

## ORIGINAL ARTICLE

## Pattern of Liver Function Tests in Spectrum of Acute Viral Hepatitis

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## ABSTRACT

**Objective:** To find out the pattern of Liver Function tests (LFTs) in different spectrums of Acute Viral Hepatitis (AVH).

**Study Design:** Cross sectional.

**Place and Duration of Study:** The study was conducted at Pathology Department of Combined Military Hospital, Malir Karachi from March 2017 to August 2017.

**Materials and Methods:** A total of 360 subjects of all age groups, both male and female, with biochemical features of acute viral hepatitis (AVH) were included. After clinical history and examination, liver function tests (LFTs) were performed that included total bilirubin, alanine amino transferases (ALT), alkaline phosphatase (ALP), followed by viral markers for hepatitis A virus (HAV), hepatitis B virus (HBV) hepatitis C virus (HCV) and hepatitis E virus (HEV).

**Results:** Among the 360 patients studied, males (n=308, 86%) outnumbered females (n=52, 14%). Biochemical pattern showed ALT value reaching >75 times the upper limit of normal (ULN). Similarly rise of serum total bilirubin was up to 30 times of ULN while rise of serum ALP was not more than 5 times of ULN. HEV was found to be the most common (28%) in seropositive AVH in the study group. Highest number (24.4%) of HEV infection was found among males in the age group of 20-30 years. ALT and bilirubin were significantly raised in patients with HEV as compared to other causes of AVH.

**Conclusion:** Pattern of LFTs varies in spectrum of AVH. Highest rise of ALT indicates extensive liver damage in HEV infection.

**Key Words:** AVH, HEV, LFTs.

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## Introduction

Viral hepatitis is an epidemic worldwide and over 13 million people suffer in Pakistan while in Asia pacific region one person dies every 30 second from hepatitis.<sup>1</sup> Deaths of 1.44 million, were identified by Global Burden of Disease Study 2010 (GBD 2010) due

to viral hepatitis, this accounted for 2.7% of all deaths in that year.<sup>2</sup> World Health Organization (WHO) and other collaborators conduct “World Hepatitis Day” on 28th of July every year to enhance the public awareness and intensify the preventive and control measures for viral hepatitis.<sup>2</sup>

In Pakistan, major cause of acute viral hepatitis (AVH) is hepatitis E virus (HEV) especially in adults belonging to lower socioeconomic groups.<sup>3</sup> Hepatitis A virus (HAV) and HEV accounted for 159,400 deaths globally in 2010.<sup>2,4</sup> Pakistan Field Epidemiology and Laboratory Training Program (FELTP) supported by the Center for Disease Control and Prevention (CDC) USA reported 712 new cases of viral hepatitis during June 2010 and March 2011 with Hepatitis C virus (HCV) infection accounting for 53.2% of newly reported cases, followed by HAV (19.8%) and HEV (12.2%).<sup>5</sup> Till now six distinct types of hepatitis viruses have been isolated and named as hepatitis A, B, C, D, E and G viruses.<sup>6</sup> More than 10 million people in Pakistan are living with HCV infection.<sup>7</sup> The

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mortality rate for HEV is low (1-2%), except in pregnant females (15-20%).<sup>8</sup> Chronic HEV is now sporadically seen in organ transplant recipients, patients on hemodialysis, HIV patients and those with hematological malignancies.<sup>9</sup> If left untreated, it may eventually progress to cirrhosis among immunocompromised patients.<sup>10,11</sup> An outbreak of HEV infection had also occurred in cruise ship because of use of seafood.<sup>12</sup> In severe instances, it can result in acute fulminant liver failure, disability and death.<sup>13</sup>

Hepatitis A and E are enterically transmitted, self-limiting AVHs. The risk factors identified for HAV and HEV infections include unsafe or contaminated food and water and poor sanitary conditions<sup>5</sup>, while HBV and HCV infections are transmitted through blood and other body fluids.<sup>6</sup> The onset of acute hepatitis is typically 2 to 24 weeks after exposure and it is unlikely to occur after 52 weeks or earlier than 4 days.<sup>13</sup> Patient presents with insidious onset of symptoms including fever, malaise, nausea, vomiting, deep yellow color of urine and pain abdomen, while signs include jaundice, pallor and tender hepatomegaly. At present HEV of two distinct origins has been identified in Pakistan based on genotype, namely Sar-55 from Central Asian origin and Abb-2B from South Asia. Of these, Abb-2B is believed to be endemic in Pakistan.<sup>14</sup> Early diagnosis of HEV infection is very important and timely management can prevent life threatening condition like acute fulminate hepatic failure but investigation for confirmation of HEV is routinely not performed, however monitoring of biochemical parameters of liver function tests (LFTs) remains very helpful in this situation. There are few published studies on biochemical pattern of LFTs to help in differentiating the causes of AVH especially in our population. This study was planned to highlight the importance of LFTs in different spectra of AVH.

