POSTER REFERENCE NUMBER: 217

Improving Access to Care and Treatment of Viral Hepatitis in Kiribati

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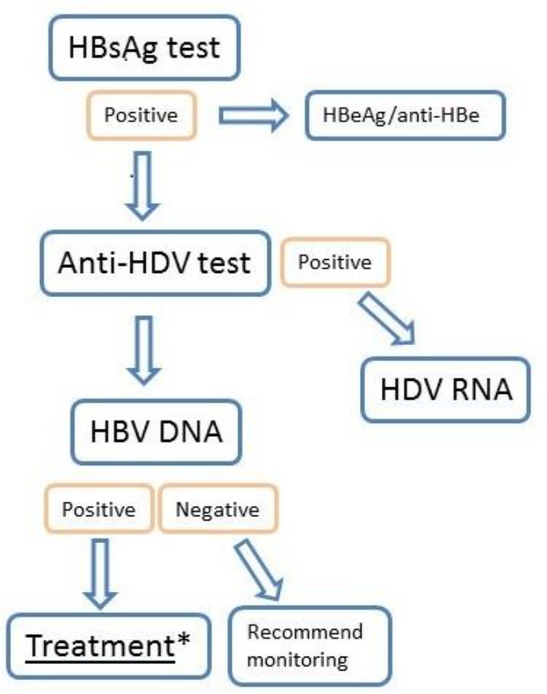
BACKGROUND

Hepatitis B is highly endemic in Kiribati, with previous studies and recent laboratory data indicating an adult HBsAg positive prevalence of at least 15% (1). Hepatitis B immunization was introduced into the routine schedule in 1989, however a serosurvey in 2014 showed childhood prevalence of 3.3% among 5 year olds. At present, data collection is limited and the treatment burden is unknown. Testing for staging of liver disease is unavailable, and medical care was confined to symptomatic treatment when patients present with liver-related complications of chronic hepatitis infection. However, access to HBV therapy has recently become available, with Tenofovir disoproxil fumarate (TDF) included on the National Essential Medicines list.

Hepatitis C prevalence in Kiribati is low and the prevalence of hepatitis A, D and E is unknown. A recent study testing samples from the 1990s indicated that HDV was highly endemic with 37% of HBsAg positive patients also HDV RNA positive (2). There is limited laboratory capacity in Kiribati, and the quality of refrigeration for sample storage is unreliable, with tests often referred to out of country laboratories.

This project consists of two objectives; a pilot study to identify patients with chronic hepatitis B infection who qualify for treatment, and to determine the current prevalence of hepatitis delta in HBsAg positive patients

Testing Procedure



* From the enrolled patients, a treatment cohort will be established according to the WHO criteria for HBV treatment.

METHODS

Implementation of this project is occurring at Tungaru Central Hospital (TCH), the national referral hospital. Patients are recruited through the general medical clinic, outpatient clinic, emergency unit and wards. There is currently no specific hepatitis clinic. Specific ethics approval for this project is not required as the samples are collected for clinical service provision.

Patients are enrolled prospectively, with HBsAg testing carried out by rapid diagnostic test (RDT) (Alere Determine, US) and ALT and APRI score testing being carried out in Kiribati. Serum samples from HBsAg positive patients are collected and transported to the Victorian Infectious Diseases Reference Laboratory (VIDRL) for confirmatory laboratory testing, including HBV serology (confirmation of HBsAg positive, HBeAg, anti-Hbe (LIAISON platform, Diasorin, Italy), HBV viral load (m2000 RealTime assay, Abbott, US), anti-HDV serology (EIA, Diasorin, Italy) and HDV RNA (VIDRL in-house protocol) if positive.

The planned enrolment is 1,000 HBsAg positive patients. In addition, matched dried blood spots (DBS) are being collected along with serum samples from 100 individuals. Separate DBS cards for serology and molecular testing will be analysed at VIDRL to determine if the DBS technology is a feasible method of sample collection in this setting.

A total of 96/104 samples were confirmed HBsAg positive, with 27/99 (27%) HBeAg positive. Samples from 7 patients were positive for both HBeAg and anti-HBe.

