ACUTE VIRAL HEPATITIS IN SINGAPORE

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SYNOPSIS

A comprehensive study of acute viral hepatitis was conducted in a major hospital in Singapore between January 1975 and March 1976. Acute viral hepatitis caused by HAV, HBV and HNANBV was found to be 30%, 46% and 24% respectively. The mean age of patients with HNANBV hepatitis was significantly higher than that of patients with HAV and HBV hepatitis. The male to female ratio was highest in HBV hepatitis (3.4) followed by HAV hepatitis (1.9) and HNANBV hepatitis (1.3).

Viral hepatitis is endemic in many parts of the world including South East Asia. In the Republic of Singapore with a population of 2.2 million, the number of clinical viral hepatitis infections per year ranged from 300 to 1,000 in the last four years (Epidemiological News Bulletin vol 3, 4, 5, 6). The accepted method of diagnosis of Hepatitis B infection is by detection of Hepatitis B surface antigen (HBsAg) in the acute serum sample of patients with viral hepatitis and diagnosis of Hepatitis A in many countries is, by exclusion of Hepatitis B. Diagnosis of Hepatitis B based on the detection of HBsAg presents no problem in countries where HBsAg carrier rates are low. In countries like Singapore where the frequency of HBsAg in normals can be as high as 13% (1) there will be a tendency to over diagnose Hepatitis B infection if specific markers for Hepatitis A virus (HAV) were not performed. Furthermore the frequency of Hepatitis non A non B infection in the non-Hepatitis B patients could not be estimated.

In 1975 a comprehensive study of liver diseases was conducted in a major hospital in Singapore and the Hepatitis B virus (HBV) and alphafetoprotein (AFP) status have been reported previously (2, 3). Recently the availability of commercial Hepatitis A specific IgM kits makes accurate diagnosis of HAV infection possible. We have retested the sera of viral hepatitis patients from that previous study and reported here are the results.

PATIENTS AND METHODS

Peripheral blood samples were taken from patients with acute viral hepatitis on admission to three Medical Units of the Singapore General Hospital between January 1975 and March 1976. The serum was separated immediately, aliquoted and stored at $-20°C$ until tested. All patients had liver biopsy and biochemical tests on admission and some also had repeated tests at 6 and 12 months. Diagnosis was based on clinical and biochemical criteria and confirmed by histopathology.

HBV markers performed were HBsAg by counter-immunoelectrophoresis (CIE) and reverse passive haemagglutination (rPHA, Wellcome Laboratory) and antibody to Hepatitis B core antigen (anti HBcAg) by radioimmunoassay (Core Ab, Abbot Laboratories, Chicago). HAV markers performed were total antibody to HAV by RIA (HAVAB, Abbot Laboratories) and IgM antibody to HAV by RIA (HAVAB-M, Abbott Laboratories). Alphafetoprotein (AFP) was performed by CIE and supplementation CIE methods (2, 4).

HAV hepatitis was defined by a positive specific IgM response to HAV and HBV hepatitis by a positive HBsAg in the absence of IgM to HAV. Hepatitis non A non B virus (HNANBV) infection was defined by exclusion of Hepatitis A and B infections.

RESULTS

There was a total of 67 patients with acute viral hepatitis confirmed by histopathology in this study. As defined by the above criteria the frequencies of Hepatitis A, Hepatitis B and Hepatitis non A non B infections were 30%, 46% and 24% respectively (Table 1). The mean age of patients with Hepatitis A infection was similar to those with Hepatitis B infection ($p>0.1$). However the mean age of those with Hepatitis non A non B infection was significantly higher than those with Hepatitis A ($p<0.001$) or Hepatitis B ($p<0.02$). The male to female ratio was highest in Hepatitis B (3.4) followed by Hepatitis A (1:9) and lowest in Hepatitis non A non B (1.3).

Exposure rates to HAV as indicated by the frequency of total anti-HA Ag was very high in patients with Hepatitis B (74.2%) and Hepatitis non A non B (100%) infection (Table 2). Similarly exposure rates to HBV as indicated by anti HBcAg was also high in patients with Hepatitis A (70%) and Hepatitis non A non B (75%) infection. Three (15%) of 20 Hepatitis A patients were HBsAg positive. AFP by supplementary CIE was positive in 5 patients (3 Hepatitis A and 2 Hepatitis B).

