

ETIOLOGY OF ENDEMIC VIRAL HEPATITIS IN URBAN NORTH INDIA

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Abstract. This study was carried out to determine the presence of markers of hepatitis viruses in patients with acute liver disease. Coinfection of HAV, HBV, HCV, and HEV was studied. Sera from 306 patients with a clinical diagnosis of acute liver disease were tested for the presence of anti-HAV antibody, HBsAg, anti-HBc antibody, anti-HBs antibody, anti-HCV antibody and IgM anti-HEV antibody by ELISA. Liver function tests were correlated with the presence of infection. Of the 306 cases, 7 (2.3%) had IgM anti-HAV, 9 (2.9%) had IgM anti-HBc, 37(12.1%) had HBsAg, 84 (27.4%) had anti-HBs, 10(3.3%) were HCV infected and 63 (20.6%) had IgM anti-HEV. There was no significant difference in the clinical and liver function profiles of infected and uninfected patients. Similarly, no difference was observed in cases coinfecting with more than one virus compared with those infected with a single pathogen. HEV had the highest prevalence amongst our cases. There was no difference in the clinical profiles of patients with non-A, non-B, non-C, non-E hepatitis by antibody assays and testing for viremia could be helpful in making the correct diagnosis.

INTRODUCTION

In India, viral hepatitis is an important public health problem that, at times, assumes epidemic proportions. Most of the acute, sporadic cases are due to hepatitis A virus (HAV) and hepatitis E virus (HEV). Hepatitis B virus (HBV) and hepatitis C virus (HCV) account for a small proportion of cases, while approximately 50% may be non-A-E (Tandon *et al*, 1984; Nanda *et al*, 1994; Nejdard *et al*, 1994). The transmission of hepatitis A and hepatitis E viruses is by the fecal-oral route, primarily via water; hepatitis B and C viruses are transmitted by parenteral routes (Khuroo, 1980; Tandon *et al*, 1984; Irshad *et al*, 1995; Singh *et al*, 1997). We studied 306 cases of acute sporadic viral hepatitis: we attempted to determine the presence of different viral hepatitis markers.

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MATERIALS AND METHODS

A hospital-based study of acute hepatitis was conducted at Lok Nayak Hospital, New Delhi over a period of one year as a part of routine investigation.

Study subjects

Subjects were 306 consecutive patients (177 adults and 129 children) with signs and symptoms compatible with acute viral hepatitis (*eg* dark urine, scleral and generalized jaundice) were enrolled. The age of the patients ranged from 1 to 68 years, while the mean age was 26 years \pm 2.5 years. More males were included (male: female ratio 1.5:1) because of their presenting in greater numbers. Voluntary informed consent was obtained and 5 ml of blood were collected from each patient. Serum was separated within 4 hours of collection and stored at -20°C in aliquots for testing by ELISA. Serum samples from 50 healthy voluntary controls were also tested in parallel by ELISA.

Study design

The history, clinical examination, and

Table 1
Viral markers in 306 cases of acute hepatitis.

Marker	Number (Percentage)	Comments
IgM anti-HAV	7 (2.3)	Three co-infection with HAV and HCV
IgM anti-HBc	9 (2.9)	Five had IgM HBc only
HBsAg	37 (12.1)	Two patients had coinfection with HCV
Anti-HBsAg	84 (27.4)	Eight patients had HBsAg; two had IgM anti-HBc and anti-HBs
Anti-HCV	10 (3.3)	-
Anti-HEV	63 (52.5)	One patient had multiple infection with HBV (IgM HBc), HCV, and HEV; three were infected with HBV and HEV; Seven were infected with HCV and HEV; One was infected with HAV and HEV

Table 2
Distribution of viral markers in adults and children with acute hepatitis.

Viral marker	Adult		Children	
	Total tested	Positive (Percentage)	Total tested	Positive (Percentage)
IgM anti-HAV	177	3 (1.7)	129	4 (3.1)
HbsAg	177	32 (18.1)	129	5 (3.9)
Anti-HBc	177	3 (1.7)	129	6 (4.7)
Anti-HBs	177	55 (31.1)	129	29 (22.5)
Anti-HCV	177	6 (3.4)	129	4 (3.1)
IgM anti-HEV	111	57 (51.4)	9	6 (66.3)

possible risk factors were noted. Those with a history of alcoholism were excluded from the study. Biochemical investigations were: a hemogram with ESR, blood glucose, serum urea and electrolytes, and liver function tests.

