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Acute Sporadic Hepatitis in Sudanese Children

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Eighty consecutive cases of acute viral hepatitis and 80 controls selected from a public pediatric clinic were entered into a study of acute sporadic hepatitis in Khartoum, Sudan. Study subjects were 14 years of age or younger and were mainly from a low socioeconomic level. Non-A, non-B hepatitis was diagnosed by exclusion in 35 (43.8%) patients, hepatitis A in 27 (33.8%), acute hepatitis B in 8 (10.0%), possible Epstein-Barr virus (EBV) hepatitis in 1 patient; and dual hepatitis A and B infection in 1 patient. Eight acute cases were positive for HBsAg but negative for anti-HBc IgM and anti-HAV IgM. Delta hepatitis was not identified in any study subject. A household case of jaundice and acquaintance with an individual outside of the household with jaundice during the prior 6 months were associated with non-A, non-B hepatitis. There was no association between parenteral exposure and non-A, non-B hepatitis. These findings suggest that enterically transmitted non-A, non-B hepatitis may be a major cause of acute sporadic hepatitis in children in this area, as well as a cause of epidemic hepatitis.

KEY WORDS: Epstein-Barr virus, jaundice, enteric transmission

INTRODUCTION

The importance of non-A, non-B hepatitis as a cause of acute sporadic hepatitis in developing countries is not well understood, although numerous outbreaks of non-A, non-B hepatitis associated with contaminated drinking water have been reported [Byskov et al., 1989; Gust and Purcell, 1987; Kane et al., 1984; Khuroo, 1980; Wong et al., 1980; Zakaria et al., 1988]. In Sudan, non-A, non-B hepatitis has been found to be a major cause of sporadic hepatitis in adults, and an outbreak of enterically transmitted non-A, non-B hepatitis has been described in a refugee camp [Al-Arabi et al., 1987; CDC, 1987a]. In the present study, the causes and risk factors of acute sporadic hepatitis in Sudanese children were investigated.

PATIENTS AND METHODS

The study was conducted at the Pediatric Outpatient Clinic of the Khartoum University Teaching Hospital, Khartoum, Sudan. Children 14 years of age or younger presenting with acute clinical jaundice of not more than 1 month's duration were consecutively entered into the study as cases. A control group of subjects was selected at the same time from patients presenting to the pediatric clinic with medical complaints but without evidence of liver pathology. One control subject was matched with each case by sex, age (within 1 year of the case), and admission date (within 1 week of case admission). It was not possible to follow patients after discharge from the hospital.

The parents of nearly all study subjects were urban laborers from a low socioeconomic level and were living in Khartoum or Omdurman, Sudan. Informed consent was obtained from the parents of all study participants.

An epidemiologic questionnaire was completed for each study subject. Along with basic demographic data, the parents of study subjects were asked about exposure to potential risk factors of hepatitis transmission during the 6 months prior to the onset of symptoms. The number of people actually living in a study subject's home and the number of major rooms in the home were recorded to determine whether crowding was a factor in hepatitis transmission [Hyams et al., 1989].

An acute serum sample was drawn from each study participant upon entry into the study. Sera were tested for the presence of serologic markers of acute hepatitis A (anti-HAV IgM) and hepatitis B (anti-HBc IgM) using commercial ELISA test kits (Abbott Laboratories, North Chicago, IL). HBsAg-positive and anti-HBc-IgM-positive samples were additionally tested for anti-delta antibody, and HBsAg-negative samples were tested for anti-HBs (Abbott). Sera samples were also tested for heterophile antibody (Trend Kit IM, V-Tech, Inc., Pomona, CA) and anti-CMV IgM (Enzygnost, Hoechst, Behringwerke AG, Marburg, Germany). Sera were not tested with the newly developed hepatitis C ELISA assay because it was not possible to follow study

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subjects for extended periods to detect seroconversion to hepatitis C antibody [Alter et al., 1989].

Along with serologic tests, serum samples were analyzed for aspartate aminotransferase (AST), alanine aminotransferase (ALT), and total serum bilirubin by standard methods. Only patients with AST and ALT levels greater than two and one-half times the upper limit of normal were considered cases of acute hepatitis. Patients with evidence of surgical or toxic liver pathology were excluded from the study.

