Gastroenterologia Japonica
Vol. 26, Suppl. 3

Hepatitis C virus infection is the major cause of severe liver disease in India

B.N. TANDON, M. IRSHAD, S.K. ACHARYA, and Y.K. JOSHI
Department of Gastroenterology, Rajgarhia Liver Unit, All-India Institute of Medical Sciences, New Delhi, India

Introduction

The diagnostic marker for HCV infection is now well established, though it is expected that the assay method, sensitivity and specificity will further improve in the near future. Reports on clinical and seroepidemiology studies of HCV are being published from different parts of the world, mostly from the developed countries[1-3]. The global status of HCV hepatitis will emerge when these studies are extended to all the regions of the world, particularly to include the tropical and developing countries. Fulminant hepatitis failure (FHF) and Subacute hepatic failure (SAHF) are common manifestations of hepatitis in India. We report here HCV as the major cause of the severe form of liver disease in India, which includes fulminant hepatic failure (FHF), subacute hepatic failure (SAHF) and chronic active hepatitis (CAH).

Patients and Methods

A total number of 167 patients which included 81 cases of fulminant hepatitis, 53 of subacute hepatic failure and 33 of chronic active hepatitis were investigated for anti-HCV antibodies and the markers of hepatitis A and B infections. The diagnosis of fulminant hepatitis, subactue hepatic failure and chronic active hepatitis were established on accepted clinical, biochemical and histological criteria[4,5].

The serological markers for hepatitis A and B were tested using EIA-kits from Abbott (USA). HBsAg was detected by a modified micro-ELISA technique[6,7]; IgM anti-HAV and IgM anti-HBc were investigated in sera samples using HAVAB-M and CORZYME-M kits respectively. Anti-HCV antibody was tested in sera samples using HCV-EIA kit from Ortho Diagnostic.

The diagnosis of hepatitis A and B infections were confirmed by the presence of IgM anti-HAV and IgM anti-HBc respectively in sera samples. Sera negative for both these markers were diagnosed as due to NANB infections. Further sera positive for HBsAg but negative for IgM antibodies were labelled as HBV carriers associated with other hepatitis viral infections. The presence of anti-HCV antibody in HBsAg-positive but IgM anti-HBC negatives sera indicated superinfection of HCV in HBV carrier, where as the presence of both anti-HCV and IgM anti HBc together established coinfection of HCV with HBV infection.

Results

Table 1 presents the anti-HCV positivity rate in FHF, SAHF and CAH. The results show that HCV antibodies were present in 43%, 47% and 42% respectively. **Table 2** shows that HCV was the exclusive etiological agent for 20.9% cases of FHF, 18.7% of SAHF and 15.2% of CAH respectively. Further, HCV infection has made an additional contribution to the severe form of liver diseases either as superinfection or coinfection with HBV virus. These data have been an-

Gastroenterol Jpn 1991:26(Suppl 3)192-195
Address for correspondence: B.N. Tandon, M.D., Professor & Head, Department of Gastroenterology & Human Nutrition, All India Institute of Medical Sciences, Ansari Nagar, New Delhi-110029, India.

Table 1 Anti-HCV positivity in FHF, SAHF and CAH

Group	No. tested	No. positive	% positive
FHF	81	35	43.2
SAHF	53	25	47.2
CAH	33	16	42.1
Total	167	79	44.9

Table 2 HCV as single etiological agent in FHF, SAHF and CAH

Disease group	No. tested	No. anti-HCV+ (exclusively)	%HCV infection (single agent)
FHF	81	17	20.9
SAHF	53	10	18.7
CAH	33	5	15.2

alyzed in **Tables 3 and 4**. Single HCV infection as the cause of severe liver disease was recorded in 43.6%, 41.7% and 50% respectively in FHF, SAHF and CAH. HCV superinfection in HBsAg carriers was recorded in 54% of FHF, 60% of SAHF and 42% of CAH cases (**Table 4**). Further, coinfection of HCV and HBV was recorded in 27.8% of FHF, 42.9% of SAHF and 75% of CAH respectively (**Table 4**).

