

Hepatitis A and Indian childhood cirrhosis

S. S. AGARWAL, U. C. LAHORI, S. K. MEHTA, P. C. BAJPAI, B. WERNER, AND D. W. BRADLEY

King George's Medical College, Lucknow, India, Institute for Cancer Research, Philadelphia, USA, and Hepatitis Laboratories Division of Bureau of Epidemiology, Phoenix, Arizona, USA

SUMMARY Antibody to hepatitis A virus (anti-HAV) was found in 50% of patients with Indian childhood cirrhosis; this was not significantly different from the prevalence of anti-HAV in age- and sex-matched controls.

Indian childhood cirrhosis (ICC) is an important cause of mortality in young children in India (Indian Council of Medical Research Liver Diseases Sub-committee, 1955) but its aetiology has remained obscure (Nayak and Ramalingaswami, 1975). It has been suggested that the disease may be a sequel to infection with the virus of viral hepatitis (Achar

et al., 1960), but this has been questioned (Nayak *et al.*, 1972). Studies of hepatitis B surface antigen (HBsAg) in patients with ICC have not been conclusive (Chandra, 1970; Nayak *et al.*, 1975). In our experience, evidence of infection with hepatitis B virus can be found in 33% of patients with ICC. HBsAg was found by radioimmunoassay to be present in 18.8% of patients with ICC, and in another 14.2% patients, anti-HBsAg or HBe, or both, could be detected. Although this incidence is significantly higher than in control populations, infection with hepatitis B cannot account for all cases of ICC. Tests for the diagnosis of infection with hepatitis A virus are now available (Bradley *et al.*, 1977), and sera from patients with ICC were,

therefore, tested for antibodies to hepatitis A virus (anti-HAV) by radioimmunoassay.

Materials and methods

The serum samples from patients with ICC and controls were collected during 1971–73 at the Children's Hospital, King George's Medical College, Lucknow. The clinical diagnosis and staging of ICC were made according to the criteria adopted from the report of the Indian Council of Medical Research Liver Diseases Sub-committee (1955). The sera were kept frozen at -20°C . Control studies have shown that anti-HAV is stable under these conditions.

Anti-HAV was measured by radioimmunoassay, as described by Bradley *et al.* (1977), in the hepatitis laboratories at the Center for Disease Control, Phoenix, Arizona. In this assay a ratio of equal to, or greater than, 2.1 between the test sample (P) and negative (N) sample (P/N ratio) was considered positive for anti-HAV.

Results and discussion

A total of 50% of the patients with ICC were positive for anti-HAV (Table 1). This number, however, was not significantly different from the prevalence of antibody in age-matched children who were admitted to the hospital for various illnesses other than those of the liver (Table 2). Although the prevalence of anti-HAV was higher in patients with stage I and stage II ICC than in those with stage III disease, the difference was not significant. There were also no great differences in the age distribution of patients in the three stages of the disease. The average P/N ratio for anti-HAV in patients with ICC was 14.6 ± 9.1 SD (range 3.1–31.3) and that in controls was 12.1 ± 8.3 (range 2.3–32.4).

In an endemic area the acquisition of antibody to an infectious agent is a function of age. This is clearly demonstrated by the age-related prevalence of anti-HAV in the patients with ICC as well as in their age-matched controls (Table 2). The prevalence of anti-HAV was no higher for ICC patients between birth and 2 years (42%) than in an age-matched

Table 2 *Antibody to hepatitis A virus in relation to age*

Age group (months)	Patients with ICC		Children with diseases other than those of liver admitted to hospital*	
	Tested	No. (%)	Tested	Positive
				No. (%)
0–12	6	2 (33)	6	1 (17)
13–24	13	6 (46)	13	8 (62)
25–36	13	7 (53)	14	9 (64)
37–48	1	1	4	4 (100)

*Protein calorie malnutrition 5 (4 positive); nephrotic syndrome 5 (1 positive); Down's syndrome 4 (2 positive); bronchopneumonia 3 (3 positive); diarrhoea 3 (3 positive); normal children 3 (2 positive); poliomyelitis 2 (2 positive); miscellaneous 12 (5 positive), including one patient with kwashiorkor, one with intracranial space occupying lesion, one with eventration of left dome of diaphragm, one with splenomegaly of unknown cause, and one with short pyrexia of unknown origin.

control population (47%). These results do not support an aetiological relationship of hepatitis A to ICC. However, the possibility that ICC may result from an abnormal response to infection with the virus of hepatitis A cannot be excluded. Determination of anti-HAV in serial serum specimens from patients with ICC may help to resolve this issue.

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Table 1 *Antibody to hepatitis A virus in patients with Indian childhood cirrhosis*

Stage	Age (months) mean ± 1 SD	No. of boys		No. of girls		Total	
		Tested	Positive	Tested	Positive	Tested	Positive
I	26.1 \pm 13.5	7	4	4	3	11	7 (64)
II	21.3 \pm 10.3	6	2	4	4	10	6 (60)
III	23.0 \pm 9.4	11	3	2	1	13	4 (31)
		24	9	10	8	34	17 (50)

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- Correspondence to Dr S. S. Agarwal, Reader in Medicine, King George's Medical College, Lucknow, India.