CLINICAL AND ETIOLOGICAL PROFILE OF ACUTE VIRAL HEPATITIS

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ABSTRACT

There is a paucity of data on the incidence of sporadic viral hepatitis in Indian children. Clinical, biochemical and etiological profile of 54 patients with acute viral hepatitis was evaluated. Of these, 32 (59.25%) patients had Hepatitis A, 18 (33.33%) had NANB, 2 (3.7%) had Hepatitis B and 2 (3.7%) concurrent Hepatitis A and B infection. It was not possible to distinguish the etiological agents on the basis of the clinical and biochemical profile. Fulminatnt hepatitis was documented in 8 (14.8%) cases. Children with NANB infection were at a greater risk ($p<0.05$) of developing fulminant hepatitis as compared to Hepatitis A infection.

Key words: *Viral hepatitis, Hepatitis A, Hepatitis B, Non A-non B hepatitis.*

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Received for publication November 6, 1991; Accepted January 16, 1992

Acute viral hepatitis, though a global problem, is more serious in nature in tropical and developing countries like India due to poor hygiene and sanitation(1). Little data is available on the incidence of sporadic viral hepatitis in Indian pediatric population because the disease is not notifiable and has a relatively benign course in children. Most of the earlier studies have concentrated on epidemics. With the recent availability of viral markers, sporadic viral hepatitis is attracting considerable attention. However, there are only limited reports in this context from India(2-5). The present investigation was, therefore, designed to evaluate the etiological and clinical profile of acute sporadic viral hepatitis in children.

Material and Methods

The study was carried out in the Pediatrics Department of LNJPN Hospital, New Delhi, from July 1986 to August 1987. It included both the anicteric and icteric cases on the basis of their history, symptomatology and liver function derangements. Cases with history suggestive of drug indicted hepatic injury and chronic liver disease were excluded.

The clinical profile was recorded in a special proforma. Serum was collected for biochemical tests (bilirubin, aspartate aminotransferase (AST), alanine aminotransferase (ALT) and alkaline phosphatase) and for viral markers. 2 to 3 ml sera taken from each patient was stored at –20° C till they were processed for viral markers. The viral markers studied included HBsAg (surface antigen of hepatitis B virus), IgM anti-HBc (IgM antibody against core antigen of hepatitis B virus) and IgM anti-HAV (IgM antibody against hepatitis A virus). HAVAB-M, Auszyme and Corzyme M Elisa kits supplied by Abbots Laborato-

ries, USA were used for viral markers(6).

A diagnosis of acute hepatitis A was made if the sera showed presence of IgM-anti HAV antibody. Diagnosis of acute hepatitis B infection was based on the presence of IgM antibody against hepatitis B core antigen (IgM anti-HBc) with or without hepatitis B surface antigen (HBsAg). Patients with HBsAg in the absence of IgM anti-HBc in their acute sera were labelled as carriers of hepatitis B infection. Non A-non B (NANB) hepatitis was diagnosed by excluding acute hepatitis A and B infections by the criteria enumerated above(2).

Non-parametric statistical tests were used for the analysis of the results.

Results

The study was performed on 54 children who fulfilled the criteria and were between 1 and 12 years of age. There were 34 males and 20 females (1.7 : 1). The etiological spectrum with respect to age groups is depicted in *Table I*. Hepatitis A virus was the commonest agent (59.25%) followed by non A-non B virus (33.33%). Hepatitis B infection was relatively uncommon (3.7%). Two patients (3.7%) had evidence of concurrent infection with hepatitis A and B viruses. Hepatitis B carrier stage was documented in 8 patients (14.8%). Hepatitis cases irrespective of the etiological agents were distributed equitably in all the age groups. However, hepatitis A virus infection occurred more commonly in patients below 6 years of age. No case was seen below one year of age.

Fifty of fifty-four (92.6%) patients had the classical prodromal illness of varying duration (2-20 days) and severity, consisting of fever, nausea, vomiting, anorexia and high colored urine (*Table II*). Four patients did not have icterus at the time of first contact. Of these, two developed jaundice and the other two who remained anicteric had deranged liver functions, bilirubinuria and tender hepatomegaly. Even after a careful search none of the commonly reported complications like arthritis, glomerulonephritis, *etc.* were documented. One of the patients had a clinical relapse within a week of symptomatic recovery from the

TABLE I—*Age Distribution of Cases According to Etiology*

Etiology	Age groups (months)			
	0-36	37-72	73-108	108+
Hepatitis A (n = 32)	9 (28.1)	14 (43.7)	6 (18.7)	3 (9.4)
Hepatitis B (n = 2)	–	1 (50.0)	–	1 (50.0)
Non A-non B (n = 18)	5 (27.8)	2 (11.1)	6 (33.3)	5 (27.8)
Concurrent HAV & HBV (n = 2)	1 (50.0)	1 (50.0)	–	–
Total (n = 54)	15 (27.8)	18 (33.3)	12 (22.2)	9 (16.7)

Figures in parentheses indicate the row percentages.