Table 5 summarizes the etiological spectrum due to hepatitis viruses in three severe types of clinical hepatitis in our patients. It may be noted that hepatitis A infection has not been recorded in any patient in this series. Hepatitis C as a single infection or superinfection/coinfection with hepa-

Table 3 Relative contribution of HCV infection to NANB hepatitis group of patients

Group	Total	NANB infection		Anti-HCV positivity in NANB group of cases		
		No.	Percentage	No.	+VE	%+VE
FHF	81	39	48.2	39	17	43.6
SAHF	53	24	45.3	24	10	41.7
CAH	33	10	30.3	10	5	50.0

Table 4 HCV coinfection and superinfection with HBV

Group	HCV superinfection			HCV coinfection		
	No.*	anti-HCV+	%+VE	No.**	anti-HCV+	%+VE
FHF	24	13	54.2	18	5	27.8
SAHF	15	9	60.0	14	6	42.9
CAH	19	8	42.1	4	3	75.0

*: All sera positive for HBsAg, **: All sera positive for IgM anti-HBc

Table 5 Etiological spectrum of FHF, SAHF and CAH patients

Type of hepatitis	FHF (n=81)		SAHF (n=53)		CAH (n=33)	
	+VE	%+VE	+VE	%+VE	+VE	%+VE
Hepatitis A	0	0	0	0	0	0
Hepatitis B	18	22.2	14	26.4	4	12.1
(i) Single infectin	17	20.9	10	18.8	5	15.2
(ii) Superinfection in HBV carrier	13	16.1	9	16.9	8	24.2
(iii) HBV and HCV coinfectin	5	6.2	6	11.3	3	9.1
(iv) Hepatitis-NANBNC						
(i) Single infection	22	27.2	14	26.4	5	15.2
(i) Superinfection in HBV carrier	11	45.8	6	40.0	11	57.8

titis B has been recorded in 43.2% of FHF, 47% of SAHF and 48% of CAH of patients. A group of patients comprising 27.2% of FHF, 26.4% of SAHF and 15.2% of CAH patients did not have positive serology for HAV, HBV or HCV infection. The patients in this group may have been infected due to HEV or a second type of a yet unidentified HCV virus (referred to by some as HFV or some yet unknown hepatitis virus).

Discussion

In 1985[7], we reported that NANB hepatitis is a public health problem in India. The confusion about the NANB hepatitis group has significantly cleared after the discovery of serological test for HCV[8] and isolation of the HEV virus[9]. It is now well established that what was labelled as NANB hepatitis includes the following diseases: (a) hepatitis C virus infection, (b) hepatitis E virus infection, and (c) an unkown hepatitis infection which may be a variant of HCV or yet another hepatitis virus which in future may be labelled as hepatitis F infection.

Recent studies, particularly from the USA[10], Japan[11] and Europe[12] have described the epidemiology and clinical spectrum of hepatitis C virus infection. It has been reported that fulminant cases are rare in prospectively followed patients with transfusion-associated NANB hepatitis which now is believed to be primarily due to HCV infection. However, when patients presenting as fulminant hepatitis were categorised by etiology, NANB has been attributed as the primary cause[13]. The earlier reports[7] from our department indicated the etiological spectrum of 130 fulminant hepatitis cases recording hepatitis A, B, NANB and associated NANB in HBsAg carriers infections in 15%, 27%, 53% and 9% cases respectively. The serological tests for HCV were not developed when this study was carried out. The present report in 81 cases of FHF reveals a major etiological role of HCV. In 21% patients it was noted as exclusive infection, 16% had superinfection of HCV in HBV carriers and 6.2% had coinfection of HCV and HBV. Thus overall 43% of all FHF cases had HCV infection. We do not know the exact etiology in reference to type of hepatitis virus in 27% of patients where markers of HAV, HBV and HCV were all negative. These patients may include cases of HEV infection, a second type of HCV virus or some other unkown hepatitis virus. None of them had a history of injection or consumption of drugs known to be associated with fulminant hepatic failure.

Subacute hepatic failure has been described in a large series of patients of acute viral hepatitis with bridging necrosis from our department. It is a distinct entity[14], different from FHF and CAH. It has a high mortality in the same range as FHF. HCV as a single or superinfection in HBV carriers or coinfection with HBV has been recorded in 47% of patients in this group. Earlier, our laboratory reported NANB hepatitis as the etiology of SAHF in 37% of the patients[7]. It was noted in the present series that 26% of patients did not have seropositivity for hepatitis A, B, or C. The infection in this group may be due to hepatitis E or a second type of hepatitis C or some unknown hepatitis virus.

