

MOLECULAR EPIDEMIOLOGY OF HEPATITIS DELTA VIRUS IN OCEANIA

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Background: Hepatitis D or delta virus (HDV) is an incomplete RNA virus with a genome of around 1700nts that uses the hepatitis B virus (HBV) surface antigen (HBsAg) for entry and exit from the hepatocyte. Co-infection or super-infection of HBV with HDV usually results in more severe liver disease. With 8 genotypes recognized worldwide, HDV has an irregular geographical distribution. High prevalence areas include the Amazon Basin, Eastern and Mediterranean Europe, the Middle East and parts of Asia and Africa. Some Pacific Islands such as Kiribati also have a high seroprevalence of HDV and high viraemia rates. In Australia, the prevalence is relatively low but comparable with rates in the US and UK. The epidemiology of HDV infection in Australia appears to be shifting away from being predominantly associated with injecting drug use to being more commonly associated with migration from endemic areas. The aims of this study were to sequence/genotype isolates from Kiribati, as well as isolates from Australian patients collected over a 6 year period and perform phylogenetic analyses to assist in our understanding of the source and epidemiology of HDV.

Methods: Sera collected in 1998 from 184 HBsAg- positive Pacific Islanders living in Micronesia, Polynesia and Melanesia was tested for HDV RNA. 897 serum samples from 2009-2014 from Australian patients were also tested for HDV RNA. Genotyping and phylogenetic analysis using full or partial genome sequencing was performed on positive isolates. If available, patient country of birth was utilized to assist with epidemiological analysis.

Results: HDV RNA was detected in the sera of 20 of 54 patients with chronic hepatitis B from Kiribati (37%) but not detected in the sera of patients from Tonga (59), Fiji (42) and Vanuatu (29). Phylogenetic analysis revealed the Kiribati HDV isolates were genotype 1 and grouped with a previously published isolate from Nauru, forming a distinct clade of Pacific HDV.

Samples from 139 Australian patients also had detectable HDV RNA; 127 of these isolates were sequenced and genotyped. 105 isolates were genotype 1 (83%); 2 genotype 2; and 20 were genotype 5 (16%). Phylogenetic analysis of the Australian strains confirmed the transmission of HDV within two families and revealed that six strains from Queensland clustered with the Kiribati "Pacific clade". Phylogenetic analysis also identified an apparent association with region/country of birth for the remaining strains, particularly the genotype 5 isolates.

Conclusion: This study has confirmed endemic HDV infection in Micronesia and identified Kiribati as having amongst the highest prevalence of HDV viraemia in HBsAg-positive patients. This study also demonstrated the increasing proportion of HDV infections in Australia which were acquired overseas prior to migration. Of note, the prevalence of genotype 5 strains (predominantly found in African patients) is increasing in Australia, reflecting changing migration patterns. Understanding the genotypes and country of origin of HDV may play a role in the diagnosis and management of an infection that is poorly recognized.