### Materials and Methods

The study was conducted at Department of Pathology, Combined Military Hospital, Malir Karachi from March to August 2017, after the approval of the institutional review committee. Patients with clinical or biochemical features of acute hepatitis were included in the study. Patients with clinical or ultrasonographic evidence of biliary obstruction, chronic hepatitis B and C or chronic liver disease

were excluded. A total of 360 patients were selected over a period of six months with nonprobability random sampling technique. Clinical profiles of the patients were recorded and LFTs were performed on Selectra Pro M chemistry analyzer, that includes serum bilirubin done by modified Jendrassik and Groff method. Serum ALT and ALP were done by Kinetic methods. Upper limit of normal (ULN) was 17umol/L for bilirubin, 40 IU/L for ALT and 170 IU/L for ALP. All patients were tested for hepatitis B surface antigen (HBsAg) by Enzyme Labeled Immuno Sorbent Immunoassay (ELISA). Antibody to hepatitis C Virus (anti-HCV) was measured by 3<sup>rd</sup> generation ELISA. Sample for IgM HAV and HEV were sent to Armed Forces Institute of Pathology Rawalpindi (AFIP) for analysis. All patients were followed up for complete clinical and biochemical recovery. Statistical analysis was done on SPSS 20.

### Results

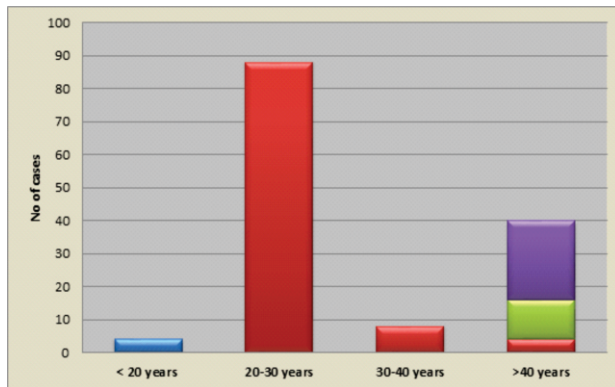
Among the 360 patients studied, males (86%) outnumbered females (14%) (Table 1). Maximum numbers of cases were young adults. Most common age group was 20 to 30 years (Figure-1). Seronegative hepatitis significantly outnumbered (n=220, 61%) the seropositive hepatitis (n=140, 39%) cases. Highest number (24.4%) of HEV infection was found among the age group of 20-30 years (Figure-1). HEV infection was found to be the most common (28%) in seropositive AVH in the study group (Figure-2). Surprisingly all were males. HCV infection was found in 24 (7%) patients, whereas HBV infection in 12 (3%). HAV was positive only in 4 (1%) patients in age group <20 years (Figure-1). We found a relative sparing of age groups below 10 years.

Biochemical spectrum of LFTs in seronegative AVH showed that maximum rise of serum bilirubin was up to 540 umol/l about 30 times of ULN. Maximum rise of ALT was >75 times of ULN (3210 U/L) with an average rise up to 1763 U/L seen in 68 cases and maximum rise of serum ALP was 2890 in a single case whereas it was 2-5 times of ULN seen in 184 cases (Table 2). In seropositive AVH, maximum rise of bilirubin was 130 umol/l in HEV, 57 umol/l in HBV, 109 umol/l in HAV and 31 umol/l in HCV (Figure 3), while maximum rise of serum ALP was 680 and 508 U/L in AVH A and E respectively. ALT was raised in almost 90% of AVH patients, being remarkably raised (1020 U/L) in HEV, whereas maximum rise noted in

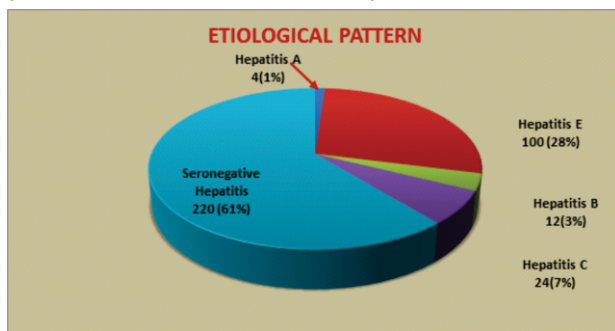
HAV was 723 U/L, 363 U/L in HBV and 63 U/L in HCV, which was statistically significant,  $p$  value < 0.05 (Table 3). Four patients progressed to acute fulminate hepatic failure. Two cases were diagnosed with hepatitis E and the other two cases had seronegative hepatitis. Except for these four patients, all gradually recovered. In general, there was greater rise of all parameters of LFTs in HEV indicating extensive liver damage than other types of seropositive AVH.