Comparisons of proportions were done using the χ^2 test with Yates' correction or the Fisher's exact test. Mean values (reported as ± 1 SD) were analyzed using the Student's t test.

RESULTS

Eighty cases and 80 controls were entered into the study from January 1987 to May 1988. Sixty-seven percent of cases were male. The mean age of cases (6.1 ± 3.4 years; range, 1–14 years) was similar to control study subjects (6.3 ± 3.6 years; range, 1–14 years). Cases had been ill with jaundice for a mean of 6.3 days (range, 1–25 days).

Based on serologic test results (Table I), hepatitis A was diagnosed in 27 (33.8%) acute cases, hepatitis B in 8 (10%) patients positive for anti-HBc IgM, possible Epstein-Barr virus (EBV) hepatitis in 1 (1.3%) patient and dual hepatitis A and B infection in 1 patient. Eight acute cases were positive for HBsAg but negative for anti-HBc IgM and anti-HAV IgM, indicating reactivation of chronic hepatitis B or chronic hepatitis B with superimposed non-A, non-B hepatitis. By exclusion, non-A, non-B hepatitis was diagnosed in 35 (43.8%) patients.

None of the cases or controls was positive for anti-cytomegalovirus IgM. No control study subject was positive for anti-HBc IgM or heterophile antibody, but three controls were positive for anti-HAV IgM. HBsAg was found in 7.5% of controls and in 27.5% of cases. One control, one hepatitis B case, and five hepatitis non-A, non-B cases had a previous history of acute jaundice.

The sex, number of people living at home, and the number of major rooms in the home were similar for controls and cases of hepatitis A, B, and non-A, non-B. Acute hepatitis A patients tended to be younger (mean, 4.1 ± 2.8 years) than other cases of hepatitis (mean, 7.1 ± 3.3 years). It is noteworthy that a higher percentage of acute hepatitis cases (including hepatitis A and non-A, non-B) reported the presence of running water (59%) and electricity (66%) in their homes than did controls (33% and 44%, respectively).

Analysis of hepatitis non-A, non-B cases for potential transmission risk factors indicated that a household case of jaundice and acquaintance with a case of jaundice outside the household was more common in cases of non-A, non-B hepatitis than in controls (Table II). The occurrence during the prior 6 months of parenteral risk factors of infection (transfusion, hospitalization, medical injection, dental care) were no more common in cases of hepatitis non-A, non-B than in controls. When hepatitis A cases were evaluated, acquaintance with a case of jaundice outside the household was more common in hepatitis A cases than in controls (Table II). Too few patients had acute hepatitis B to make meaningful comparisons of risk factors. There was no relation between the occurrence of risk factors of transmission and the age and sex of study subjects.

There was no significant difference between the various types of hepatitis and presenting complaints or physical findings. One acute hepatitis B case and two HBsAg-positive/anti-HBC-IgM-negative cases were known to have died. Higher AST, ALT, and total bilirubin levels were found in hepatitis non-A, non-B cases compared with hepatitis A and hepatitis B, but the differences were not statistically significant (Table III).

DISCUSSION

Non-A, non-B hepatitis was found to be the most common cause of acute sporadic hepatitis in this pediatric population living in an urban area of Sudan. In a previous study of adults in Omdurman, Sudan, non-A, non-B hepatitis was also found to be the most frequent cause of acute hepatitis [Al-Arabi et al., 1987]. The additional finding in this study that hepatitis A was a major cause of acute hepatitis in children is consistent

TABLE I. Number of Study Subjects With Positive Serologic Markers of Viral Hepatitis Infection

Marker	Control (n = 80)	Hepatitis class: A (n = 27)	Non-A, non-B (n = 35)	Acute B (n = 8)	Chronic B[a] (n = 8)	Dual A/B (n = 1)	EBV (n = 1)
Anti-HAV IgM	3	27	0	0	0	1	0
Anti-HBc IgM	0	0	0	8	0	1	0
HBsAg	6	8	0	6	8	0	0
Anti-delta	0			0	0	0	
Anti-HBs	5	2	5	3	0	0	0
Heterophile antibody	0	0	0	0	0	0	1
Anti-CMV IgM	0	0	0	0	0	0	0

[a]HBsAg-positive/anti-HBc-IgM-negative.

