



Clinico-Serological profile of Acute Sporadic Viral Hepatitis in Kashmiri Adults: Hospital based Prospective Study

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Abstract

Background: *There is no report on clinico-serological profile of acute viral hepatitis from the state of J & K since the discovery of hepatitis E and hepatitis C.*

Methods: *A prospective hospital based study was conducted in a large referral hospital in Kashmir India. 56 consecutive patients with acute viral hepatitis were studied for their presentation, etiology and clinical features.*

Results: *Acute viral hepatitis was more common in males with MF ratio of 1.33:1. Forty (71.4%) belonged to rural and 16(28.57%) to urban areas. Most commonly involved age group was 21-30 years (37%) followed by 14-20 years (25%). Most commonly observed symptoms were Jaundice (82%), Anorexia (76.8%), and dark urine (73.2%). Only 7% patients had cholestatic features. 5.4% patients had anicteric hepatitis. Hepatomegaly was observed in 68.8% and splenomegaly in 19.6%. Clinical and biochemical characteristics were not helpful in differentiating various types of hepatotropic viral hepatitis. Most common viral infections was hepatitis E(50%), followed by hepatitis B(26.7%), hepatitis A(16%), hepatitis C (3.5%) and dual infection of hepatitis A and E in(3.5%).*

Conclusion: *Acute viral hepatitis is an important public health problem in developing countries. Most cases are due to hepatitis E, and hepatitis A continues to be an important cause of acute viral hepatitis in developing countries even in adults. Clinical and biochemical characteristics were not helpful in differentiating different types of hepatotropic viral hepatitis.*

Key words: *viral hepatitis, hepatitis E, hepatitis A, clinico-serological profile.*

INTRODUCTION

Acute viral hepatitis is a systemic infection affecting the liver predominantly. It is characterized by diffuse necroinflammatory infection of liver. Hepatotrophic viruses cause 98.99% cases of acute viral hepatitis. Among Hepatotrophic viruses almost all are caused by one of the five viral agents' viz. hepatitis A virus (HAV), hepatitis B virus (HBV), hepatitis C virus (HCV), hepatitis D virus (HDV) and hepatitis E (HEV) while as only 1-2% are caused by non-hepatotrophic viruses ^[1].

In under developed and developing countries, hepatitis E is commonest cause of acute viral infection constituting about 44% of all cases, followed by hepatitis B(29.7%), hepatitis A (5%), hepatitis C (1%) and hepatitis D (0.9%) ^[2]. Hepatitis E and A are transmitted by faeco-oral route while as hepatitis B,C and D are transmitted by parenteral route. Hepatitis E has also been shown to be transmitted by parenteral transmission also ^[3]. There is also evidence that hepatitis E is a zoonotic disease being transmitted from animals to humans ^[4]. In India, both sporadic and epidemic cases of viral hepatitis are common. The outbreaks of adult population had mostly been caused by hepatitis E virus (HEV) and are related to sewage contamination of drinking water supplies. In contrast to adults, HAV is the most common cause of acute hepatitis in children ^[4]. Overall 40-50% of sporadic cases are due to HEV, while as HBV and HAV account for 16-40% and 2-30% respectively. HCV is less frequent cause being seen in less than 10% of all cases.

All types of acute viral hepatitis produce clinically similar illnesses, ranging from asymptomatic infection to fulminant liver failure at one end and subclinical persistent infection to rapidly progressive disease with cirrhosis at other end. The usual icteric attack in adults is marked by a prodromal period of about 3-4 days. Initial Flu like illness is common to almost all infections which may follow or may be accompanied by loss of appetite, aversion to smoking, distaste for food, pain upper abdomen and abdominal discomfort ^[5]. Prodromal period is followed by darkening of urine and lightening of faeces. This heralds development of yellowish discoloration of eyes. Pruritis may appear transiently for few days ^[5]. Physical findings include jaundice, tender hepatomegaly, lymphadenopathy and splenomegaly. Hepatomegaly occurs in 70% and splenomegaly in 20% of patients.

