A clinical and molecular epidemiological survey of hepatitis C in Malawi suggests an historic mechanism of transmission

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1 INTRODUCTION

Hepatitis C virus (HCV) is a leading cause of liver disease worldwide. There are no previous representative community HCV prevalence studies from southern Africa (with the exception of island nations) and very limited genotypic data.[1-3] We addressed these research needs with representative community and hospital-based studies, to inform an effective public health response.

2 AIM

We aimed to estimate HCV prevalence and describe the molecular epidemiology among participants of a community serosurvey and among inpatients with cirrhosis or HCC in a tertiary hospital in Blantyre, Malawi

3 METHOD

We conducted a community census-based random sampling serological survey, and a hospital-based study of prospectively-enrolled patients with cirrhosis and hepatocellular carcinoma (HCC) in Blantyre, Malawi.

We tested participants with a 4th generation HCV antigen/antibody ELISA (Monolisa, Bio-Rad), confirmed with PCR (GeneXpert, Cepheid), used line immunoassay (Inno-LIA HCV, Fujiribio) for RNA-negative participants.

We did target-enrichment whole-genome HCV sequencing (NextSeq, Illumina).

4 RESULTS

COMMUNITY HCV EPIDEMIOLOGY

Among 96,386 censused individuals, we randomly selected 1661 people aged ≥16 years for HCV testing and sampled in participants' homes.

Population-standardised HCV RNA prevalence was 0.2% (95% CI 0.1–0.5).

PATIENTS WITH CIRRHOSIS AND HCC

Among 238 prospectively recruited hospital patients, HCV RNA prevalence was 1.9% in patients with cirrhosis and 5.0% with HCC.

ASSOCIATIONS WITH HCV INFECTION

Mapping showed that HCV RNA+ patients were from peri-urban areas surrounding Blantyre (Figure 1)

Community and hospital HCV RNA+ participants were **significantly older** than comparator HCV RNA negative populations **(median 53 vs 30 years for community**, p=0.01 **and 68 vs 40 years for hospital** patients, p<0.001). (Figure 2)

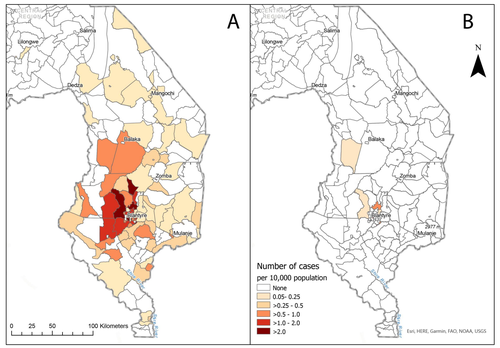

Figure 1 : Residence of patients with HCC and cirrhosis referred to Queen Elizabeth Central Hospital over an 18 month period, per 10,000 population A: HCV RNA negative patients B: HCV RNA positive patients

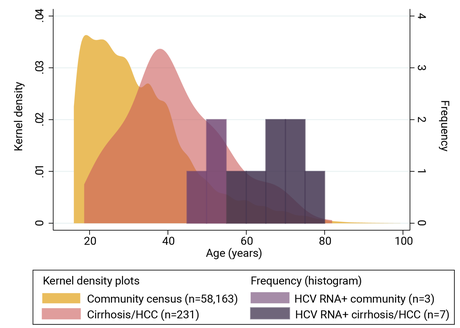

Figure 2 : Age distribution of patients with HCV infection from community and inpatients with cirrhosis and HCC (histograms), relative to control populations (density plots)

MOLECULAR EPIDEMIOLOGY

Endemic HCV genotypes from full length HCV sequencing were 4v (50%), 4r (30%) and 4w (10%). (Figure 3)

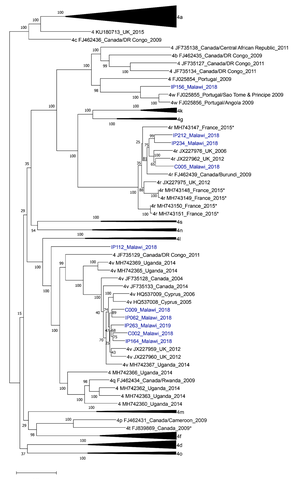

Figure :3 Maximum likelihood phylogenetic tree: full-length hepatitis C sequences from Malawi aligned to 117 genotype 4 full genome sequences

5 CONCLUSIONS

In the first representative census-based community serological study in southern Africa, HCV was uncommon in the general population, centred on **peri-urban areas**, and was **attributable for <5% of liver disease.**

HCV was observed **among older people**, suggesting an historic mechanism of transmission. Genotype **4r**, which has been associated with treatment failure with ledipasvir and daclatasvir, is endemic

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