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Original Research

Current Condition of Chronic Hepatitis B Virus Infection in Cuban Adults

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ABSTRACT

Background: The reduction of the incidence of hepatitis B virus (HBV) infection in Cuba can be attributed to the effectiveness of the national immunization program. However, the number of patients with chronic HBV observed in clinical practice is not negligible.
Objective: A cross-sectional study was conducted to describe the main clinical characteristics of patients with chronic hepatitis B virus infection.
Methods: A total of 146 patients who had at least a 6-month history of hepatitis B surface antigen positivity were recruited between 2013 and 2015. Descriptive statistical analysis of the epidemiologic, clinical, biochemical, and virologic variables was performed.
Results: Men accounted for 67.8% of patients, and the median age was 43 years. The median time since diagnosis of infection was 9 years. Among the patients, 59% had chronic hepatitis, 34% had liver cirrhosis, and 7% were inactive carriers. Concomitant diagnoses demonstrated that 16.4% of patients had malignancies, predominantly lymphoma. Only 64.4% of patients had received antiviral treatment, and lamivudine was the most commonly used (61.6%) drug. Moreover, 70% of patients were identified during an inactive phase.
Conclusions: Patients with chronic HBV infection are still a health problem in the adult Cuban population, especially in patients with concomitant malignancies.

Introduction

The hepatitis B virus (HBV) is a major cause of morbidity and mortality. Approximately one-third of the world's population has serologic evidence of past or present HBV infection, and 350 to 400 million people are chronic HBV surface antigen (HBsAg) carriers.[1] In the most recent global epidemiologic reports on HBV, European guidelines have confirmed that there is a decreasing prevalence of this infection in most regions of the world. The slight decrease in its incidence and prevalence, particularly evident in central sub-Saharan Africa, tropical Latin America, central Latin America, Southeast Asia, and central Europe, may be the result of expanded immunization in the latest decades. However, the absolute number of HBsAg-positive persons increased from 223 million in 1990 to 240 million in 2005. This increasing overall number of individuals chronically infected with HBV and the widespread global differences in HBV prevalence is shocking. HBV infection prevalence data are needed at country and subnational levels to estimate disease burden to update the vaccination policy.[2]

In Cuba, HBV was an important health problem during the 1980s. The reporting of cases between the years 1989 and 2007 was variable, but the highest (20.3/100,000 habitants) was reported in 1992. The national immunization program against this virus in the population up to age 25 years and in high risk groups has resulted in a decline in the incidence and prevalence of this disease over the past 15 years.[3] Despite the significant reduction in the incidence of new infections, there are still important numbers of chronic cases observed in clinical practice. However, there is not enough epidemiologic data to accurately estimate the number of HBsAg-positive people in the country. It is known that this infection is among the causes of liver cirrhosis, a disease that ranks

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10th among the leading causes of death in Cuba.[4] This study was performed to identify the main epidemiologic and clinical characteristics of adult Cuban patients chronically infected with HBV.

Material and Methods

A prospective study was conducted at the National Institute of Gastroenterology, Havana, Cuba, between November 2013 and April 2015. The study was approved by the institution's ethics committee. Written informed consent was obtained from patients before enrollment in the study. A total of 1978 patients were admitted to the outpatient clinic during the period of the study. Of 150 patients recruited, 146 satisfied the inclusion criteria. The study included men and women who had had a positive serum surface antigen (ie, HBsAg) for more than 6 months. Exclusion criteria were other known chronic liver diseases, including autoimmune, metabolic, or hereditary diseases, as well as positivity for serological markers of human immunodeficiency virus or hepatitis C infection.

Variables collected in the study

Epidemiologic characteristics

Sex, age, origin (rural or urban), occupation, date of diagnosis of infection, smoking history, previous vaccination for HBV, concomitant diseases, and exposure to known risk factors were identified.

Virology

Reverse transcription polymerase chain reaction was used for the quantitative determination of viral load using commercially available kits (cobas AmpliPrep/cobas TaqMan/cobas TaqMan 48, Roche Diagnostics, Switzerland/U.S.). The lower limit of detection of HBV DNA was 20 IU/mL (2.0 E + 1 IU/mL), and the maximum was 1.70 E + 8 IU/mL. The HBsAg, HBV E antigen (HBeAg), and HBV E antibody (HBeAb) were measured with ELISAs.

Clinical

Definitive diagnosis of chronic hepatitis was determined by liver biopsy, liver cirrhosis (by a complete medical history), inactive carrier (normal transaminases, HBV DNA < 20,000 UI/mL, and normal or minimal inflammation histology), and the prior or concurrent use of antiviral treatments.

