Sero-Diagnosis for Viral Hepatitis in 93 Patients Admitted with Acute Hepatitis in Three Different Teaching Hospitals in Lahore

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Abstract

Serodiagnosis was done in 93 patients admitted with acute viral hepatitis (AVH) to three teaching hospitals in Lahore. Five (5.4%) had hepatitis A, 39(41.9%) hepatitis B (2 of these were anti delta positive), 44 (47.3%) probable hepatitis E and 3(3.2%) had HAVIHBV co-infection. Antibody to hepatitis C (anti HCV) was detected in 6 patients (6.4%); 2 with HBV and 4 with probable HEY infection. Excluding 39 patients with hepatitis B and 3 with HBV as part of co-infection, there was evidence of previous HBV infection in 39 out of the remaining 51 patients. In the subset of 6 children, 3 had hepatitis A and 3 hepatitis E Of these, Shad evidence of previous exposure to HBV and one was also positive for anti HCV. Our results are suggestive of a strong background of HBV infection raising concern about its chronic sequelae in the community (JPMA 44:182, 1994).

Viral hepatitis is a worldwide problem, but is particularly rampant in the developing countries including Pakistan. In these countries viral hepatitis is endemic and is punctuated by periodic outbreaks[1]. Apart from the widespread morbidity caused by acute phase of infection there is a predilection to chronicity by HBV, I{DV and HCV in a certain proportion of patients. There are 300 million carriers of HBVin the World[2]. The pattern of infection by hepatitis vimses differs in various countries and geographical areas[3-8]. In Pakistan sporadic studies have been undertaken on seroepidemiology of AVH in hospitalized patients by workers in Rawalpindi[9] and Karachi[10], which showed differences in frequencies of NANB and B hepatitis adult in cases of AVH. These studies used acute phase serological markers for hepatitis A and B to categorize their patients. In this study of serodiagnosis of AVH, we used a range of seromarkers for HAY, HBV, HDV as well as a second generation seromarker for HCV In addition, our patients were drawn from three different hospitals in the metropolitan city of Lahore sewing localities of relatively different socioeconomic background.

Patients and Methods

This was a collaborative hospital based study carried out by the Liver Study Group in Lahore, between May, 1991 to December, 1991 after approval by the ethical committee of the group based on the criteria laid down in the declaration of Helsinki. The Group comprised of senior investigators from three teaching hospitals and Institute of Experimental Medicine, Lahore. The three hospitals i.e. Mayo, Services and Shaikh Zayed are located in the different areas of the city serving patients of relatively different socioeconomic strata; for instance, Mayo Hospital near the old walled city serves the lower class area, while Shaikh Zayed is located in a relatively upper class suburb. The Services Hospital is located between these two and the patients sewed are of a mixed type. Ninety-three unselected

hospitalized patients with clinical diagnosis of AVH were investigated after obtaining informed consent from the patients or their guardians in those below 18. Thirty-five patients were from Mayo, 39 from Services and 19 from Shaikh Zayed Hospital. The diagnosis was based on history, clinical findings and raised alanine amino transferase (ALT) levels of more than 2.5 times the maximum limit. Relevant information regarding their socioeconomic background, history of drug intake, injections, transfusion, vaccination and contact with a case of hepatitis was recorded. Monthly family income was used to determine the socioeconomic class. Besides seromarkers for hepatitis, laboratory investigations in all patients included CBC, urinalysis, serum bilirubin, transaniinases and alkaline phosphatase. Other causes of jaundice were excluded by careful history and physical examination. Screening tests for infectious mononucleosis (I.M Quick, Human) and IgM antibody to cytomegalovirus (Abbott CMY-M-EIA) were also done. Blood samples were collected in vacutainers for seromarkers, sera separated by centrifugation and stored at -70°C until analyzed. The in-vitro, qualitative enzyme immunoassay serodiagnostic tests were performed in duplicate by ELISA test system of Abbott Laboratories, Chicago (USA) according to the procedure recommended by the manufacture. The serodiagnostic criteria for AVH due to hepatitis viruses were: i)acute HAy: positive for IgM anti HAY, ii)HBV: positive for IgM anti HBc; iii) HEV (NANB): negative for IgM anti HAY and IgM anti HBc; iv)HDY: positive for anti HDY in}{Bs Ag positive patients and v) co-infection: when two acute phase semmarkers were present Since acute phase tests for HCV are not available, anti HCVpositivity was considered as denoting past HCY infection.

Results

There were 70 males and 23 females and except for 6 children (age <12 years), all were adults. The mean age of adult patients was 32 years and that of children 7 years. The age distribution showed 18 patients (13 males and 5 females) between 0-19 years, 49 (40 males and 9 females) between 20-39 years and 26 patients (17 males and 9 females) of 40 years or above. Sixty-eight of 93 patients (73%) were drawn from u than or semi-u than areas and 25 (27%) from rural setting. The number of patients was almost equally distributed between lower and middle class i.e., 46 and 44 subjects respectively with only 3 patients from the upper class. History of contact with a case of hepatitis during the preceding 6 months was present in 20(21.5%) and of injections during the similar period in 29(30.2%) patients. There was a past history of jaundice in 10 and blood transfusions in 3 patients. History of vaccinations against hepatitis B was negative in all. The serum bilirubin ranged between 2.5-21 mg/dl. In 44 patients, serum bilirubin was more than 10 mg/dl and in 49 patients less than 10 mg/dl. The ALT levels ranged between 95-2865 I.U./L with levels of more than 10 times of up perlimit in 38 patients. The screening tests for infectious mononucleosis and 1gM anti-CMV were negative in all patients. The results of serodiagnosis for hepatitis viruses in 93 patients of AVH are shown in Table I.