The course of acute viral hepatitis varies from patient to patient ranging from subclinical disease to self limiting symptomatic illness to fulminant liver failure ^[6]. Clinical and biochemical recovery is usually within six months of onset of illness. Severe cases of acute hepatitis may progress rapidly to acute liver failure, marked by poor hepatic synthetic function. Fulminant hepatic failure may occur in as many as 1 percent of cases of hepatitis B or A. Hepatitis E is a common cause of fulminant hepatic failure in Asians. In hepatitis B, 95-97 percent of patients recover completely while as 3-5 percent develop chronic infection. In case of hepatitis C, 85 percent of newly infected

patients remain viremic and may develop chronic liver disease.

MATERIAL AND METHODS

This hospital based study was conducted in Postgraduate department of Medicine, SMHS hospital Srinagar, Kashmir from July 2009 to December 2010. Patients of acute viral hepatitis of age more than 14 years were selected from both inpatient and outpatient departments. There were no controls. The diagnosis of acute viral hepatitis was based on accepted clinical and biochemical criteria. A detailed history and meticulous examination was performed. Liver function tests (LFT) were performed every 15 days till clinical and biochemical recovery. The exclusion criteria include age less than 14 years, history of intake of known hepatotoxic drug, previous hepatitis like illness, congestive hepatopathy, patients with ischemic hepatitis, patients with severe infection or multisystemic failure, known cases of HBsAg positivity or Chronic liver disease, patients with extrhepatic biliary obstruction and seronegative acute hepatitis patients. All biochemical liver function tests along with serum transaminases were performed using HITACHI Boehringer Mannheims 912 Auto-Analyzer. Ultrasonography was performed by a single expert sonologist who was aware of the patients symptoms and presumptive diagnosis. The USG machine GE Logic 200 Pro-Series was used. The serology of hepatitis A-E was performed using following ELISA kits:

- ✓ Immunovisions ELISA kit for anti-HAV IgM and anti-HEV IgM.
- ✓ J. Mitras HEPALISA kit for HBsAg and anti-HDV IgM.
- ✓ Adaltis Italia Spa EIGN, HCV Ab (H4) kit for anti-HCV.
- ✓ Immunovisions ELISA kit/J. Mitras HEPALISA kit for anti-HBc IgM.

The diagnosis of acute viral hepatitis was based upon an illness with less than one month of duration with symptoms compatible with acute viral hepatitis, an initial serum level of alanine aminotransferase (ALT) of more than fivefold the upper limit of normal, and exclusion of the other potential nonviral causes of hepatocellular injury and ruling out alcoholic hepatitis, chronic liver disease, anoxic hepatitis, drug induced hepatitis and systemic disease such as a malaria, typhoid and brucellosis by conventional clinical and laboratory studies wherever needed.

Acute hepatitis A was diagnosed if serum sample tested positive for IgM anti-HAV. Acute hepatitis B was diagnosed if serum sample tested positive for HBsAg and IgM anti- HBc. Hepatitis C was diagnosed if serum tested positive for anti-HCV at initial visit and 3 months later. Hepatitis E was diagnosed if serum tested positive for IgM anti-HEV. The statistical inference was deduced after the whole patient data was fed in computer using Statistical Package for Social Sciences (SPSS) Ver. 17.0. The frequency distribution was compared using chi-square tests. The student 't' test was used for comparison of mean values. All

values were expressed as mean±SD. A p-value of <0.05 was considered as statistically significant.

