EVOLUTIONARY HISTORY OF HEPATITIS B VIRUS SUB-GENOTYPE D3 IN BOTSWANA

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Doreen Ditshwanelo[1,2], Wonderful T.Choga[2], Motswedi Anderson [3], Bonolo Phinius, Ontlametse T. Bareng, Rosemary Musonda, Sikhulile Moyo , Kebaneilwe Lebani, Simani Gaseitsiwe

1Botswana Harvard AIDS Institute Partnership Gaborone, Botswana; 2Department of Biological sciences and Biotechnology, Botswana International University of Science and Technology, Palapye, Botswana; 3Department of Medical Sciences, School of Allied Health Professions, University of Botswana, Gaborone, Botswana, 4Harvard T.H. Chan School of Public Health, Boston, MA, USA.

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BACKGROUND

- This study was conducted to describe the origins, introduction (time to Most common recent Ancestor (tMRCA), diversity and evolutionary patterns of HBV sub genotype D3 circulating in Botswana.
- Botswana has intermediate HBV prevalence rate of 2-7% with three subgenotypes (A1,D3 and E) reported at the following prevalence rates; 80%,18.6% and 1.4% respectively. The evolutionary history of all subgenotypes in Botswana remains unexplored. Such analysis aid in tracking disease evolution over time thus helping in theoretical HBV prevention and management.

METHODS

- **Study design**: Cross-sectional study utilizing (n = 154) HBV near-full length sequences.

Diversity analysis

- Non-recombinant, BW sequences (n = 24) were partitioned into 7 corresponding HBV ORFs using Babylon translator http://hvdr.bioinf.wits.ac.za/babylon

- Pairwise distances were calculated based on MEGA v.7.0.

Inter-diversities were represented using violin plots as implemented in R package v.4.0.1

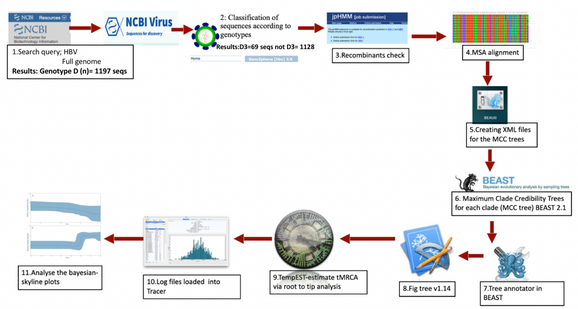


Fig 1. Phylogenetic analysis flow chart

RESULTS

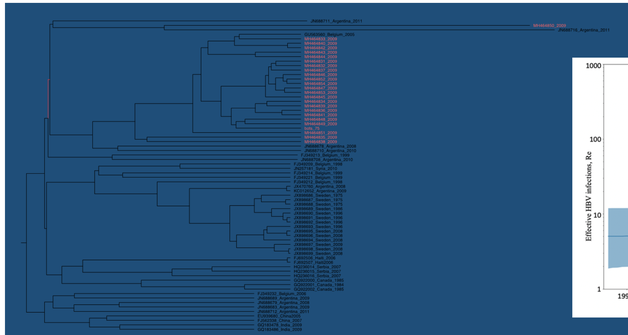


Fig 2. HBV/D3 Botswana (red) sequences related to the Argentina and Belgium isolates suggesting European and North American origin.

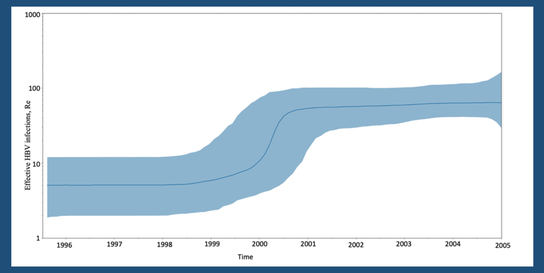


Fig 3. Bayesian skyline plot for HBV/D3 sequences showing an increase in the number of effective infections around the years 1999-2000

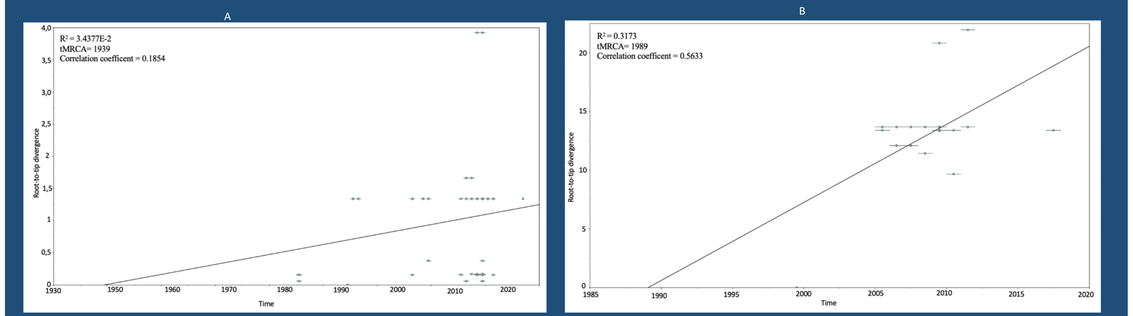


Fig 4. Root to tip regression estimating the tMRCA and the clock rates of the entire HBV sub-genotype D3 sequences(A) and D3 clade consisting most of Botswana sequences(B). Average tMRCA = 1939+1989/2= 1964

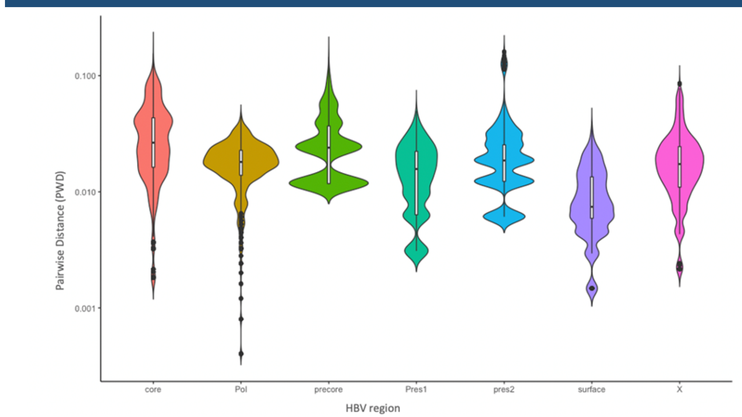


Fig 5. Violin plot showing nucleotide diversity of each HBV sub-genotype D3 ORFs. Core is the most diverse ORF (high median) while the surface ORF is the least diverse (lower median).

CONCLUSIONS

- First study to give insights of HBV/D3 evolutionary dynamics in Botswana aiding in theoretical HBV management and disease tracking.
- HBV/D3 sequences related to the Argentina and Belgium isolates suggesting European and North American origin.
- HBV sub-genotype D3 tMRCA dated back to 1964 with 95% highest posterior density range of 1939-1989.
- Increase in HBV/ D3 infections in Botswana population reported around years 1999-2000, which could be associated with reported HIV increase around the same years due to shared means of transmission.
- Nucleotide diversity of Botswana sequences revealed core as the most diverse ORF and the surface as the most conserved ORF.
- The study results confirmed that the surface region should continue to be the targeted region for vaccine developments.
- More studies with larger sample sizes recommended to address HBV evolution in Botswana to track disease evolution over time.

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Contact info: doreenditshwanelo@gmail.com