

Viral Hepatitis: Recent Experiences from Serological Studies in Bangladesh

W. I. Khan¹, R. Sultana¹, M. Rahman¹, H. Akhter¹, J. A. Haq², L. Ali², M. A. Mohsin¹ and A. K. A. Khan²

Viral hepatitis is a major public health problem throughout the world affecting several hundreds of millions of people. Hepatitis literally means inflammation of the liver. This disease can range from being subclinical to life threatening. Viruses are the most common and significant causes of hepatitis. Nevertheless, excessive consumption of alcohol, use of certain hepatotoxic drugs or other types of infectious diseases can also cause hepatitis.

Viral hepatitis is caused by a unique group of viruses that attack the liver and the currently known types are Hepatitis A (HAV), Hepatitis B (HBV), Hepatitis C (HCV), Hepatitis D (HDV), Hepatitis E (HEV) and Hepatitis G (HGV). Infections due to HAV, HBV, HCV and HDV viruses are associated with significant morbidity and mortality in developing countries. Infection with HDV virus occurs only in individuals already infected with HBV, as its replication depends on HBV.² Re-

SUMMARY Infections due to hepatitis A (HAV), hepatitis B (HBV), hepatitis C (HCV) and hepatitis E (HEV) viruses are the major causes of hepatitis and are associated with significant morbidity and mortality in developing countries like Bangladesh. The present study was carried out to determine the prevalence of HBsAg, anti-HCV antibody, anti-HAV antibody and anti-HEV antibody in patients suspected of having infection by HBV, HCV, HAV and HEV, respectively. Antibody to HAV was detected in 39% of subjects investigated. HBsAg was identified in 19% of subjects. Antibody to HCV and HEV was detected in 13% and 53% subjects, respectively. Infection with HAV was very high among children ≤ 6 years of age (100%). On the contrary, exposure to HEV was higher in adult persons ≥ 30 years of age (52%) compared to that in children ≤ 6 years of age who had 0% incidence. Our study clearly indicates a high prevalence of those viruses, particularly of enterically transmitted HAV and HEV in Bangladesh, which appeared to be a serious health problem in this developing country. Control measures should be taken on an urgent basis to prevent the spread of infections by these viruses.

cently, another virus, i.e. HGV has been identified³ and precise information regarding the importance of this virus seems to be becoming available soon. Viruses causing hepatitis can be transmitted by either fecal-oral routes, as in the case of HAV and HEV or it can be blood-borne, as in the case of HBV, HCV, HDV, and HGV. Individual hepatitis viruses are distinct with characteristic clinical illness and complications caused by them.

HAV and HEV mainly cause acute hepatitis and are only rarely associate with the chronic form. Both of the viruses are spread through ingestion of water or food contaminated with infected faecal material. HAV mostly affects

From the ¹Department of Immunology, National Diagnostic Network, Panthopath, Dhaka-1205, Bangladesh, ²Research Division, BIRDEM Academy, Dhaka, Bangladesh

Correspondence: W. I. Khan

young children⁴ and infection with this virus is very common among preschool children in the developing world. HAV is endemic in many developing countries in Asia and Africa.^{5,6} Most cases of HAV infections are subclinical or mild and self-limited. Infected adults tend to have a more severe or prolonged illness, sometimes accompanied by fulminant hepatitis. However, it is usually followed by complete recovery and life-long immunity. HEV was first recognized following epidemics of hepatitis in India unrelated to HAV or HBV.⁴ Epidemics of infection with HEV have also been observed in Southeast and Central Asia, Africa, and recently in Mexico.^{7,8} HEV mainly affects young adults and does not seem to confer good protective immunity, so re-infection is possible.⁹

The major mechanisms of HBV transmission are close personal contact involving salivary exchange, sexual contact, vertical transmission from mother to offspring, and exposure to infected blood.¹⁰ It has been reported that in areas of hyperendemicity such as in Asia and Oceania, HBV is transmitted primarily via the perinatal route.¹¹ HBV infection also occurs sporadically in Western Europe, North America and other developed countries.⁴ Infection with HCV is also a world-wide health problem. The incidence of HCV is high in Japan, Italy, the Middle East and it is particularly prevalent in developing countries.¹² HCV is thought to be less infectious than HBV and is mainly spread through blood transfusion, although sexual transmission may rarely occur.¹³ Most cases are clinically undetectable and in contrast with HBV, 70-80% of people who are acutely infected

progress to chronic active hepatitis.¹⁴

Recent years have seen advances in laboratory assays for investigating antibodies against HAV, HEV, HCV and also for various markers for HBV. However, the high cost of those assays has limited assessment in developing countries like Bangladesh. Precise information regarding the present situation of infections in this country caused by hepatitis viruses is still scanty. The present study was carried out to determine the prevalence of HBsAg, anti HCV antibody, anti HAV antibody and anti HEV antibody in patients suspected of having infection by HBV, HCV, HAV and HEV, respectively in Bangladesh with a view to throwing some light on the prevalence of those viruses in this country.