The strongest association of HCV has been reported with chronic active hepatitis in Western literature and from Japan[1-3]. Prospective studies have shown that nearly 50% of the post-transfusion and community-based acute sporadic hepatitis due to HCV progress to chronic hepatitis. It is reported that in community-acquired chronic active hepatitis up to 80% cases are due to HCV infection[15]. The present data of our department reveals that 48.5% cases of chronic active hepatitis (community-acquired) had HCV infection which included exclusive infection due to HCV as well as super-and coinfection with HBV. As in the case of FHF and SAHF a group of patients less in number than those with the previous two diseases was serologically negative for hepatitis A, B or C markers. This group may have hepatitis E infection or a second type of HCV disease.

In conclusion, the data of the present study establish that HCV is an important etiological agent in nearly half of the cases in the three severe forms of community-acquired hepatitis namely FHF, SAHF, and CAH in India.

Summary

The present study describes the status of hepatitis C virus infection in 167 patients with severe forms of liver diseases in India. The anti-HCV positivity rate was recorded as 43%, 47% and 42% in patients with FHF, SAHF and CAH respectively. HBV and HCV coinfection was recorded in 28% of FHF, 43% of SAHF and 75% of the CAH cases. Superinfection of HCV in HBsAg carriers was recorded in 54% cases of FHF, 60% of SAHF and 42% of the CAH. None of these 167 patients was positive of HAV-IgM. Further, 27.7% of FHF, 26.4% of SAHF and 15.2% of CAH cases were neither HBV nor HCV markers positive. These can be labelled as non-A, non-B and non-C infections.

References

1. Morgan C, Hyland C, Young FF: Hepatitis C antibody and transaminase activities in blood donors. Lancet 1990;335:921-922
2. Poel CLV, Reesink HW, Schaasberg W, et al: Infectivity of blood seropositivity for hepatitis C virus antibodies. Lancet 1990;335:558-560
3. Tremolodo F, Bennegnu L, Casarin C, et al: Antibody to hepatitis C virus in hepatocellular carcinoma. Lancet 1990;335:300-301
4. Tandon BN, Joshi YK, Tandon M: Acute liver failrue: Experience with 145 patients. J Clin Gastroenterol 1986;8:664-668
5. Anad AC, Irshad M, Acharya SK, et al: Fibronectin in acute and subacute hepatic failure. J Clin Gastoroenterol 1989;11:314-319
6. Gandhi BM, Tandon BN: A low cost micro-ELISA test for hepatitis B surface antigen. Trop Gastroenterol 1984;5:142-148
7. Tandon BN, Gandhi BM, Joshi YK, et al: Hepatitis virus non-A, non-B: the cause of a major public health problem in India. Bulletin of WHO 1985;63:931-934
8. Choo QL, Kuo G, Weiner AJ, et al: Isolation of c DNA clone derived from a blood borne non-A, non-B viral hepatitis genome. Science 1989;244:359-362
9. Reyes GR, Purdy MA, Kim JP, et al: Isolation of c DNA from the virus responsible for enterically transmitted non-A, non-B hepatitis. Science 1990;247:1335-1339
10. Alter MJ, Margolis HS, Krawezyushi K, et al: Parenterally transmitted non-A, non-B hepatitis in the United States and its association with hepatitis virus antibody. Proceeding of Int Symp on non-A, non-B hepatitis and blood borne infectious diseases Tokyo, Japan 1989;58
11. Kuo G, Choo QL, Alter G, et al: An assay for circulating antibodies to a major etiological virus of human non-A, non-B hepatitis. Science 1990;244:362-364
12. Roggendorf M, Deinhardt F, Rasshofer R, et al: Antibodies to hepatitis C virus. Lancet 1989;ii:324-325
13. Gimson AES, White YS, Eddleston ALWF, et al: Clinical and prognostic differences in fulminant hepatitis A, B and non-A, non-B. Gut 1983;24:1194-1198
14. Tandon BN, Joshi YK, Krishnamurthy L, et al: Subacute hepatic failure: Is it a distinct entity. J Clin Gastroenterol 1982;4:343-346
15. Alter HJ: The hepatitis C virus and its relationship to the clinical spectrum of NANB hepatitis. J Gastroenterol Hepatol 1990; Suppl1:78-94