DISCUSSION

This study showed for the first time the distribution of the different types of acute viral hepatitis in Singapore, 30% was due to HAV, 46% to HBV and 24% to HNANBV. There is a paucity of information regarding viral hepatitis, particularly to the different types of viral hepatitis in this whole region. In the United States during 1976 there were 56,000 cases of viral hepatitis reported, of which 59% were due to HAV, 27% to HBV and 14% to HNANBV (5). Prevalent studies of viral hepatitis in countries closer to this region showed that between 1971 and 1976 there was a progressive fall in HAV and a concomittant rise in HBV and HNANBV infection rates. In 1971 the prevalences of HAV, HBV and HNANBV infections in Fairfield Hospital, Melbourne was 71.1%, 21.7% and 8.3% respectively. This relative proportion changed to 46.1%, 38.0% and 15.9% respectively by 1976 (6). The relative proportion of the different types of viral hepatitis in Singapore is closer to those of Melbourne than those of the United States.

In agreement with other studies we found a high male to female ratio of 3.4 in HBV hepatitis. This male predominance was still observed in HAV hepatitis but almost disappeared to HNANBV hepatitis. Patients with HAV and HBV hepatitis tended to be young and had mean ages of 24.3 and 28.9 years respectively. On the other hand patients with HNANBV hepatitis were significantly older with a mean age of 40.2 years.

Our present study was hospital based and therefore would tend to increase the proportion of HBV and HNANBV infections because of the more severe nature of these infections. The relative proportions of the different types of viral hepatitis in the general population may well be different. Hepatitis B infection

TABLE 1
ACUTE VIRAL HEPATITIS IN SINGAPORE

TYPE OF HEPATITIS	NUMBER (%)	AGE	MALE : FEMALE RATIO
Hepatitis A	20 (30%)	*24.3 ± 6.2	1 : 9
Hepatitis B	31 (46%)	28.9 ± 13.7	3 : 4
Hepatitis non A non B	16 (24%)	40.2 ± 16.0	1 : 3
TOTAL	67		

*Mean ± 1 SD

TABLE 2
HEPATITIS A AND B MARKERS IN PATIENTS WITH ACUTE VIRAL HEPATITIS

TYPE OF HEPATITIS	NO	ANTI HA Ag		HBsAg		ANTI-HBcAg
		IgM	TOTAL	CIE	rPHA	
Hepatitis A	20	*20 (100%)	20 (100%)	2 (10.0%)	3 (15.0%)	14 (70%)
Hepatitis B	31	0	23 (74.2%)	19 (61.3%)	31 (100%)	31 (100%)
Hepatitis non A non B	16	0	16 (100%)	0	0	12 (75%)
TOTAL	67	20 (29.9%)	59 (88.1%)	21 (31.3%)	33 (49.3%)	57 (85.1%)

*Number positive (%)

in this study was based on the presence of HBsAg and the absence of IgM specific anti HA Ag. Some infections due to HNANBV could therefore still be classified under HBV infection. During the convalescent period of HBV infection, HBsAg may be absent and the only indication of a recent HBV infection is the presence of anti HBcAg. However this type of misdiagnosis in this study would be minimum because the blood samples were obtained during the acute phase, within the first two days of admission. Three HAV hepatitis patients in this study were HBsAg carriers and would have been wrongly classified as HBV hepatitis if IgM anti HA Ag had not been performed.

HAV infection may be underdiagnosed in this study. It is possible that IgM anti HA Ag may be affected by prolonged storage of sera. However against this possibility is that IgM anti HA Ag was detectable in this study and in several sera tested, this antibody was in high titre. In support that IgM could withstand prolonged storage at −20°C was the finding that the titre of IgM anti Epstein Barr virus in patients with infectious mononucleosis was not affected after prolonged storage at −20°C (unpublished data).

Both HAV and HBV are highly endemic in Singapore. This is reflected not only in the presence of clinical HAV and HBV infections but also by the high HBsAg carrier rate and the high exposure rate as indicated by anti HBcAg and anti HA Ag. In this study previous exposure to HBV in non HBV hepatitis patients as indicated by anti HBcAg was 72.2% (26/36). Similarly previous exposure to HAV in non HAV hepatitis patients was 83%. These findings were supported by the high frequency of anti HBcAg and anti HA Ag in our normal population (7, unpublished data).

LIST OF ABBREVIATIONS

HAV	: Hepatitis A Virus
HBV	: Hepatitis B Virus
HNANBV	: Hepatitis non A non B Virus
RIA	: Radioimmunoassay
CIE	: Counterimmunoelectrophoresis
AFP	: Alphafetoprotein
HBsAg	: Hepatitis B surface Antigen
HA Ag	: Hepatitis A Antigen
Anti HBcAg	: Antibody to Hepatitis B core Antigen
Anti HA Ag	: Antibody to Hepatitis A Antigen
IgM Anti HA Ag	: IgM Specific antibody to Hepatitis A Antigen

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