Serology

All sera were tested by ELISA for IgM anti-HAV antibodies (Murex Diagnostics, England), HBsAg (Hepalisa or Eliscann Microelisa Strips, Ranbaxy Diagnostics, England), IgM anti-HBc (Murex Diagnostics, England), anti-HBs antibody (Clonatec, France), anti-HCV antibodies (Murex anti-HCV antibody Kit, England) and IgM anti-HEV (MHEV Elisa, Genelabs) according to the manufacturer's in-

structions. Any positive samples or those with doubtful results were tested once again by ELISA.

RESULTS

A total of 7/306 (2.3%) patients with liver disease were found to be infected with HAV, while a large proportion (63/306, 52.5%) were HAV-infected. As shown in Table 1, 110 (36%) patients had evidence of infection (carriage with HAV, HBV, HCV or HEV) while 84 (27.5%) showed anti-HBs antibody. About half of the patients had no viral markers and the etiology remained unclear in these cases. Four patients with HCV infection were coinfect-

3 with HAV and 1 with HBV. Most of the HAV-infected cases were children (57%).

The percentage positivity of IgM anti-HAV declined between childhood (3.1%) and adulthood (1.7%). A much larger proportion of adults were HBsAg positive (18.1%) compared with children (3.9%). HEV was also seen more often in adults: very few pediatric sera were positive for HEV. HCV infection was found in similar proportions (~ 3-3.5%) of children and adults (Table 2).

Signs and symptoms did not vary with different types of hepatitis, regardless of age. Jaundice and dark urine were the commonest features. No significant difference in liver function was seen among those with serological markers.

DISCUSSION

Studies from different parts of India have reported 15-32% HAV infection, 1.8-57% HBV infection, and 0-12.5% HCV infection in acute viral hepatitis (Irshad *et al*, 1995; Singh *et al*, 1997; Kar *et al*, 1997).

Our study indicates a very low percentage of HAV infection: this finding may have been due to the hospital-based nature of the study. Sub-clinical or mild HAV infections may not present to the hospital. The prevalence of HBV and HCV is in accordance with the prevalence reported by the three research teams that are mentioned above.

Anti-HEV antibodies were found in 52.5% of the 120 patients whose serum was tested. This finding is similar to that of other studies, in which 44-84% HEV in acute viral hepatitis (AVH) and 23-62% in the fulminant hepatic failure (FHF) were reported (Tandon *et al*, 1984; Nanda *et al*, 1994; Nejdard *et al*, 1994; Tan *et al*, 1995).

Coinfection with HAV and HCV was noted in three cases (1%) while HEV coinfection with other hepatotropic viruses (HAV, HBV and HCV) was seen in 12 cases (4%). The symptoms, signs, and biochemical derange-

ment were no different to those produced by single pathogens.

HBV is a cause for major concern: it causes acute hepatitis, as shown in our study, and it plays a role in chronic liver disease, including hepatocellular carcinoma. HEV was the most common etiological agent in the causation of acute viral hepatitis and could exist concurrently with other hepatotropic viruses. In about half the patients, no viral marker was detected; these patients may have been infected with other hepatitis viruses or may not have undergone seroconversion. Testing for viremia in these cases would have been helpful. The reduced seroprevalence of HAV infection in adults may also indicate the improvement in living standards of the urban population, which has been noted earlier in Thailand (Tandon *et al*, 1984; Poovorawan *et al*, 1993). This co-existence might be a result of superinfection by HEV in a patient already carrying HBV/HCV, but it is difficult to predict whether both agents are synergistically responsible for the disease. Similar cases of co-infection have been reported by many workers (Jameel *et al*, 1992; Thomas *et al*, 1993; Nanda *et al*, 1994; Nejdard *et al*, 1994).

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