SUBJECTS AND METHODS

Between June 1996 and May 1998, a total number (N) of 1,823 patients suspected of suffering from HBV infection based on clinical findings were referred to the National Diagnostic Network (NDN), Dhaka, Bangladesh by clinicians throughout Bangladesh, to investigate hepatitis surface antigen (HBsAg). During the same period a total number 320, 98 and 180 suspected cases of HCV, HAV and HEV infection were also referred to NDN for investigating antibody against HCV, HAV and HEV, respectively. In all cases, blood samples were collected and sera were subjected to enzyme-linked immunosorbent assay (ELISA). HBsAg was assessed using commercially available enzyme immunoassays (Sorin, Biomedica, Italy). Anti-HAV IgM

(Sorin, Biomedica, Italy), Anti-HCV (Sorin, Biomedica, Italy) and Anti-HEV IgM (Genelab) antibodies were also determined by ELISA. Positive samples for HBsAg were confirmed by repeat ELISA (Organon Teknika, Netherlands).

RESULTS

A total number of 352 out of 1,823 (19%) suspected cases of HBV infection were found positive for HBsAg (Table 1). The prevalence rate in males (22%) was higher than females (13%). Most of the positive cases were over six years of age. Among the total 320 cases referred for investigating antibody against HCV, sera of 40 persons were found anti-HCV antibody positive, yielding a prevalence rate of 13% among the suspected cases (Table 2). The prevalence of antibody against HCV was also slightly higher in males (14%) compared to that in females (9%). Out of a total of 98 suspected cases of HAV infection, we detected 38 positive cases (39%) suffering from acute HAV infection as revealed by the presence of anti-HAV IgM antibody, which is considered to be the indicator of the acute phase of HAV infection (Table 3). In addition, we observed a 100% prevalence rate in children \leq 6 years of age and 0% prevalence rate in persons \geq 30 years of age among the cases suspected of HAV infection. On the contrary, among the suspected cases of HEV infection, prevalence of HEV seropositivity was higher in persons \geq 30 years of age (52%) compared to that in children \leq 6 years of age who had 0% prevalence (Table 4). We also observed a high prevalence for acute HEV infection among the

Table 1 Prevalence of hepatitis B surface antigen (HBsAg) by age and gender in patients suspected of suffering from HBV infection

	N	HBsAg Positive	
		N	(%)
Overall	1,823	352	(19)
≤ 6 years	67	6	(9)
7~12 years	91	21	(23)
13~18 years	129	33	(26)
19~30 years	686	154	(23)
≥ 30 years	850	138	(16)
Male	1,321	288	(22)
≤ 6 years	44	3	(7)
7~12 years	59	13	(27)
13~18 years	76	21	(28)
19~30 years	484	123	(25)
≥ 30 years	658	128	(19)
Female	502	64	(13)
≤ 6 years	23	3	(13)
7~12 years	32	8	(25)
13~18 years	53	11	(21)
19~30 years	202	31	(15)
≥ 30 years	192	11	(5)

Table 2 Presence of anti-HCV antibody in patients suspected of suffering from HCV infection

	N	Anti-HCV antibody	
		N	(%)
Overall	320	40	(13)
≤ 6 years	3	1	(33)
7~12 years	7	1	(14)
13~18 years	20	0	(0)
19~30 years	79	10	(13)
≥ 30 years	211	28	(13)
Male	243	33	(14)
≤ 6 years	2	1	(50)
7~12 years	3	0	(0)
13~18 years	14	0	(0)
19~30 years	62	10	(16)
≥ 30 years	162	22	(14)
Female	77	7	(9)
≤ 6 years	1	0	(0)
7~12 years	4	1	(25)
13~18 years	6	0	(0)
19~30 years	17	0	(0)
≥ 30 years	49	6	(12)

cases suspected of HEV infection. Among 180 persons investigated, 95 had detectable anti-HEV IgM antibody (53%) suggestive of recent HEV infection. Moreover, we observed a marked increase in HEV seropositive cases during the rainy season (June to August) of Bangladesh (data not shown).