TABLE II—*Clinical Features of Acture Viral Hepatitis in Relation to Etiology*

Features	HAV (n = 32)	NANB (n = 18)	HBV (n = 2)	HAV + HBV (n = 2)	Total (n = 54)
History of exposure	2 (6.2)	1 (5.55)	–	–	3 (5.5)
Fever	31 (96.8)	16 (88.9)	1 (50)	2 (100)	50 (92.6)
Lassitude	14 (43.7)	5 (27.7)	–	1 (50)	20 (37)
Nausea	24 (75)	8 (44.4)	1 (50)	1 (50)	34 (63)
Vomiting	21 (65.6)	7 (38.9)	1 (50)	1 (50)	30 (55.5)
Anorexia	25 (78.1)	11 (61.1)	–	1 (50)	37 (68.5)
Change in bowel habits	3 (9.37)	2 (11.1)	1 (50)	–	6 (11.1)
High colored urine	32 (100)	18 (100)	2 (100)	2 (100)	54 (100)
Clay colored stools	17 (53.1)	6 (33.3)	–	2 (100)	25 (46.3)
Itching	1 (3.1)	1 (5.5)	–	–	2 (3.7)
Altered sensorium	2 (6.2)	5 (27.8)	–	1 (50)	8 (14.8)
Hemorrhage	2 (6.2)	2 (11.1)	–	–	4 (7.4)
Icterus	30 (93.7)	18 (100)	2 (100)	2 (100)	52 (96.3)
Hepatomegaly	27 (84.4)	13 (72.2)	1 (50)	–	41 (75.9)
Decrease in liver span	1 (3.1)	4 (22.2)	–	1 (50)	6 (11.1)
Splenomegaly	11 (34.4)	4 (22.2)	–	–	15 (27.7)

Figures in parentheses indicate column percentages.
Differences between HAV and NANB groups were not significant ($p > 0.05$; Chi square test).
HBV and concurrent infection group could not be compared due to small sample size.

first episode. None of the clinical syndromes could distinguish between either of the three etiological agents.

Table III shows that all the biochemical parameters tested tended to be more deranged in non A-non B and hepatitis B

TABLE III—*Biochemical Profile of Hepatitis Cases in Different Etiological Groups*

Etiological groups	Biochemical tests (Range and mean ± SD)			
	Bilirubin (mg/dl)	AST (IU/L)	ALT (IU/L)	Alk. Phosph. (KAU/L)
Hepatitis A	0.8-10 (4.2±1.85)	62-186 (103.2±31)	64-210 (125.6±38)	4--50 (28.5±14.4)
Hepatitis B	12-14.5 (13.2±1.25)*	152-168 (160±8)	170-174 (172±2)*	25.8-42 (34±8)
Concurrent HAV+HBV	4.8-24 (4.8±.05)	121-152 (136±15.5)	172-202 (187±15)	24-25 (24.5±.05)
Non A-Non B	2.8-24 (6.9±5.5)	56-178 (118±30.5)	80-236 (144.5±47)	3.2-60 (25.7±16.4)
Total	0.8-24 (5.46±4)	56-186 (111.5±32)	64-236 (136±42.5)	3.2-60 (27.6±14.6)

* These parameters attained significance when compared with HAV group ($p<0.05$; Wilcoxan's rank summation test).

patients. However, these differences attained significance ($p<0.05$) only for alanine aminotransferase and serum bilirubin in HBV Group in comparison with HAV Group. It is obvious that the types of viral hepatitis could not be reliably distinguished on the basis of signs, symptoms and biochemical profile alone.

Fulminate hepatitis, *i.e.*, altered sensorium with acute viral hepatitis in the absence of pre-existing liver disease was documented in only 8 of 54 cases (14.8%). Of these, five (62.5%) had NANB infection, 2 (25%) had hepatitis A and 1 (12.5%) had concurrent hepatitis A and B infection. Children who had NANB infection were at a significantly higher risk ($p<0.05$; Fischer's exact test) of developing fulminant hepatic failure in comparison to those with hepatitis A (5/18 *vs* 2/34 cases). Interestingly, 50% of the fulminate hepatitis cases were hepatitis B carriers with superimposed NANB virus infection. The sample size of carriers is too small for a meaningful statistical analysis.