RESULTS

A total number 56 sero-positive patients, including 32 males and 24 females, 40 patients from rural and 16 from urban areas were included in study. 35(62%) patients were from 14-30 years of age with 14(25%) in age group of 14-20 years and 21(37%) in the age group of 21-30. Mean age of presentation was 30 years. The commonest symptoms observed were jaundice (82.10%), anorexia (76.8%) and high colored urine in 73% of cases. Cholestatic features were present in only 4(7.10%) of patients. 53(94.60%) patients were icteric at presentation, 38 (67.80%) had hepatomegaly and 11 (19.60%) patients had splenomegaly. 11 (19.64%) patients had serum bilirubin less than 3mg/dl while as only 2 (3.5%) had a serum bilirubin more than 24mg/dl. The mean bilirubin elevation was 8.61 mg/dl. The mean AST level was 983.4 IU/ml and mean ALT

level was 993.2 IU/ml. Out of 56 cases 28 (50%) were sero-positive for hepatitis E, 15 (26.70%) had serology positive for hepatitis B. Nine had hepatitis A and 2 cases had dual infection with hepatitis E and A [Table 1]

There was a uniform involvement of males and females by various viral infections, with no Statistical significance. There was no demographic difference of involvement in various viral infections, all the viruses involving both urban and rural areas equally. Hepatitis A and hepatitis E infections were more common in younger patients, age less than 30 years while as hepatitis B was more common in age group of 31-40 years [Table 2].

Mean serum bilirubin for hepatitis A was 8.11mg/dl, for hepatitis B 6.73mg, for hepatitis C 5.95mg/dl and for hepatitis E it was 10.23 mg/dl. Mean serum AST, ALT in various infections also varied with hepatitis A and hepatitis E showing higher levels than hepatitis B and C.

Table 1: Hepatitis Virus Sero-positivity among cases (n=56)

Viral Marker	No. of Cases	Percentage
Anti-HAV IgM	09	16.00
Anti-HAV IgM & Anti-HEV IgM	02	03.50
HBsAg	15	26.70
Anti-HCV	02	03.50
Anti-HEV IgM	28	50.00
Total	56	100.00

$\chi^2 = 42.03$; $p = 0.000$

Table – 2 Hepatitis Virus Sero-positivity among cases with respect to age (n=56)

Age (Years)	Anti-HAV IgM		Anti-HAV IgM and Anti-HEV IgM		HBsAg		Anti-HCV		Anti-HEV IgM		Total	
	No. of Cases	Percentage	No. of Cases	Percentage	No. of Cases	Percentage	No. of Cases	Percentage	No. of Cases	Percentage	No. of Cases	Percentage
14-20	07	12.50	00	00	01	1.70	01	1.70	05	08.90	14	25.00
21-30	02	03.50	02	3.50	03	5.30	0	0.00	14	02.50	21	37.50
31-40	00	00	00	00	07	12.50	0	0.00	6	10.70	13	23.00
41-50	00	00	00	00	02	3.50	0	0.00	2	03.50	04	07.00
51-60	00	00	00	00	01	1.70	1	1.70	1	01.70	03	05.00
61-70	00	00	00	00	01	1.70	0	0	0	00.00	01	01.70
Total	09	16.0	02	03.50	15	26.78	2	03.50	28	50.00	56	100.00

$\chi^2 = 33.14; p = 0.001$

Table 3: Mean Serum Bilirubin/AST/ALT of the Cases at presentation

Serology	Mean bilirubin at First contact (n=56)	Mean AST at First Contact (n=56)	Mean ALT at First Contact (n=56)	Mean ALP at First Contact (n=56)
Anti-HAV IgM	8.11	1474.9	1589.2	129.53
Anti-HAV IgM and Anti-HEV IgM	4.95	653.5	881.5	117
HBsAg	6.73	1134.6	821.86	238.2
Anti-HCV	5.95	143	179.0	367
Anti-HEV IgM	10.23	1511	1494.71	280.8

DISCUSSION

Out of 56 patients, the mean age of presentation was 30±12.4 years, the youngest one 14 years and oldest one 70 years. The male to female ratio was 1.33:1. This difference was statistically insignificant. This clarifies the fact that acute hepatitis affects males slightly more than females.