Liver biopsy

Histologic evaluation was performed using the METAVIR (Algorithm for Evaluation of Histological Activity) scale. Measurements of hepatic hardness in kilopascals (kPa) were made with the FibroScan Echosens 402, Paris, France (M probe; ultrasonic frequency 3.5 MHz) and expressed as degree of fibrosis (F) (reference values: F0–F1, < 7 kPa; F2, 7–8 kPa; F3 and F4, 8-10 kPa, and F5 > 10.5 kPa).

Phases of chronic HBV infection

- Immune phase: Immune tolerant (HBeAg-positive, normal transaminases, and HBV DNA > 20,000 IU/mL, mild or no liver necroinflammation, and mild or no fibrosis.
- Immunoreactive: Increased or fluctuating levels of transaminases and HBeAg-positive, HBV DNA < 20,000 IU/mL, moderate to severe activity of liver necroinflammation, and fibrosis.
- Nonreplicative or inactive carrier: At the 1-year follow-up visit (checked every 4 months), normal serum aminotransferases, normal histology, or minimal inflammation, HBeAg-negative, and HBeAb-positive. Serum HBV DNA levels undetectable or below 20,000 IU/mL.

Biochemical determinations were performed in the clinical laboratory of the Gastroenterology Institute using routine validated methods (Roche Hitachi 902 Chemistry Analyzer, Switzerland).

Statistical analysis

The variables were recorded and processed in a database created in the Statistical Package for Social Sciences for Windows version 21.0 (IBM-SPSS Inc, Armonk, New York). The medians, means, SDs, and frequencies were defined. The χ^2 test was used to assess the relationships between categorical variables. A P value of 0.05 was used to determine statistical significance. The estimated prevalence rate of each specific disease was determined as the number of patients with HBV/clinic population during the period × 100.

Results

HBV represented 8.5% among all liver diseases observed during the period of study. Men were more affected, and the median age was younger than 45 years. The HBV patients mostly lived in urban areas of the western region of Cuba. More than 80% of patients were professionals, and 6 of them (4.1%) were health workers, mainly nurses. Seven new patients were diagnosed during the study period, whereas 89 patients (61%) were diagnosed with chronic infection during the prior 10 years. There were 40 patients (27.3%) younger than age 35 years who were not immunized, and 10 of these patients were between ages 23 and 31 years who had a previous history of malignancies diagnosed during childhood or adolescence.

Malignancy was the most common concomitant disease: 9 patients had non-Hodgkin lymphoma, 5 had Hodgkin lymphoma, 3 patients had leukemia (2 had acute lymphoblastic leukemia and 1 patient had acute promyelocytic leukemia), and 2 patients had nervous system neoplasms (neuroblastoma and medulloblastoma). Other malignancies (adenocarcinomas) were reported, each them in a different patient: uterus, laryngeal, thyroid, prostate, colon, and malignant histiocytosis. Two patients with non-Hodgkin lymphoma also had other malignancies (**Table I**).

HBV infection was first detected in 74 patients (50.7%). Of these patients, 64 had chronic liver diseases, and 10 had acute hepatitis. Fifty-nine patients (40.4%) were identified by routine medical checkups for other comorbidities. In addition, 6 (4.1%) patients were infected perinatally and 4 (2.7%) were blood donors. Three patients (2.1%) were diagnosed during pregnancy. Ninety-four patients (64.4%) had received previous treatment, with lamivudine being the most common drug used in 90 patients (61.6%) followed by interferon in 31 patients (21.2%). Other treatments included adefovir in 15 patients (10.3%) and tenofovir in 11 patients (7.5%). Most patients had undergone more than 1 treatment since being diagnosed. The definitive diagnoses, differences in age, biochemical indicators, and virologic indicators are shown in **Table II**.

Most patients (71.2%) had low viral loads (< 20,000 IU/mL). Liver necroinflammation was observed in 85% of patients, whereas fibrosis was reported in 53% of patients. Coinciding with histology, the highest proportion of patients had mild or no fibrosis on liver elastography (**Table III**).

The majority of patients were in the nonreplicative phase (70%) with HBV DNA levels below 20,000 IU/mL, and 10 patients were inactive carriers with normal histology. Fifty-four patients had chronic hepatitis and 37 patients had liver cirrhosis. An additional 19.2% of patients (5 with cirrhosis and 23 with chronic hepatitis) were in an immune-tolerant phase, and 11.6% of patients (8 with cirrhosis and 9 with chronic hepatitis) were in an immunoreactive phase. Of the patients in an immunoreactive phase, 70% had received antiviral treatment.