The median duration of illness and alteration of sensorium was four and one days, respectively. The biochemical derangements were considerably higher in fulminant cases as compared to nonfulminant hepatitis patients (*Table IV*). There

TABLE IV—*Biochemical Profile of Fulminatnt and Non-fulminant Cases (Range, Mean ± SD)*

Liver functions	Fulminant cases	Non-fulminant cases
Bilirubin (mg/dl)	4.4-24 (9.87±7.26)	0.8-12.4 (4.7±2.6)
AST (IU/L)	90-178 (136.6±26.8)	56-186 (107.2±31.8)
ALT (IU/L)	80-236 (180.5-26.8)	64-220 (126±35.5)
Alk. Phosph. (KAU/L)	12-50 (32.6±12.7)	3.2-60 (26.4±14.7)

Differences in total bilirubin, ALT and alkaline phosphatase were statistically significant ($p<0.001$, $0.001<p<0.01$, $0.001<p<0.01$, respectively; Student's 't' test).

were only two survivors, of which one recovered completely (Hepatitis B carrier with NANB infection) and the other patient with hepatitis A had a symptomatic relapse within 7 days of clinical recovery from the initial episode. It is unlikely that the patient who had a relapse had suffered a second infection because the interval between the two episodes was too small.

Concurrent infection with hepatitis A and hepatitis B virus was seen in two cases who had HBsAg, IgM anti-HBc and IgM anti HAV in their acute sera. The clinical profile of these two patients differed considerably. One of them had a fulminant hepatic failure and died whereas the other had a benign course of illness with complete recovery.

Discussion

Despite the severe magnitude of the problem of acute viral hepatitis in India, there are only few published reports on the etiology of this disease in children. In conformity with other reports(2-5), hepatitis A virus was the commonest cause of acute viral hepatitis occurring sporadically in Indian children (59.25%). A comparison of the various Indian and western studies on etiological spectrum(2-5,7-9) is shown in *Table V*. Although the incidence of viral hepatitis has declined considerably in the western population, in this population also, helatits A virus is still the commonest cause(7-9). Non A-non B hepatitis occurred in 33.33% of our children. The importance of NANB virus infection in Indian adults is well established(2). It seems to play an important role in childhood hepatitis as well (*Table V*). Hepatitis B virus infection is a relatively uncommon cause in this age group; its incidence in the present study (3.7%) was amongst the lowest reported.

On the basis of clinical and biochemical profiles it was not possible to make a reliable diagnosis of the etiological agent. Similar observations have been made earlier(10). The clinical profile and observations were in conformity with the classical description(11).

In our study, children with NANB infection were at the maximal risk of developing fulminate hepatitis (63%) in contrast to the earlier report from India(3) which showed that HAV and HAB were

TABLE V—*Comparison of Etiological Profile of Acute Sporadic Childhood Hepatitis in Different Populations*

Country	Year	No. of cases	HAV	HBV	NANB	Concur. HAV+HBV
USA(6)	1979	50	88	–	12	–
USA(7)	1984	54	79	5	16	–
Germany(8)	1979	199	80	14	6	–
India(2)	1984	78	67	9	24	–
India(3)	1986	88	76	10	14	–
India(4)	1989	496	56	20	23	1
India(5)	1990	75	75	9	13	3
India (present study)	1987	54	59	4	33	4

responsible for most of the fatal cases (40% each). The frequency of the three agents in any series of fulminant viral hepatitis will depend to some extent on the frequency with which these agents are prevalent in the community and is the probable explanation for the difference in the above mentioned studies. The higher rate of NANB infection in fulminant cases in the present series could also be due to a relatively higher prevalence of NANBV infection in the present series. However, in the present series, children with NANB infection were at a significantly higher ($p<0.05$; Fischer's exact test) risk of developing fulminant hepatitis in comparison to hepatitis A. In conformity with earlier experience, the biochemical indices (serum bilirubin, alanine aminotransferase and alkaline phosphatase) were significantly more deranged as compared to non-fulminant cases (*Table IV*).

Interestingly, four out of the seven of our patients who were carriers of HBV and had intercurrent NANB infection developed fulminant hepatitis. Earlier studies in adult patients have made similar observations(12,13).

We observed two cases of concurrent infection with hepatitis A and B viruses, which is a relatively rare etiological form. Most of the published reports of such cases are in adults(14-16) except for two reports of six such cases in Indian children(4,5). The clinical profile of these patients varied from a benign course to filminant hepatitis with death. The variation in clinical profile of these patients as observed has been reported earlier also(14,15). We also had a patient with clinical relapse a week after recovery from the initial episode of hepatitis A. The relapse of hepatitis may have been due to incomplete elimination of HAV after the first episode leading to a second clinical illness. Secondly, HAV may have triggered an auto-immune response leading to a second illness(17).

It is concluded that hepatitis A is the commonest form of sporadic hepatitis in children and NANB infection is associated with a higher risk of fulminate hepatic failure.

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NOTES AND NEWS

UPDATE IN PEDIATRIC RESPIRATORY DISORDERS

A one day Seminar on "Update in Pediatric Respiratory Disorders" is being organized under the joint auspices of Respiratory Chapter of IAP, Department of Pediatrics, Seth G.S. Medical College, K.E.M. Hospital, Bombay and Bombay Branch of IAP on *14th June, 1992* at Jivraj Mehta Hall (MLT) from 9 am to 5 pm.

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