The same has been reported by many other authors [7, 8, 9, 10, 11, and 12]. Majority of our cases were in the age group of 21-30 years (37%) and 14- 20 years (25%). This age distribution was statistically significant with a P value of < 0.001. This observation was in accordance with

observations of H. Kaur et.al, Subrat et.al, and Nandi et.al^[10, 12,13]. The most common symptoms observed were jaundice (86.10%), anorexia (76.80%), high colored urine (73%), fever with chills (66.1%) and abdominal pain in 39.3%. Less common symptoms were clay colored stools and itching. Commonest^[13] clinical signs were icterus (94.6%), hepatomegaly (61.8%) and splenomegaly (19.60%). These results were in conformity with results of H. Kaur et al^[10], Nandi et al^[13], Khuroo et al^[14].

Total mean bilirubin among cases was 8.61 mg/dl ranging from 0.4mg to 27mg. Eleven patients had anicteric hepatitis with bilirubin levels less than 3mg/dl. In Khuroo's study^[14], mean bilirubin was 5.58±3.73mg/dl ranging from 2-22mg/dl. H. Kaur et al^[10] also observed that the mean serum bilirubin in patients who recovered from acute hepatitis was 10.5mg/dl. In this study hepatitis E was found to be most common cause of acute viral hepatitis accounting for 50% of patients. 15 cases (26.70%) had acute hepatitis B (HBsAg +ve, HBc IgM positive), nine patients(16%) had acute hepatitis A(anti-HAV IgM positive). These observations were consistent with other studies from India. H. Kaur et al^[10] study reported that Hepatitis E was encountered most frequently (44.56%) followed by hepatitis B (29.7%), whereas hepatitis D occurred least frequently 0.99%. Nandi et al reported from his study that Hepatitis-E was detected in 45.4%, hepatitis A in 33% and hepatitis B in 12.5% patients. Acute hepatitis C was detected in 0.01% of patients. Kunal Das et al^[15] found that 53.3% of sporadic

acute viral hepatitis cases were due to hepatitis E virus while 11% were due to hepatitis B virus. Hepatitis C virus was responsible for 8% of the sporadic AVH cases and hepatitis A was found in 5% of the cases. Khuroo, M. S. et al^[14] reported that etiology in sporadic acute viral hepatitis was hepatitis E virus (HEV) in 49.6%, hepatitis B virus (HBV) in 15%, hepatitis A virus (HAV) in 1.5%, hepatitis C virus (HCV) in 1.7%, hepatitis D virus (HDV) co-infection in 1.5%. Tandon et al^[16] reported non-A non- B hepatitis viruses to be the cause for 44% of sporadic acute viral hepatitis in adults. J Bansal et al^[17] observed that 42 percent of cases of sporadic viral hepatitis were positive for anti-HEV antibodies. Subrat Kumar et al^[18] reported from his study that 38.6 % of the patients with acute viral hepatitis were positive for anti-HEV IgM, 17.5% were positive for anti-HAV IgM, 7.3% were positive for HBsAg, 2.8% were positive for anti-HCV. Jagir Singh et al^[19] observed that hepatitis A and Hepatitis E combined together contributed 68% of acute sporadic viral hepatitis and hepatitis B,C,D contributed together for about 32% of acute viral hepatitis. Our observations were according to the above discussed studies. Two of our patients (3.50%) had dual infection with acute hepatitis A and E. Ayobanji et al^[20] also observed dual infection in 4 out of 246 (0.02%) of their patients. In study by Nandi et al^[13], out of 252 patients 0.063% were shown to have dual infection with hepatitis A and E. No one among 56 of our cases was positive for hepatitis D serology. In the study from Chau et al. out of 444 patients, none had hepatitis D coinfection or superinfection. The

same results were shown by M Irshad and others [21]. In H Kaur's [10] series, 0.99 % of his patients had serology positive for hepatitis D, Hepatitis E and A patients had highest transaminases levels. Mean AST in hepatitis E was 1511.07IU/L and for hepatitis A was 1474 IU/L. Highest mean AST levels for hepatitis E was 1494 IU/L and for hepatitis A it was 1589 IU/L. Same observations were made by H. Kaur et al, however in their study hepatitis B patients also had high levels of aminotransferases, more than that of hepatitis A.

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