CLINICS

RAPID COMMUNICATION

Clinical outcome of a patient cohort with acute hepatitis B

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INTRODUCTION

Viral hepatitis is a public health problem in Brazil and worldwide. According to the World Health Organization (WHO), 2 billion people have had contact with the hepatitis B virus (HBV); approximately 5% of these individuals are considered carriers (1).

The risk of chronicity after infection is 90% in the newborns of mothers with positive hepatitis B early antigen (HBeAg), 25 to 30% in children under 5 years of age, and less than 5% in adults (2). Chronic carriers have an increased risk (15 to 40%) of developing cirrhosis, hepatic decompensation, and hepatocellular carcinoma, resulting in 1 million deaths each year (3).

The most effective hepatitis B preventive measure is vaccination. Since 1998, a policy of universal vaccination has been implemented for children younger than 1 year in Brazil. The policy was subsequently extended to people younger than 20 years (4). Vaccination was also extended to vulnerable populations (e.g., injected drug users or healthcare workers) in 2001 and to people up to 29 years of age in 2010 (5). It is estimated that 75% of the under-29 population is vaccinated (6).

Because HBV carriers are the source of infection and chronic hepatitis B is a major cause of cirrhosis and hepatocellular carcinoma, it is important to understand the incidence, prevalence, and chronification associated with HBV infection (7).

The objective of this study was to describe the clinical outcomes of patients with confirmed acute hepatitis B (AHB) in the South region of Brazil in the city of Porto Alegre from 1999 to 2007.

PATIENTS AND METHODS

This retrospective-prospective cohort study was based on secondary data (retrospective data) obtained from the Information System for Notifiable Diseases (SINAN) and primary data collected from patients who completed structured and semi-structured questionnaires (prospective data).

No potential conflict of interest was reported.

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A case was defined as any individual reported to SINAN in Porto Alegre, a city of 1.5 million inhabitants, from January 1999 to December 2007, and who had positive HBsAg and positive immunoglobulin M antibody to the hepatitis B core antigen (anti-HBc IgM). The patients were contacted at their addresses and phone numbers, and the records of individuals whom we were unable to find were checked through the Mortality Information System or the Health Care Unit registers.

After signing informed consent forms, the patients answered questionnaires evaluating epidemiologic data, the risk factors for hepatitis B acquisition and their participation in consultation and preventive measurements (i.e., vaccination). They were asked to supply copies of laboratory tests performed at least 6 months after their AHB diagnoses. If no information could be obtained, serological tests were performed in a Public Health Service unit.

Patients were considered to have resolved hepatitis B if they had negative HBsAg and positive antibodies to the hepatitis B surface antigen (anti-HBs) after 6 months and, in cases of chronic carriers, if they presented with positive HBsAg in the same period (8).

To determine the number of coinfected patients, the authors examined notification forms with information related to coinfection with hepatitis C virus (HCV) and human immunodeficiency virus (HIV).

This study was approved by the Ethics Committee of the Universidade Federal de Ciências da Saúde de Porto Alegre.

In the statistical analysis, Pearson's Chi-squared test was used, with a 5% level of significance.

RESULTS

Between 1999 and 2007, 103 confirmed cases of AHB were reported to SINAN in Porto Alegre: 67 (65%) patients were male, and 77 (74.8%) were aged between 20 and 49 years.

Of the 103 eligible patients, it was possible to identify outcomes in 78 (75.7%) cases: 56 (71.8%) were considered resolved; 11 (14.1%) became chronic carriers; and 11 (14.1%) died. Four (36.4%) of the 11 deaths (5.1% of the 78 evaluated patients) resulted from fulminant hepatitis.

Hepatitis became chronic in patients older than 22 years: 8 of these patients (72.7%) were between 20- and 49-years-old, and 3 (27.3%) were over 50-years-old. The Caucasian race was prevalent, and female patients became chronic carriers more often than males.

Seventeen (16.5%) of the 103 reported patients had associated coinfections: 12 (70.6%) had HIV; 4 (23.5%) had HIV/HCV; and 1 (5.9%) had HCV. There was no association

Table 1 - Studies that have assessed the chronicity of acute hepatitis B in adult populations.

