Spectrum of Acute Viral Hepatitis in Southern India

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Abstract

Background: The incidence of hepatitis-A among adults in India is on the decline as majority develops protective immunity to it by late adolescence. Most of these studies are from northern India. Clinical spectrum of sporadic acute viral hepatitis from southern India has not been well documented.

Methods: A prospective hospital based study was conducted in a large military hospital in southern India. 224 consecutive patients with acute viral hepatitis were studied for their presentation, etiology and clinical features.

Result: Hepatitis-E was detected in 102 (45.4%), hepatitis A in 74 (33%) and hepatitis B in 28 (12.5%) patients. Acute hepatitis C was detected in two patients. 15 patients had a mixed infection. Hepatitis A constituted 41.2% and 31.3% of all cases in the age groups 11-20 and 21-30 years respectively. Cholestasis was present in 68 (30.4%) patients with hepatitis E accounting for most (61.8%) cases. There were four (1.8%) cases of acute liver failure. Two cases were due to hepatitis E and one case each was due to hepatitis A and hepatitis B. A relapsing course was seen in four cases due to hepatitis-A.

Conclusion: Hepatitis A remains a significant cause of sporadic acute viral hepatitis in young adults in southern India.

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Key Words: Viral hepatitis; Hepatitis A

Introduction

Acute viral hepatitis (AVH) remains a public health problem in India despite improving sanitation, health awareness and socio-economic conditions. Hepatitis E is the commonest cause of acute hepatitis in adults and hepatitis A is the commonest cause in pediatric age group [1-3]. India is hyper-endemic for Hepatitis A and E [1]. Numerous studies based on IgG anti-hepatitis A virus (HAV) seropositivity in healthy population have shown that majority above the age of 15 years have already been exposed to HAV and recommendations have been made that vaccination against HAV is not required in our country as majority of people above 15 years are protected against HAV [1-4]. However, there are only few studies from southern India on prevalence of HAV exposure and infection. To the best of our knowledge there is no published study on clinical profile of acute viral hepatitis in adults as seen in armed forces. This study has been done in an armed forces hospital of South India to study the clinical spectrum of sporadic AVH.

Material and Methods

This study was conducted at a large multi-specialty military hospital located at Bangalore, India over a period of one and half years from 01 Jul 2003 to 31 Dec 2004.

Patients with acute onset of jaundice suggestive of acute hepatitis, with at least one positive serological viral marker

(IgM HAV, IgM HEV, hepatitis B surface antigen and anti-HCV) were included in the study. Patients with clinical or ultrasonographic evidence of biliary obstruction or chronic liver disease were excluded. Hepatitis B surface antigen (HBsAg) positive but IgM-anti-HBc negative patients and anti-HCV positive but HCV RNA negative patients were also excluded.

All the patients were admitted to the hospital and clinical profile recorded. Complete liver function test (LFT), prothrombin time and ultrasonography was done on admission for each patient. Upper limit of normal for AST and ALT was 40 IU/L and for alkaline phosphatase was 170 IU/L. All patients were tested for HBsAg (ELISA, J Mitra & Co, India), anti-HCV (3rd generation ELISA, J Mitra & Co, India), IgM HAV (ELISA, General Biologicals Corp., Taiwan) and IgM HEV (ELISA, Smart Test Diagnostics, Israel). IgM and IgG anti-HBc and HCV RNA was done in patients who were HBsAg positive and anti-HCV positive respectively. All patients were followed up for complete clinical and biochemical recovery. All patients received normal diet. Symptomatic treatment for nausea and vomiting was given where indicated.

Statistical analysis was done using EP 16 software. Univariate and bivariate frequency tables were generated based on categorical data. Association between parameters was studied using chi-square test at appropriate level of significance. Association was considered to be statistically significant if $p < 0.05$.

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Results

A total of 252 cases of acute hepatitis were seen during the period of study. Twenty eight cases were excluded due to various reasons (no serological marker was positive in 26 cases and 2 cases were IgM and IgG anti-HBc positive at onset of illness). 224 cases of acute viral hepatitis were included in the study. There were 175 males and 49 females in the mean age group of 22.5 years.

