn N, Sintusek P, et al. Towards the elimination of viral hepatitis in Thailand by the year 2030. *J Virus Erad.* 2020;6(3):100003. https://doi.org/10.1016/j.jve.2020.100003. PMID: 33251021; PMCID: PMC7646674.
7 Mokaya J, Burn EAO, Tamandjou CR, et al. Modelling cost-effectiveness of tenofovir for prevention of mother to child transmission of hepatitis B virus (HBV) infection in South Africa. *BMC Public Health.* 2019;19(1):829. https://doi.org/10.1186/s12889-019-7095-4. PMID: 31242901; PMCID: PMC6595556.
8 Pan CQ, Duan Z, Dai E, et al. China study group for the mother-to-child transmission of hepatitis B. Tenofovir to prevent hepatitis B transmission in mothers with high viral load. *N Engl J Med.* 2016;374(24):2324–2334. https://doi.org/10.1056/NEJMoa1508660. PMID: 27305192.