Hepatitis B and C Single and Co-infection in Chronic Liver Disease and their effect on the Disease Pattern

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Introduction
Approximately 5% of the world's population (350 million people) are infected with HBV and 1% (60 million people) with HCV. Chronic infection by these viruses leads to slow progressive liver disease that over a period of up to 30 years may result in cirrhosis, chronic liver failure and hepatocellular carcinoma (HCC). An infection with both viruses B and C is frequent, particularly in areas where the two viruses are endemic and among populations at high risk for perinatal infections. Thus chronic viral hepatitis ranks as the fifth most common cause of death globally. Several studies regarding the prevalence of Hepatitis viruses in the causation of CLD have documented the presence of co-infection of HCV and HBV besides single infection. This study reports the frequency of HBV and HCV infection in chronic liver diseases and differences in the clinical features of patients' with single or co-infection with the two viruses.

Patients and Methods
In this prospective hospital based study adult patients over 15 years of age admitted to Military Hospital Rawalpindi in years 1999-2000, with clinically recognizable chronic liver disease were included. The diagnostic criteria for the selection of chronic liver disease patients were based on the presence of:

a) Clinical signs like ascites, hepatomegaly, splenomegaly with other clinical features including jaundice, palmar erythema, clubbing, edema, axillary and pubic hair loss, Spider nevi, flapping tremors, drowsiness, confusion and coma.

b) Ultra sound showing coarse hepatic texture, changes in liver size, increased portal vein diameter, and splenomegaly.

c) Impaired liver function tests including raised level of alanine amino transferase (ALT). Patients with acute hepatitis were excluded.

Patients included in the study were subjected to serology for Hepatitis B and C. HBsAg was detected by Clone System EIAGEN HbsAg, Biochem Immuno System Italia, S.P.A and anti-HBc by Monolisa® Anti BHc, Sanofi Diagnostics Pasteur, France an immunoenzymatic technique (sandwich method). Detection of HCV was done using Abbott HCV EIA 3.0 kit. Statistical analysis were done by SPSS version 10.0 Chi-square test was applied to calculate the probability (p-value) of diseases, age, HBV and HCV markers, co-infection and clinical symptoms.

Results
A total of 97 patients were included in the final analysis, out of which 45 (46.4%) were females and 52 (53.6%) were males. No significant difference (P=0.084) was found
between the gender on acquisition of disease.

The cases of CLD comprised 18 (18.6%) Ch. Hep patients, 72(74.2%) cases of cirrhosis and 7 (7.2%) cases of HCC. The occurrence of cirrhosis among the complications of chronic liver disease was significantly higher than Ch Hep in the study population (P<0.0001).

The mean age of CLD patients was 51.6 years, (range 16-75). In both the sexes CLD was distributed almost equally in all age groups except 3rd and 5th group (Table 1). In these age groups frequency was significantly higher in males as compared to females (P<0.00001). Females were dominating in older age groups ranging 61-70 and 71-80 years.

In 97 CLD patients one fourth (24.7%) were positive for HBsAg , and 61.1% for anti Hbc (Table 2). The overall frequency of seromarkers was highest in cirrhotics followed by Ch. Hep and HCC patients.

The percentage of HBsAg positively was 27.8% in Ch. Hep patients (5/18). In cirrhotics it was 23.6% (17/72)and in HCC patients, 28.5% (2/7). Anti-HBc positivity was almost same, 55.5% and 59.7% in chronic hepatitis (10/18) and cirrhotics (43/72), whereas it was 71.4% in (5/7) HCC patients.

Out of total CLD cases, 64.9% were positive for anti HCV. The frequency of anti-HCV was significantly higher in cirrhostics (P<0.003) as compared to Ch. Hep and HCC patients ( Table 3). Anti-HCV positivity was positive in 61.1% (11/18) of Ch. Hep patients, 68.1% (11/18) of cirrhotics (49/72) and 42.9% (3/7) of HCC cases.

In 97 CLD patients a total of 58 patients were positive for anti-HBc and out of these, 34(58.6%) patients were positive for anti-HCV as well. The detection of additive co-infection with both HBV & HCV in CLD patients was based on presence of combination of anti-HCV+anti HBc and anti-HCV+HbsAg. Highest frequency of anti HCV+anti-HBC and anti HCV+HBsAg was found in cirrhotics, followed by Ch. Hep and HCC patients (Table 4).