Hepatitis B Virus	N=104
Confirmed HBsAg positive	96
HBV Viral Load: (n=104) (>20,000IU/mL) (>2,000IU/mL)	 19 21
HBeAg: (n=99) HBeAg positive anti-HBe positive anti-HBe equivocal HBeAg & anti-HBe pos	 27 (27%) 76 (77%) 2 7

From the 96 confirmed HBsAg positive samples, 52 (54%) were positive for anti-HDV, with 36 (37.5%) positive for HDV RNA.

Hepatitis D Virus	N=96
Anti-HDV positive Anti-HDV negative	44 (46%) 52 (54%)
HDV RNA positive (LOD <375IU/mL)	36 (37.5%)

RESULTS

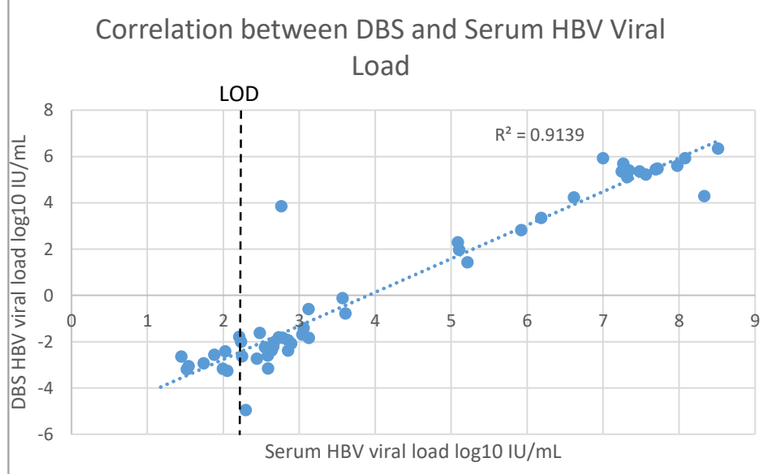
An implementation plan and timeline was developed by the Kiribati working group. An awareness and training meeting was held before sample collection was started to ensure all staff were aware of the study, with monthly follow up meetings planned for monitoring and evaluation of the project progress. A one day training workshop was also held to introduce staff to the collection, labelling and documentation guidelines recommended for the project. Sample collection commenced in March 2017.

To date, 104 serum samples have been received at VIDRL for confirmatory serology and molecular testing, as well as 100 matched DBS (both for serology and molecular testing).

Clinical Characteristics	N=104
Age (median, IQR)	29 (25-34)
Gender (%)	55 female (53%) 49 male (47%)
ALT (median, IQR) N=50	14 (9-21)

To date, testing the DBS for HBV viral load has been done for half of the samples received. HBsAg testing is in progress.

The lower limit of detection for HBV viral load from the DBS samples was determined to be 171 IU/mL.



CONCLUSIONS

This project is ongoing, with continuing sample collection in Kiribati, and further testing to be carried out at VIDRL in Australia. Due to technical reasons, APRI testing was not carried out for the initial patients. This testing will be important to assess patients for the presence of cirrhosis to identify those eligible for treatment. Negotiations are well advanced to provide HBV antiviral treatment for use in Kiribati.

The detected prevalence of HDV in the samples received is similar to that detected previously (37%). This is amongst the highest HDV prevalence rates worldwide.

Preliminary data suggests the HBV viral load determined from the DBS sample shows good correlation to the matched serum sample, the lower limit of detection for the DBS was 171 IU/mL. Analysis of further samples is ongoing to confirm the use of DBS in this setting.

This screening program will identify those with advanced hepatitis B related disease who qualify for treatment. By identifying and initiating treatment for those with advanced disease this study will help reduce the burden due to HBV infection in Kiribati.

REFERENCES

1. Wilson et al, 2000 Vaccine. 18:3059
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CONFLICTS OF INTEREST

S Locarnini has received consulting fees from Gilead Sciences Inc, Arrowhead Research Corp, Roche Molecular and Janssen (J&J), and research funding from Gilead Sciences Inc, Arrowhead Research Corp and Spring Bank Pharmaceuticals Inc.
All other authors declare that they have no conflicts of interest, and have not received any money or support from industry or pharmaceutical companies.

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MINISTRY OF HEALTH & MEDICAL SERVICES
Government of Kiribati

World Hepatitis Summit 2017
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