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Acute Viral Hepatitis A, B and Non-A, Non-B in Stockholm in the 1950s and 1970s: A Comparison

**Summary:** The incidence of hepatitis types A (HA), B (HB) and Non-A, Non-B (NANB) and their epidemiology were studied in all patients admitted to the Roslagstull Hospital for acute viral hepatitis during five consecutive months in 1953-54 (Group I). This was before i.v. drug addiction had been encountered in Stockholm, Sweden. The results were compared with the findings in patients with acute viral hepatitis admitted during six consecutive months in 1970 (Group II) and during 13 consecutive months in 1977-78 (Group III), when i.v. drug addiction had become prevalent in Stockholm. Sera from all patients were tested for antibodies against hepatitis A virus (anti-HAV), for hepatitis B surface antigen (HBsAg) and the corresponding antibody (anti-HBs), and for antibody against hepatitis B core antigen (anti-HBc) using radioimmunoassay techniques (RIA) (HAVAB, AUSRIA II, AUSAB, and CORAB, Abbott Laboratories). HAVAB-positive sera were tested for anti-HAV-IgG and anti-HAV-IgM by a solid phase RIA. Hepatitis A was diagnosed in 31% (20/64), 28% (42/151), and 30% (84/277) in Groups I, II, and III, respectively. Hepatitis B was diagnosed in 55% (35/64), 62% (93/151) and 47% (129/277) in Groups I, II, and III, respectively. By excluding infections with HA and HB viruses, cytomegalovirus, and Epstein-Barr virus, NANB was diagnosed in 14% (9/64), 10% (15/151), and 23% (63/277) in Groups I, II, and III, respectively. HB dominated both before and after i.v. drug addiction had become prevalent. The relative number of HA cases was constant, irrespective of the year under investigation. NANB existed as early as the 1950s, and if i.v. drug addicts were excluded, the relative number of these infections was found to be constant, i.e. 14% and 14.8% in 1953-54 and 1977-78, respectively. I.v. drug addiction was found to have changed the epidemiological situation by decreasing the mean age of hepatitis patients, by increasing the male preponderance of HB and NANB patients, and by increasing the relative number of NANB cases.


Received: 23 March 1981

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Introduction

Reliable serological techniques are now in general use for the diagnosis of hepatitis A (HA) and hepatitis B (HB). Using serological means to exclude HA und HB as well as cytomegalovirus (CMV) and Epstein-Barr virus (EBV), which are rarer causes of hepatitis, a third form of acute viral hepatitis, called hepatitis Non-A, Non-B (NANB), has been recognized (1, 2, 3, 4, 5, 6).

In the 1970s most cases of sporadic acute viral hepatitis were shown to be HB in the United States, in Central Europe, and in Scandinavia (1, 2, 3, 4, 5) whereas most were HA in Australia (6). NANB accounted for 10-25% of the sporadic cases (1, 2, 3, 4, 5, 6). Epidemiologically, sporadic HA has often been associated with trips to endemic areas (7) and sporadic HB and NANB with parenteral routes of transmission (8). By testing sera stored since the 1950s, Hoofnagle et al. (9) showed that parenterally transmitted NANB existed in the U.S. at that time. NANB has also been implicated as an epidemic agent in the mid 1960s and has been an increasing problem ever since (13).

Up until now no Swedish study has been published comparing the epidemiology and relative number of HA, HB, and NANB in patients with acute viral hepatitis before and after i. v. drug addiction had become prevalent. Hence, the following study was undertaken in patients with acute viral hepatitis who were admitted to the Roslagstull Hospital in the 1950s and 1970s.

Patients and Methods

Patients: Our data consisted of clinical, epidemiological and laboratory findings from three groups of patients with acute viral hepatitis who were treated at the Roslagstull Hospital for infectious diseases. All patients were from the Stockholm region. Group I consisted of 64 patients hospitalized sometime between October 1953 and February 1954, and Group II of 150 patients hospitalized sometime between January and June 1970. Serum specimens stored at -20°C were available from these patients. Group III consisted of 277 inpatients and outpatients who were studied prospectively from September 1977 to October 1978. This group has been described in detail elsewhere (5).