DISCUSSION

The list of hepatitis viruses has been growing since the human volunteer studies of Krugman and his colleagues in New York over 30 years ago.¹⁵ At that time, there were only HAV and HBV but now there are HCV, HDV, HEV and HGV. The present data indicate a high prevalence of HAV, HBV, HCV and HEV in patients suspected of suffering from those viral infections in Bangladesh. Although our data do not represent the overall prevalence rate of viral hepatitis in Bangladesh and are based on investigations in suspected cases only, they probably show the current situation related to viral infections causing hepatitis in this country, particularly the incidence of acute HEV and HAV infections which seems to be quite alarming. Both HEV and HAV infections usually occur in crowded residential areas and are spread by the fecal-oral route. One intriguing issue is the very high prevalence of HAV in children in the age group ≤ 6 years and HEV in the age group ≥ 30 years. This demonstrates that HAV infection is acquired usually in the first few years of life. Our study corroborates with the findings of Arankalle and his colleagues⁵ in relation to the prevalence of those two viruses in India. In their study, they found that about 85% of children by the age of 5 years acquired HAV infection mainly through

Table 3 Incidence of presence of anti HAV IgM antibody in suspected cases of HAV infection

	N	Anti HAV IgM antibody	
		N	(%)
Overall	98	38	(39)
≤ 6 years	16	16	(100)
7~12 years	26	16	(62)
13~18 years	8	4	(50)
9~30 years	6	2	(33)
≥ 30 years	42	0	(0)
Male	68	22	(32)
≤ 6 years	8	8	(100)
7~12 years	14	8	(57)
13~18 years	6	4	(67)
19~30 years	6	2	(32)
≥ 30 years	34	0	(0)
Female	30	16	(53)
≤ 6 years	8	8	(100)
7~12 years	12	8	(67)
13~18 years	2	0	(0)
19~30 years	NA*	-	-
≥ 30 years	8	0	(0)

*NA: not available

Table 4 Prevalence of anti HEV IgM antibody among cases suspected of HEV infection

	N	Anti HEV IgM antibody	
		N	(%)
Overall	180	95	(53)
≤ 6 years	6	0	(0)
7~12 years	12	3	(25)
13~18 years	13	5	(39)
19~30 years	61	41	(75)
≥ 30 years	88	46	(52)
Male	119	62	(52)
≤ 6 years	3	0	(0)
7~12 years	6	3	(50)
13~18 years	7	3	(43)
19~30 years	40	24	(60)
≥ 30 years	63	32	(51)
Female	61	33	(54)
≤ 6 years	3	0	(0)
7~12 years	6	0	(0)
13~18 years	6	2	(33)
19~30 years	21	17	(42)
≥ 30 years	25	14	(56)

subclinical infection. The higher prevalence of antibody against HEV among adults compared with children is also similar to that reported for population-based studies in Somalia,¹⁶ Hong Kong⁷ and India.⁵ It is not clear why this infection occurs so predominantly in adults, but one possibility is that increased exposure of adults to increased volumes of contaminated food and water compared with infants and children can cause the adults to be more susceptible to infection caused by HEV. Extensive studies on this issue in different geographical situations can reveal the facts. The high prevalence of HEV infection in the rainy season seems to be related to the fecal contamination of the water supply, particularly during the flood, which often threatens the life of many people in this country. Even though Hepatitis B vaccine has been available for about 20 years, there are still many people in the world who do not benefit from its protection, mainly due to its high cost. We also observed a high prevalence of HBsAg in suspected cases of HBV infection in our study. Transmission of HBV can result from either vertical (mother to child) or horizontal (between other relatives or other unrelated children or adults) routes. In Bangladesh, 3-5% of the pregnant women were reported to be positive for HBsAg.¹⁷ Therefore, transmission through this route and also by transfusion of improperly screening blood, increased drug abuse and unsterile injections are likely to be responsible for the spread of this infection in this country. The number of HCV-infected patients is also quite alarming. The precise reasons remain to be determined but again unsterile injections and blood transfusion without proper screening, seem to be responsible for the

spread of this viral infection in this country.

We observed a high prevalence of HAV, HBV, HCV and HEV in the Bangladeshi population suspected of having suffered from those viral infections, particularly the situation with enteric viruses. HEV and HAV appeared to cause a serious health problem in this poor country with a large population. Extensive studies based on randomized selection of persons will give us more precise information on the overall prevalence rate of those viral infections in this country. Control measures must be taken immediately to prevent the spread of those viruses. Implementation of standard public health approaches like provision of clean water, proper disposal of sewage and improved personal hygiene through health education can help control HAV and HEV infections. To prevent HBV infection, vaccination should be encouraged, but as most of the people of this country cannot afford to go for vaccination due to financial reasons, prevention of hepatitis B can also be achieved probably by educational programs related to the practices that increase the risk of horizontal transmission. Proper screening of blood before transfusion and use of sterile syringes should be encouraged at all levels. Increasing awareness in dealing with blood and blood products will also decrease the spread of HCV infection. Bearing in mind that chronic hepatitis may follow an inapparent acute hepatitis and the disease having an indolent course of many years, nonetheless progres-

sing silently to cirrhosis, necessary measures should be taken immediately to combat those viruses causing hepatic diseases.

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