**Table 1: Gender Wise Distribution of the AVH Cases (N=360)**

Gender	No of Cases	Percentage
Male	308	86%
Female	52	14%
Total	360	100%



**Fig 1: Age Wise Distribution of the AVH Cases (N=360)**  
(□=HEV, □=HAV, □=HCV, □=HBV)



**Fig 2: Etiological Pattern of AVH Cases (N = 360)**

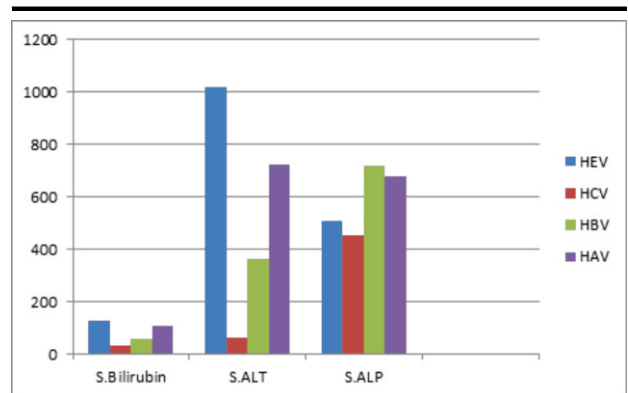
**Table 2: LFTs in Seronegative AVH Cases (N =220)**

LFTs	Maximum Rise	Values	No of Cases	Mean
S. Total Bilirubin	540	10 – 200	312	57
		> 200	48	346
S. ALT	3210	40 – 1000	292	216
		> 1000	68	1763
S. ALP	2890	300 – 500	184	326
		> 500	176	818

**Table 3: LFTs in Seropositive AVH Cases (N = 140)**

	Chi-Square Statistics			Row Totals
	ALT	T BIL	ALP	
Hepatitis E	1020 (730.74) {114.50}	130 (110.17) {0.01}	508 (796.10) {104.26}	1658
Hepatitis A	723 (684.31) {2.19}	109 (103.17) {6.98}	680 (645.52) {5.76}	1512
Hepatitis B	363 (509.33) {42.04}	57 (56.79) {5.10}	721 (554.88) {49.73}	1141
Hepatitis C	63 (244.62) {134.85}	31 (30.88) {0.94}	454 (266.50) {131.92}	548
Total	2169	327	2363	4859 (G. Total)

The chi-square statistic is 598.269. The  $p$ -value is < 0.05. The result is significant at  $p < 0.05$



**Fig 3: LFTs in Seropositive AVH Cases (N = 140)**

### Discussion

Viral hepatitis is a major cause of morbidity and mortality worldwide and an increasing cause of concern in Asian population. Whether it is water, food or blood born hepatotropic virus, increasing burden is alarming. According to the guidelines and recommendation given by National Academy of Clinical Biochemistry on use of laboratory tests in the diagnosis and monitoring of hepatic injury, AVH can be diagnosed by ALT >10 times of ULN and ALP >2 times of ULN.<sup>15</sup> In our study, we have found that ALT can rise > 75 times of ULN whereas ALP >2 but <5 times of ULN. The commonest cause of AVH was seronegative hepatitis (61%) than seropositive hepatitis. HEV was the major cause of seropositive AVH (28%), same was also observed by Butt AS<sup>16</sup> where in HEV infection occurred in 20-22% of AVH cases. In our study, prevalence of HEV infection in the age group of 20-30 years was 24.4% and same was also found by Malik IA.<sup>17</sup> Predominantly, males were

affected and this was also observed by Bengu said et al.<sup>11</sup>; but contrary to the findings of Teshale EH<sup>18</sup> which reported higher number of females. Biochemically, HEV infection presentation was different than other causes of AVH as bilirubin and ALT were markedly raised in HEV as compared to HAV. Das et al.<sup>19</sup> reported no clinical or biochemical difference in spectrum of AVH, which were contrary to our findings but similar to the results reported by Azim et al.<sup>20</sup> It showed better correlation between biochemical parameters such as ALT, bilirubin and ALP in HEV, as evident by statistical significance ( $p$  value  $<0.05$ ). Significant correlation of serum bilirubin, ALT and ALP in HEV is also reported in our study, indicating both impaired conjugation and cholestasis by affected hepatocytes while less conjugation defect in other spectra of AVH. Maximum and rapid hepatocellular damage was more in HEV, it can be simply diagnosed by biochemical monitoring of patient. This study showed the significance of biochemical parameters for diagnosis and management of AVH and HEV infection. Knowledge and interpretation of these tests are vitally important. At present, no vaccine is available for HEV infection, but available against HAV and HBV.<sup>21</sup> As per the findings of our study it reinforces that HEV continues to be the commonest cause of seropositive AVH thereby emphasizing the need for rapidly available investigation like LFTs that help in diagnosis of HEV. This study was a single center study carried out at CMH Malir, not representing the entire population of Pakistan; however, it does provide valuable information on the importance of LFTs in different spectra of AVH. More multicenter studies with similar selection criteria throughout the country would better enable us to evaluate the complete biochemical pattern in AVH.

### Conclusion

HEV infection remains a significant cause of seropositive AVH. The biochemical pattern of LFTs is different in HEV than other spectra of AVH. Highest rise of ALT indicates extensive liver damage in HEV that remains a significant cause of sporadic AVH in our study population.

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