Hepatitis E was the commonest cause seen in 102 (45.5%), followed by hepatitis A in 74 (33%) and hepatitis B in 28 (12.5%) cases. There were only two cases of acute hepatitis C. Mixed infection was seen in 18 cases (A+E 16 cases, B+E and B+A in one case each respectively). Hepatitis A constituted 41.2% of all cases in the age group 11-20 years, followed by hepatitis E (35.3%). In the older age group, 21-30 years, hepatitis E was the commonest (52%) infection, followed by hepatitis A (31.3%).

Most of the patients presented within one week of onset of symptoms to the hospital. Jaundice and fatigue were the major presenting complaints followed by anorexia whilst icterus and hepatomegaly were the most frequent signs. Pruritis was present in 68 (30.4%) patients. Majority of cases (42 cases) with pruritis were due to hepatitis E.

There were four (1.8%) cases of acute liver failure. Two cases were due to hepatitis E and one case each was due to hepatitis A and hepatitis B. 114 (50.9%) cases had serum ALT in the range of 1000-2000 IU/L on admission ($p=0.71$). Only 15 (6.7%) cases had a value less than 500 IU/L and 29 (13%) cases had values above 2000 IU/L.

Majority (88.5%) of the patients with pruritis had raised serum alkaline phosphatase, upto three times the upper limit of normal ($p<0.05$) whilst only 6 (9.8%) cases had a rise above three times the upper limit of normal (Table 3).

Table 1
Etiology of acute viral hepatitis

Age (years)	Hepatitis B (n=28)	Hepatitis C (n=2)	Hepatitis A (n=74)	Hepatitis E (n=102)	Mixed (n=18)
1-10	0	0	6	2	2
11-20	12	0	35	30	8
21-30	14	2	30	50	7
31-40	2	0	3	11	1
>40	0	0	0	9	0

Table 2
Clinical features

Clinical features	Hepatitis A (n=74)	Hepatitis E (n=102)	Hepatitis B (n=28)	Hepatitis C (n=2)	Hepatitis A&E (n=16)	Hepatitis B&E (n=1)	Hepatitis B&A (n=1)
Jaundice	74	102	28	2	16	1	1
Fever	43	53	18	1	12	1	1
Pruritus	15	42	6	0	5	0	0
Fatigue	41	63	17	2	10	1	1
Pain abdomen	19	29	4	0	7	1	1
Nausea/vomiting	41	52	14	0	12	1	1
Hepatomegaly	74	102	28	2	15	1	1
Splenomegaly	10	12	5	0	5	0	0

The duration of illness was 1- 4 weeks for majority of hepatitis A (74.3%) and hepatitis E (73.5%) cases. In 17 (60.7%) cases with hepatitis B, illness lasted 4-8 weeks ($p<0.001$). Relapsing course was seen in four cases, all of which were due to hepatitis A. Two patients with acute liver failure died (one case each of hepatitis E and B). Both cases died of hospital acquired severe sepsis.

Gall bladder wall thickening on ultrasound examination was seen in two cases each of hepatitis A and hepatitis E, and one case of hepatitis B. It was normal in all other cases.

Discussion

Hepatitis E virus was the commonest cause of acute viral hepatitis in this study. Other studies have also shown that hepatitis E is the commonest cause of sporadic acute viral hepatitis among adults in India [2,5-7].

Hepatitis A is common in children [8]. Most studies have shown a low prevalence of this virus among adults [5,7,9]. Chadha et al [2], compared the etiology of sporadic and fulminant viral hepatitis a decade apart and found an increase in hepatitis A incidence in adults, especially, in those who developed fulminant hepatic failure (from 3.5% to 10.6%). We found that a third of our adult patients were infected with hepatitis A. The incidence was particularly high in late teens and young adults. Our patients, mostly recruits, were generally from low socio-economic background who were non-immune to hepatitis A infection. Our study implies that hepatitis A continues to be an important cause of acute viral hepatitis in adults, in South India. A study conducted on school children in Delhi had found that all children by age of 16 years had antibodies against hepatitis A and this study recommended that mass vaccination is not

Table 3
Serum alkaline phosphatase in patients with cholestasis (n=68)

Serum alkaline phosphatase (IU/L)	Hepatitis A (no. of cases)	Hepatitis B (no. of cases)	Hepatitis E (no. of cases)	Hepatitis A+E (no. of cases)
<170	6	0	4	0
170 - 540	7	6	34	5
>540	2	0	4	0

required in North India [1]. In light of our results, it will be interesting to know the seroprevalence of antibodies to hepatitis A in similar population of South India before re-opening the debate for mass vaccination against hepatitis A.