Among variable clinical features ascites was present in 56.4% and encephalopathy in 23.8% patients (Table 5). Comparison of these clinical features in single and co-infected HBV and HCV, CLD patients revealed that ascites and encephalopathy were present in significantly high number (P<0.00001 and P<0.015 respectively) in co-infected patients. GI bleeding was significantly more common in patients of co-infection and single HBV infection (P<0.03 and P<0.02 respectively) than HCV infection alone. Whereas hepatomegaly was a significant feature ( P<0.033) of HBV and HCV single infections than co-infection.

**Discussion**

The results of the study revealed that 58% of CLD patients were in 6th and 7th decade of life. Chronic hepatitis patients were a decade younger than cirrhotics, whereas HCC patients were a decade older at an average. Other researchers have reported similar
results. A number of them have suggested that increasing age is a higher risk to have the disease, probably due to longer exposure to multiple risk factors.7-13

Our results revealed occurrence of a relatively high percentage (42%) of CLD cases before fifty years of age. It was 2% in patients up to 20 years of age, about 10% each in second and third decade and 20% in fourth decade of life. The reason could be an early childhood infection with the hepatitis viruses. The chronic infection with hepatitis viruses leads to slow progressive liver disease. It may end up in cirrhosis, chronic liver failure, and hepatocellular carcinoma (HCC) over a period of up to 30 years.2,14 In Asians several researchers reported occurrence of HBV infection during early childhood, revealing chances of significant perinatal transmission of HBV in infection.15

Serological analysis revealed high frequency of hepatitis B and C viruses among CLD patients in our study. Similar results were presented by other researchers as well.2,11,14,15 High prevalence of HBV as compared to HCV was reported almost two decades earlier in Pakistan.12 In a few preliminary studies anti-HCV was found positive in 25% of CLD patients and HBV infection in at least half of these patients.16,17 In these studies, cases of HCV associated CLD were much less common than the HBV associated cases. Contrary to the above reports recent studies from East Asia, Japan, Southern Europe, USA, Africa and Pakistan3,6,8,9,11,16,18-23 have reported a high prevalence of HCV infection in CLD patients. The variation in result of the present study and the previous studies may reflect the availability of second and third generation assay for the detection of HCV but an actual increases in the prevalence of HCV infection appears more likely. According to our results the HCV infection was found in 65% of total CLD patients whereas HBsAg in almost 25% while 61.1% had anti-HBc indicating previous exposure to HBC infection. These results reflect high prevalence of both the viruses in this patient population. There are studies revealing similar results of occurrence and co-occurrence of anti-HBc and anti-HCV reflecting a similar distribution of HBV and HCV.18,23-27

The presence of a high proportion of co-infection in CLD patients in our study is an important finding. Since the route of transmission for these viruses are similar so patients could have co-infection with one or two viruses. Several other researchers from Pakistan also reported co-infection.3,4 Rodriguez-Rosado5 and Anne Maclennan reported triple and quadruple co-infection of HIV/HBV/HCV and HIV/HBV/HCV/HDV in similar percentage. Bruix et al23 found 50% prevalence of anti-HCV with HBsAg in HCC patients and indicated that in some patients, cancer may occur because of the combined oncogenic action of both the viruses Chiaramonte et al25 found same in patients with compensated cirrhosis.

An Italian study28 has also deducted that anti-HBc and anti-HCV occur together more frequently in patients with HCC. Previous evidence of viral infection indicate that patients infected with more than one virus are likely to develop more serious liver disease than those infected with a single agent. Dual infection may reduce histologic severity but not the chronicity.29 It increases chronicity and cirrhogenesis.25

A particular situation is the constellation of anti-HBc alone and in combination with anti-
HCV. Such patients have lower RNA levels but a higher prevalence of cirrhosis.29

Among different clinical features ascites was ranking highest followed by hepatic encephalopathy. The incidence of these features was 50% higher in co-infected patients as compared to single HBV or HCV patients. GI bleeding was also significantly higher in co-infected cases. Several other researchers also found ascites as the most common clinical feature followed by GI bleeding as complication of CLD.29-32

In summary, a high percentage of patients of CLD, in this study had evidence of HBV, HCV and coinfection. The progression of irreversible liver damage and relevant clinical features were more marked in co-infected patients as compared to patients with single virus infection.

References