

ABSTRACT:

HIGH-INTERMEDIATE ENDEMIC PREVALENCE OF HEPATITIS B VIRUS AMONGST FEBRILE PATIENTS IN BANGLADESH, INCLUDING EVIDENCE OF OCCULT INFECTION

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Introduction: With a combination of an intermediate hepatitis B virus (HBV) prevalence and a large population, Bangladesh has one of the highest burdens of viral hepatitis globally. Data on circulating genotypes remain limited, but both recombinant strains and occult infection have been previously reported in the region.

Aim: To assess the prevalence of HBV and occult HBV infection among febrile patients admitted to two medical facilities in Dhaka, including the Dhaka Medical College Hospital.

Methods: Any adult patients of ≥ 18 years with a history of fever $>38^{\circ}\text{C}$ for >48 hours admitted to the study sites between June-October 2017 were eligible to be enrolled. Blood samples were collected from patients and screened for HBV infection and previous HBV exposure, using HBsAg and anti-HBc respectively. All anti-HBc-positive patients were screened for HBV DNA to identify occult HBV infection. HBV positive patients with viral loads $\geq 3.0 \log_{10}$ IU/ml underwent a target-enrichment approach for HBV whole genome sequencing (WGS) on an Illumina Mi-Seq platform in Oxford.

Results: A total of 201 patients were recruited into the study. Exposure to HBV was common in the cohort, with 74/201 (37%) anti-HBc positive. HBsAg was present in 14/201 (7%). Additionally, 3/201 (1.5%) of the cohort were anti-HBc-positive, HBsAg-negative and HBV DNA-positive, indicating occult infection.

WGS for HBV was performed on four patients, including one patient with occult infection. A median of 60,997 HBV reads per sample and median coverage of 869 reads/site was obtained after de-duplication. Genotypes A (n=1), C (n=1) and D (n=2) were observed, with the occult infection being a genotype C isolate. None of the sequences identified were recombinants.

Conclusion: Our findings indicate a high-intermediate endemic prevalence of HBV in this setting. Occult HBV infection is present in the region, accounting for 3/17 (18%) of HBV infections. This is of relevance to clinicians assessing their patients, and is also important in informing approaches to screening blood products for transfusion. A diverse range of HBV genotypes are present in Bangladesh, and the detection of a genotype A strain supports studies suggesting that this genotype is increasingly common in Bangladesh.