TABLE II. Number of Study Subjects With Risk Factors for Hepatitis Transmission Among Controls and Acute Hepatitis A, Non-A, Non-B, and Hepatitis B Cases

Risk factor (%)	Control (n = 80)	Hepatitis A (n = 27)	Non-A, non-B (n = 35)	Hepatitis B (n = 8)
Contact with jaundiced				
Family member	3 (4)	2 (7)	5 (14)**	3 (38)
Non-household person	7 (9)	6 (22)*	9 (26)***	2 (25)
Parenteral risk factors				
Medical injection	26 (33)	7 (26)	2 (6)	4 (50)
Transfusion	1 (1)	0 (0)	1 (3)	0 (0)
Hospitalization	11 (14)	2 (7)	1 (3)	0 (0)
Dental care	0 (0)	0 (0)	0 (0)	1 (13)

*P = 0.13, hepatitis A compared with controls.
**P = 0.05, hepatitis non-A, non-B compared with controls.
***P = 0.04, hepatitis non-A, non-B compared with controls.

TABLE III. Comparison of Mean Values of Biochemical Tests Among Cases of Acute Hepatitis A, Non-A, Non-B, and Hepatitis B*

Test (mean + SD)	Hepatitis A (n = 27)	Non-A, non-B (n = 35)	Hepatitis B (n = 8)
AST (IU/liter)	754.2 ± 663.9	955.0 ± 715.3	641.8 ± 459.1
ALT (IU/liter)	583.0 ± 397.9	733.2 ± 534.8	415.0 ± 223.8
Total serum bilirubin (mg/dl)	5.7 ± 4.6	7.2 ± 5.0	6.3 ± 3.2

*$P > 0.05$, non-A, non-B hepatitis compared with hepatitis A and B for all tests.

with previous studies of pediatric hepatitis [Dienstag et al., 1978].

Non-A, non-B hepatitis was not associated in this study of pediatric hepatitis with parenteral exposure. The previous study of adult hepatitis in Sudan also found no increase in parenteral risk factors among cases of non-A, non-B hepatitis [Al-Arabi et al., 1987]. These findings suggest that enterically transmitted non-A, non-B hepatitis may be the most frequent cause of acute sporadic hepatitis in all age groups in this area, although the possibility of sexual transmission in adults has yet to be studied.

The association between non-A, non-B hepatitis and acquaintance with another case of jaundice outside the household is suggestive of shared exposure to a common source of infection, like contaminated water, as in epidemic non-A, non-B hepatitis. Because contact with a jaundiced household member was also associated with non-A, non-B hepatitis, person-to-person transmission may be a factor as well [CDC, 1987b].

Previous reports have indicated that both epidemic and sporadic non-A, non-B hepatitis are common in nearby countries, and an outbreak of non-A, non-B hepatitis has been described in Sudan [Bassily et al., 1986; CDC, 1987a; Belabbes et al., 1985; Khuroo et al., 1983; Molinie et al., 1988; Nouasria et al., 1984; Shamma's, 1984; Zakaria et al., 1988]. However, enterically transmitted non-A, non-B hepatitis has been noted to have a lower attack rate in children than in adults [CDC, 1987a,b; Khuroo, 1980; Belabbes et al., 1985].

Delta hepatitis was not found to be a cause of acute hepatitis in this pediatric population, although it was diagnosed in 13% of adult hepatitis cases in a previous study [Al-Arabi et al., 1987]. Finding few acute cases of delta hepatitis in this population endemic for this infection could have resulted either from a low level of transmission in children or from an unknown bias in the selection of patients. There was no evidence, however, of sampling bias in this study except for a higher percentage of male cases compared with female cases, which may have resulted from differential utilization of health services, as previously noted [Al-Arabi et al., 1987].

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