Table I. Sero-diagnostic profile and positivity of seromarkers in 93 patients of acute viral hepatitis.

Type of acute hepatitis; number; percent	No. of	IgM anti HAV	HBsAg	IgM ant HBc	HBeAg	IgG anti HBc	Anti HBe	Anti HBs	Anti HCV	Anti HDV
1. HAV; n=5 (5.4%)										
Alone	1	1	0	0	0	0	0	0	0	0
With past HBV infection	4	4	3	0	1	2	0	0	0	0
2. HBV; n=39 (41.9%)										
Alone	37	0	29	37	11	35	17	0	0	0
With past HCV infection	2	0	2	2	1	2	0	0	2	0
3. HEV; n=44 (47.3%)										
i) HEV (NANB, non C) n=40										
HEV with past HBV	29	0	20	0	3	23	6	5	0	0
HEV only	11	0	0	0	0	0	0	0	0	0
ii) HEV with past HCV and HBV N=4	4	0	2	0	0	3	0	1	4	0
4. HDV; N=2 (2.2%)	2	0	2	0	0	2	1	1	0	2
5. Co-infection n=3 (3.2%)										
HAV with HBV	3	3	3	3	1	3	1	0	0	0

In 3 patients in this group, positivity of other seromarkers included HBsAg(n=3), IgGanti-HBc(n=3), HBeAg(n=1), and anti- }{Be(n=1). Serodiagnostic and other features in the group of 6 children are shown in Table II.

Table II. Sero-diagnosis for AVH and other relevant featurs in the subset of 6 children in the study.

Age (yrs)	Sex	Residence	Socio-economic class	History of contact	History of injection/ transfusion	Sero-diagnostic profile
9	Male	Urban	Lower	-	-	HAV with past HBV infection (HBsAg and anti HBc+)
6	Female	Urban	Lower	-	+	HAV with past HBV infection (HBsAg+)
4	Male	Urban	Middle	-	-	HAV with past HBV infection (HBeAg+)
9	Male	Rural	Middle	-	-	NANB non-C (HEV) with past HBV infection (HBsAg and anti HBc+)
9	Male	Urban	Lower	+	-	NANB non-C (HEV)
9	Male	Rural	Middle	-	+	HEV with positive anti HCV and past HBV infection (HBsAg and anti HBc+)

Ages of 6 children ranged between 4-9 years. The socioeconomic status was equally distributed between lower and middle class. Four cases were from urban and 2 from rural areas. History of contact with a hepatitis patient during the preceding 5 months in 1, while past history of jaundice was negative in all. A history of injections and dental treatment during the past 6 months was present in 2 while none had history of recent drug intake or vaccination against HBV. Of 6 children AVH was caused by HAV in 3, and HEV(NANB) in 3, one of whom was also positive for anti-HCV. Five out of 6 children had evidence of antecedent HBV exposure which included positivity for HBsAg in 4, HBeAg in 1 and anti-HBc in 3.

Discussion

Over the past few years attempts have been made to characterize the seroepidemiology of AVH in our country. A study in adult patients from a military hospital in Rawalpindi during 1984-86[9] showed NANB as the predominant type (77%) whereas, the next major type was HBV (23%). Another report by the same investigators[10], revealed that in children HAV (59.3%) was the most frequent type followed by NANB (29.7%), HEV (6.6%) with dual infection of HAV and HBV in (4.4%) of these patients. Report from Karachi showed NANB in 53% HBV in 45% and HAV in 2% of the adult patients[11]. Our study showed that 5 patients had acute HAV of whom 4(3 of whom children), also had antecedent HBV infection; the remaining one patientum a foreign student, was positive only for IgM anti HAV. There were 3 other patients, all adults, with HAV was associated with HBV co-infection, meaning there by that HAV could still be a diagnostic consideration in adults. Acute HBV was diagnosed in 42 patients negative test for HBsAg in 8 patients supports the observation that the presence of IgM anti-HBc provides cretical diagnostic information for the acute phase of HBV infection[12]. NANB or probable HEV was another major group comprising of 44 patients, 11 of whom were negative for all sero-markers, whereas 33 had evidence of antecedent HBV infection. These cases were of hepatitis E which is common in the developing countries[13]. In countries like USA, however, HCV account for a vast majority of community acquired NANB hepatitis[5]. Anti HCV was positive in 6 patients; 4 with hepatitis E and past HBV exposure and 2 with acute HBV. It is difficult to differentiate between acute and chronic HCV on the basis of currently available assays, as it has been observed that HCV anti-bodies may take longer to appear following infection[14]. For the same reason, some clinically suspected cases may remain undetected without follow-up. The prevalence of delta super infection was low (2.2%) amongst HBsAg positive patients. A similar relatively low prevalence i.e., 3.1% was reported from Rawalpindi[15]. In conclusion, the study group showed HEV (NANB) and HBV as the major causative agents for AVH. However, there was evidence of past HBV infection in a sizeable number of patients including children. A part from HBV, HCV can pose a threat as it can last for indefinite period even after the resolution of hepatitis and has a high tendency to choronicity[16]. A recent study in patients on choronc haemodialysis in a Lahore hospital showed that the prevalence of anti HCV was 62%[17]. The predominance of antecedent and acute HBV infection raises concern for chronic liver disease and calls for extensive epidemiological studies and preventive measures.

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