Clinical and biochemical characteristics were not helpful in differentiating the viruses, thus serological testing is essential for correct etiological diagnosis. Kaur et al [5] reached similar conclusion in their study of endemic hepatitis in North India.

Cholestasis of varying severity was present in nearly a third of our patients. Cholestasis was commonest in hepatitis E as documented in earlier studies [10]. It was also seen in patients with hepatitis A and B. Majority of patients with cholestasis had serum alkaline phosphatase levels varying from 1.5-2.0 times above the upper limit of normal. Only around 10% patients with cholestasis had a significant rise in alkaline phosphatase levels (>3 times normal).

Relapsing course of hepatitis was seen in four patients. All the patients were infected with hepatitis A. Apart from the relapsing course of the disease there were no other clinical differences between the relapsing and non-relapsing hepatitis cases.

There were four cases of acute liver failure of which two had died (one each of hepatitis A and E). Both the fatal cases had three out of four adverse prognostic indices (serum bilirubin >15 mg/dl, prothrombin time >25 sec, cerebral edema on admission and age > 40 years) while the two non-fatal cases had none and one adverse prognostic factor respectively [11].

The duration of illness was less than four weeks in majority (68.4%) of our patients. Sub-group analysis showed that in 60% of hepatitis B patients, the illness lasted up to eight weeks. The severity of disease, as measured by prothrombin time, did not correlate with the duration of illness.

This study is one of the larger studies of its kind from India. Soldiers, especially military recruits, constitute a large part of our clientele. This has resulted in a bias towards inclusion of young males and less number of

women and children in our study. This is the potential limitation of this study.

Conflicts of Interest

None identified

Intellectual Contribution of Authors

Study Concept : Gp Capt B Nandi

Drafting & Manuscript Revision : Gp Capt B Nandi, Maj P Hadimani

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References

1. Acharya SK, Batra Y, Bhatkal B. Sero epidemiology of hepatitis A virus infection among school children in Delhi; implications for HAV vaccination. *J Gastroenterol Hepatol* 2003; 18:822-7.
2. Chadha MS, Walimbe AM, Chobe LP, Arankalle VA. Comparison of etiology of sporadic acute and fulminant viral hepatitis in hospitalised patients in Pune, India during 1978-81 and 1994-97. *Indian J Gastroenterol* 2003; 22: 11-5.
3. Mall ML, Rae RR, Phillip M. Seroepidemiology of hepatitis A in India. *Ind J Gastroenterol* 2001;20:130-2.
4. Batra Y, Bhatkal B, Ojha B. Vaccination against hepatitis A virus may not be required for school children in northern India. *Bull WHO* 2002;80:128-31.
5. Kaur R, Gur R, Berry N, Kar P. Etiology of endemic viral hepatitis in urban North India. *Southeast Asian J Trop Med Public Health* 2002; 33: 845-8.
6. Das K, Agarwal A, Andrew R, Frosner GG, Kar P. Role of hepatitis E and other hepatotropic virus in aetiology of sporadic acute hepatitis: a hospital based study from urban Delhi. *Eur J Epidemiol* 2000; 16: 937-40.
7. Kar P, Gangwal P. Analysis of serological evidence of different hepatitis viruses in acute viral hepatitis in prisoners in relation to risk factors. *Indian J Med Res* 2000;112:128-32.
8. Malathi S, Mohanavalli B. Clinical and viral marker pattern of acute sporadic hepatitis in children in Madras, South India. *J Trop Pediatr* 1998; 44: 275-8.
9. Ichhpujani RL, Riley IW. Demographic features of sporadic acute hepatitis as determined by viral hepatitis markers. *J Common Dis* 1991; 23: 138-43.
10. Mechnik, Laura MD. Acute Hepatitis E virus Infection Presenting as Prolonged Cholestatic Jaundice. *Journal of Clinical Gastroenterol* 2001; 33: 421-2.
11. Acharya SK, Panda SK. Acute hepatic failure in India: A perspective from East. *Journal of Gastroenterol Hepatol* 2000; 15: 473-9.

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