Methods: Sera from all the patients were analysed by routine biochemical tests – either Meulengracht's reaction, thymol turbidity and Takata (Group I), or serum-bilirubin, serum-aspartate aminotransferase, S-ALAT, and serum-alkaline phosphatase (Groups II and III). The acute-phase serum and one or more convalescent-phase sera from each patient were tested for antibody against hepatitis A virus (anti-HAV) (in Groups I and II acute-phase sera only) and for hepatitis B surface antigen (HBsAg), the corresponding antibody (anti-HBs) and antibody against hepatitis B core antigen (anti-HBc) using the available radioimmunoassay (RIA) techniques (HAVAB, AUSRIA II, AUSAB, and CORAB, Abbott Laboratories, North Chicago, Ill., USA) according to the manufacturer's instructions. Sera from patients in Groups I and II were tested with AUSRIA II only if they had been found negative for HBsAg in an immunodiffusion (ID) test (14) performed earlier. HAVAB-positive sera were titrated for anti-HAV of the IgG and IgM classes using a solid-phase RIA technique as described elsewhere (15). Sera positive for HBsAg in RIA were tested by ID (16) for verification. If too weak for ID, a positive AUSRIA II was verified in a confirmatory test (Abbott Laboratories). All sera which were ID-positive for HBsAg were subtyped, as reported in part elsewhere (14). All HBsAg-positive sera were also tested for hepatitis B e-antigen (HBeAg) and the corresponding antibody (anti-HBe) using an ID test (17). Sera from patients lacking both anti-HAV of the IgM class and HBsAg, and not positive for anti-HBe only were also tested for antibodies against CMV and EBV; the same applied to sera from two known HBsAg-carriers in Group III. A complement fixation test (18) for CMV (Group III), including late convalescent-phase sera, or an indirect immunofluorescence test (IF) for antibodies of the IgM class against CMV (19) (Groups I and II) was performed. These sera were also tested for heterophil antibodies using the Monospot reaction (Ortho Diagnostics, New Jersey, USA) and the Paul-Bunnell-Davidsohn reaction (20) (Group III), or by IF for antibodies of the IgM class against EBV (21) (Groups I and II).

Statistical analyses were made with the chi-square test using Yates's correction.

Diagnostic criteria have been published in detail elsewhere (5). Briefly, patients with anti-HAV of the IgM class in the acute-phase sera were considered to have HA; patients with HBsAg and/or anti-HBc without anti-HBs in the acute-phase sera were considered to have HB. Patients with no serological evidence of acute HA, HB, CMV and EBV infections and no evidence of alcohol abuse or medication with hepatotoxic drugs, but with an S-ALAT at least five times the upper normal limit (a criterion not valid for Group I since this test was not available in 1953-54) were classified as having NANB.

Results

The incidence of HA cases (Table 1) was similar (28-31%) in the three groups studied, whereas the relative number of HB cases was lower in Group III than in Groups I and II. The serological evidence for the diagnosis of acute HB is given in Table 2. Of the HB patients, 94-98% were diagnosed due to the presence of HBsAg, and 2-6% due to anti-HBc as the only HB marker in the acute-phase serum. In Group II there were 151 episodes of acute viral hepatitis in 150 patients. A 9-year-old girl who had HA followed by HB and another patient had HA and HB simultaneously, with anti-HAV of the IgM class and anti-HBc, as well as HBsAg in his acute-phase serum only. In Group III there were 277 hepatitis episodes classified as HA, HB or NANB in 273 patients. One patient had HA and HB simultaneously, and four patients had two consecutive episodes of acute viral hepatitis at least six months apart. As can be seen in Table 1, the overall male/female ratio increased from 1.1 in 1953-54 to 1.8 in 1977-78; the overall mean age decreased from 38 years in 1953-54 to 31 years in 1977-78. However, when the mean age and age range for i. v. drug addicts in...