Reference	Author	N	Chronicity (%)	Assessed population
9	Barker	172	7.0	Prisoners
10	Beasley	37	2.7	Students: Taiwan
11	Ferraz	357	1.7	Acute hepatitis B: Brazil
12	Gimeno	63	0	Drug addicts
13	Hoofnagle	149	4.7	Prisoners
14	Kent	35	0	Acupuncture
15	Kuruuzum	240	4.6	Acute hepatitis B: Turkey
16	Lavarini	150	4.0	Acute hepatitis B: Italy
17	McMahon	48	10.4	Eskimos (Alaska)
18	Rinker	28	0	Women who received contaminated blood
19	Roumeliotou*	13	0	Women with heterosexual contact
20	Roumeliotou*			
21	Schomerus*	58	12.0	Acute hepatitis B: Germany
22	Wiedmann*			
19	Roumeliotou*	507	0.2	Acute hepatitis B: Greece
23	Tassopoulos*			
24	Tassopoulos*			
25	Wands	17	0	Oncologic staff

*Studies published on the same population. Only data from studies with the greatest number of individuals were considered.

between the type of coinfection and patient outcomes, chronicity, resolutions or deaths ($p = 0.747$). Two of the patients who became chronic carriers were coinfected, 1 with HIV and 1 with HIV/HCV.

DISCUSSION

Since the early 70s, several published studies have evaluated the chronicity of AHB in adult patients (Table 1) and shown an evolution to chronicity of up to 12% (9-25). A meta-analysis of 10 studies with adult heterogeneous populations, without adjusting for potential differences between them, showed that the risk of chronicity was higher than 10% in 2 studies, 5% in 1 and less than 5% in 7 (7).

Note that the chronicity in this study was high (14.1%) compared to the literature. This discrepancy could most likely be explained by the fact that the evolution to chronicity is inversely proportional to the age at which infection occurs (16). For example, some authors have reported that approximately 10% of patients who become infected with HBV as adults would not clear HBsAg after 6 months (21). As shown in our sample, all the patients were older than 22 years, which could justify a higher chronicity. Note that other studies have also observed high frequencies of chronicity (10,15,17). Several factors are associated with the increased risk of chronic HBV infection, including male gender, various causes of immune deficiency, genome variations, and genetic, hormonal and nutritional factors (7).

Differences in chronicity can also be explained by the manner in which it was calculated. In the present study, the evolution to chronicity was calculated based on patients who had complete follow-ups, similar to other studies (15,24). However, some authors did not specify whether there were losses in the follow-up (17) or if they calculated the progression to chronicity based on the total number of patients or only those with completed follow-ups (11). The results of the present study could be overestimated because some patients were lost to follow-up.

Regarding deaths, it is relevant that 5.1% of patients (4 of 78) died of causes related to fulminant hepatitis. Clearly, this result is most likely overestimated by the under-reporting of AHB.

Implementing the HBV vaccination over the last 30 years in several countries, such as the United States in 1981, Taiwan in 1984 and Brazil in 1998, has promoted a change in patient outcomes (13,18,26,27).

Of the AHB patients, 77 (74.8%) were aged between 20 and 49 years; this age range is not included in the National Immunization Program. Our findings suggest the importance of revising the inclusion criteria used in the vaccination schedule currently used in Brazil.

Regarding ethnicity, the Caucasian race was prevalent. Regarding gender, female patients were more likely to become chronic carriers, although this difference was not statistically significant. This result was not in alignment with other studies, which have reported a higher evolution to chronicity in male individuals (28,29,30).

Regarding the 17 coinfected patients, 12 (70.6%) had HIV, 4 had HIV/HCV, and 1 had HCV. HBV/HIV coinfection occurs in many patients, and it is explained by the common routes of transmission for these 2 viruses, primarily sexual, parenteral and vertical (31). A study conducted in Porto Alegre involving 587 HIV patients showed that 14 of 306 (4.6%) had positive HBsAg (32).

Note that 2 patients who became chronic carriers were coinfected. Literature reports suggest that worse outcomes are more frequent in coinfected patients (33).

The abovementioned results suggest the utmost importance of control measures and epidemiological assessments of HBV patients because in the evaluated population, there were high levels of chronicity and mortality related to liver injury. Effective actions, such as universal vaccination, break the transmission chain of HBV. The appropriate follow-up of patients and their contacts (home and/or sexual) is essential for improving the well-being of our population.

AUTHOR CONTRIBUTIONS

Souza LA was responsible for all the phases of the study from conception to the manuscript draft. Mattos AA was responsible for the general coordination of the study, draft and critical review of the manuscript. Fiorini M and Ribeiro P were responsible for collecting the data and organizing the database. Tovo CV participated in drafting and critical review of the manuscript.

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