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Short research communication

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Abstract

Background: Worldwide, 5–10% of people with chronic hepatitis B virus infection are co-infected with hepatitis D virus. In Qatar, there are no data on hepatitis D virus infection among patients positive for hepatitis B surface antigen (HBsAg).

Aims: To determine the seroprevalence of hepatitis D virus infection among patients with chronic hepatitis B virus infection in Qatar and assess the characteristics of these patients.

Methods: This was a retrospective cohort study of all HBsAg-positive individuals tested for hepatitis D virus between 1 January 2010 and 29 December 2019 within the Hamad Medical Corporation. Data were retrieved from electronic records and included demographic and clinical information of the patients.

Results: Of the 2348 HBsAg-positive patients, 125 were positive for hepatitis D virus (seroprevalence 5.3%). The median age of hepatitis D positive patients was significantly higher than for hepatitis D negative patients (P = 0.001). Most of the patients with hepatitis D had a hepatitis B viral load

Conclusions: Hepatitis D virus infection is associated with lower hepatitis B virus viraemia and more advanced liver disease in the study population.

Keywords: hepatitis D, hepatitis B, co-infection, surface antigen, viraemia, liver disease, Qatar

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Introduction

Hepatitis D virus is a hepatotropic virus with a circular ribonucleic acid (RNA) genome. This virus has at least eight genotypes, of which genotype 1 is the most frequent and is distributed worldwide (1). It uses the surface protein of hepatitis B virus as its coating, and hence, its replication and transmission are closely linked to those of the latter (2). In 2015, it was estimated that 257 million people were living with hepatitis B virus infection, defined as hepatitis B surface antigen (HBsAg) positive (3). At least 5% of those people are co-infected with

hepatitis D virus, meaning 15–20 million people are infected with hepatitis D virus worldwide (4). A meta-analysis in 2019 showed that hepatitis D virus seroprevalence was 10.58% suggesting more people are infected with this virus (5).

Most people with hepatitis D virus are in Africa, Asia, Eastern Europe, Greenland, Middle East, Pacific Islands and South America (4). People with chronic hepatitis B virus and hepatitis D virus infection have a twofold higher risk of developing cirrhosis, a threefold higher risk of developing hepatocellular carcinoma and a twofold increased mortality rate than individuals only infected with hepatitis B virus (monoinfection) (6,7).

Current guidelines generally recommend treatment with pegylated interferon-alpha for at least 48 weeks for chronic hepatitis D virus infection, irrespective of response patterns while on treatment. This is because the overall rate of sustained virological response is low. However, newer drugs with novel mechanisms of action against hepatitis D virus are more promising. The United States Food and Drug Administration has granted fast-track designation to lonafarnib, a hepatitis D virus prenylation inhibitor, in combination with ritonavir for treatment of hepatitis D virus infection after a phase IIa study showed a decrease in hepatitis D virus RNA during 4 weeks of treatment (8). Another study explored the optimal regimen of lonafarnib and showed that the addition of ritonavir allowed for a lower dose and higher concentration of lonafarnib with better tolerance (9). The European Commission approved the entry inhibitor bulevirtide (also called myrcludex B) as the first drug for chronic hepatitis D virus treatment. An open-label, phase IIb clinical trial assessed the safety and efficacy of bulevirtide in combination with tenofovir in patients with hepatitis B virus and hepatitis D virus co-infection (10). The study showed a dose-dependent decrease in hepatitis D virus RNA in parallel with a decrease in alanine aminotransferase (11).

In Qatar, screening of 78 428 blood donors between January 1994 and December 2001 found that 0.98% were HBsAg positive and 10.85% were hepatitis B core antibody (HBcAb) positive. Of 915 patients with chronic liver disease in Qatar, 2.5% were attributed to hepatitis B virus (12). However, data are lacking about the hepatitis D virus infection status among HBsAg-positive patients in the country.

This study estimated the seroprevalence of hepatitis D virus antibody among HBsAg carriers in Qatar and assessed the clinical, laboratory and virological characteristics of those positive for hepatitis D virus antibody.

Methods

Study setting, design and population

Hamad Medical Corporation comprises 12 hospitals and provides secondary and tertiary medical care for all the population of Qatar (2.8 million people). This was a retrospective, cohort study conducted in all Hamad Medical Corporation hospitals. The study population included all HBsAg-positive patients (older than 14 years) who were tested for hepatitis D virus antibodies (immunoglobulin G (IgG) and immunoglobulin M (IgM)) at the time of the study.

Study outcome and data collected

The primary outcome was the seroprevalence of hepatitis D virus infection among HBsAg-positive individuals in Qatar. Data were collected on the clinical, laboratory and radiological characteristics of those positive and negative for hepatitis D antibody.

Study procedures

The electronic laboratory system of Hamad Medical Corporation was used to identify HBsAg-positive patients who had also been tested for hepatitis D virus antibody between 1 January 2010 and 29 December 2019. Demographic and clinical data were extracted from all available electronic medical records of identified patients and transcribed into a standardized data collection sheet. Data extracted included: demographic information, hepatitis D virus antibody result, hepatitis D virus polymerase chain reaction (PCR) result, hepatitis B virus serology result, human immunodeficiency virus (HIV) status, abdominal ultrasound and ultrasound elastography results, aspartate aminotransferase (AST) to platelet ratio index score, and cirrhosis and hepatocellular carcinoma status.

Statistical analysis

Demographic and clinical characteristics of individuals who were hepatitis D virus-positive and hepatitis D virus-negative were compared. Continuous data were presented as medians (interquartile ranges [IQR]) and compared using the Wilcoxon rank-sum test. As appropriate, categorical data were summarized as numbers (percentages) and compared using the Fisher exact test or Pearson chi-squared test. Statistical analyses were performed using Stata, release 15 (StataCorp., College Station, TX, USA). A P-value ≤ 0.05 was considered statistically significant.

Ethical considerations

This retrospective chart review study involving human participants was conducted in accordance with the ethical standards of the institutional and national research committee and the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The Institutional Review Board at Hamad Medical Corporation approved the study with a waiver of

informed consent (MRC-01-19-519).

Results

Between 1 January 2010 and 29 December 2019, we found 2348 patients who were HBsAg positive and screened for hepatitis D virus antibodies; 125 of them tested positive for hepatitis D virus antibodies, giving a seroprevalence of 5.3%. Missing data were reported in the entire data set. Table 1 shows the demographic characteristics of the patients by hepatitis D virus infection. The median age of patients positive for hepatitis D virus was 38 years (IQR 32–49), significantly higher than the patients negative for hepatitis D virus, 35 years (IQR 29–45), P = 0.001. There were more males in both groups: 73.6% hepatitis D virus positive and 74.0% hepatitis D virus negative. The patients were categorized by WHO region. The majority of hepatitis D virus positive and hepatitis D virus negative individuals were from the WHO Eastern Mediterranean Region. Within this region significantly more patients were hepatitis D virus positive (80.8%) than the hepatitis D virus negative (61.8%), P