

Clinical Correlates of Hepatitis B or Hepatitis C Coinfections in People Living with HIV/AIDS (PLHIV)

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Abstract

Introduction: Hepatitis B virus (HBV) coinfecting HIV patients are likely to have chronic hepatitis B infection and associated severe liver disease, however effect of hepatitis B on HIV has not been proven to be of any effect. Similarly in HIV/HCV co-infection majority of the studies have shown no significant influence of hepatitis C on the course of HIV infection, although some studies have demonstrated an association between HCV infection and faster HIV disease progression.^{14,15} Therefore, further studies are needed to study the impact of HBV/HCV co-infection on course of HIV, specially, in India.

Aims and Objectives: To study the clinical, biochemical and immunological profile of PLHIV co-infected with either hepatitis B or hepatitis C virus, the severity of liver disease and hepatitis B and hepatitis C viral loads in these co-infected PLHIV and the association of WHO stage of HIV and immunosuppression with hepatitis B and hepatitis C viral loads as well as severity of liver disease.

Method: It was an observational cross-sectional study, involving 30 PLHIV co-infected with either hepatitis B or C. A detailed history and physical examination was done. Complete Haemogram, Liver function tests, kidney function tests, Ultrasonography abdomen, CD4 cell counts, hepatitis B surface antigen (HBsAg), hepatitis B envelope antigen (HBeAg), hepatitis B Viral DNA (HBV DNA) and HCV RNA levels were done. Severity of liver disease was assessed by FIB 4 SCORE.

Results: Among the 30 PLHIV subjects 30% were co-infected with HCV 70% were co-infected with HBV (HBsAg positive). All the subjects were asymptomatic for their liver disease. All the subjects were on Anti-Retroviral Therapy (ART) and 80% were in Early WHO stage (T1 and T2) and 20% were in Advanced WHO stage (T3 and T4). It was similar in both HBV and HCV co-infected group. The mean CD4 count of the subjects was 416.70±189.50 cells/mm³ with the range of 69 – 909 cells/mm³. Five subjects (16.67%) had a CD4 count <200 cells/mm³. Fifty seven percent subjects had no fibrosis or moderate fibrosis (FIB 4 <1.45) and 13.3% (4 subjects) had extensive fibrosis or cirrhosis (FIB 4>3.25). In HCV co-infected subjects 3 of 9 (33.33%) had severe liver fibrosis and only 1 of 21 (4.7%) among HBV co-infected had severe liver fibrosis. Among the 9 HCV co-infected subjects, 3 (33.33%) had undetectable HCV RNA. More number of subjects with detectable hepatitis C viral load had severe liver disease as compared to undetectable viral

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load. In HIV and HBV co-infected subjects the HBeAg positivity was seen in 42.86% subjects and 38.1% subjects had detectable HBV DNA load. Significant correlation was seen between HBeAg positivity and HBV DNA load. No correlation could be found between FIB 4 score and hepatitis B envelope antigen (HBeAg) positivity or HBV DNA load. No correlation between severity of liver disease (FIB 4) score and WHO staging or CD4 count could be seen. WHO staging and CD4 count also did not correlate with HCV RNA load, HBeAg positivity and HBV DNA load.

Conclusions: There is no correlation of CD4 count and WHO stage with liver disease severity or hepatitis viral load in patients on HAART. In HIV and HBV co-infected patients high prevalence of HBeAg positivity is seen. Thus it becomes important to look for deranged liver enzymes and HBeAg positivity in PLHIV co-infected with hepatitis B so that ART can be initiated in these patients irrespective of CD4 count. Hepatitis C co-infected subjects are more likely to have severe liver disease in spite of good CD4 count, so specific treatment for hepatitis C virus should be considered.

Keywords: Hepatitis, HIV, CD4 count, Co- Infection

Introduction

AIDS remains one of the world's most serious health challenges.¹ There is an increase from previous years as more people are receiving the life-saving antiretroviral therapy, thus prolonging their survival. The prolonged survival of HIV/AIDS patients result in increased chances of getting ill from comorbidities, chief among them being co-infection with the hepatitis C virus (HCV) and hepatitis B virus (HBV). Liver related deaths have become the second most common cause of death among persons with HIV infection.²

The prevalence of chronic hepatitis B among HIV-infected patients is between 5- 20% and prevalence of hepatitis C infection in person living with HIV (PLHIV) is around 20-30% worldwide having similar routes such as injection drug use (IDU), blood transfusion, sexual contact, or from mother to child during pregnancy or birth.^{3,4}

The prevalence rates of co-infection with HBV/HCV in HIV patients varies worldwide and even in India depending on the geographic regions, risk groups and the type of exposure involved. In a study of 1178 HIV patients in north India HBV co-infection was seen in 9.9%, HCV co-infection was seen in 6.3% and both HBV/ HCV co-infection was seen in 1%⁵ whereas in south India with 1487 HIV patients, HCV positivity was seen to be 3.02%.⁶

Co-infections with viral hepatitis in PLHIV are of great concern. HIV infection negatively impacts all phases of the natural history of hepatitis B leading to increased rates of persistent infection, higher HBV DNA levels, lower rates of HBe Ag loss, increased cirrhosis and liver-related mortality, and increased risk of hepatocellular carcinoma.⁶⁻⁸ Liver associated mortality is about 17 times higher in HIV/HBV co-infected patients than in HIV negative patients.⁹ The negative impact of HIV infection on hepatitis C is seen with persistent HCV viremia, higher HCV viral load, and reduced response to interferon-based HCV therapy.¹⁰

HIV/HBV co-infection does not affect the course of HIV infection significantly. However the risk for ART related hepatotoxicity is increased. Some studies have shown an accelerated progression to AIDS and a reduced rate of survival among co-infected subjects. But there are many studies which have found no effect of HBV infection on the risk of acquiring an AIDS-defining condition or on overall mortality.^{3,11-13} Similarly in HIV/HCV co-infection majority of the studies have shown no significant influence of hepatitis C on the course of HIV infection, although some studies have demonstrated an association between HCV infection and faster HIV disease progression.^{14,15} Therefore further studies are needed to study the impact of HBV/HCV co-infection on course of HIV, specially, in India.

AIMS and Objectives

- To study the clinical, biochemical and immunological profile of PLHIV co-infected with either hepatitis B or hepatitis C virus.
- To study the severity of liver disease and hepatitis B and hepatitis C viral loads in these co-infected PLHIV.
- To study association of WHO stage of HIV and immunosuppression with hepatitis B and hepatitis C viral loads as well as severity of liver disease.

Materials and Methods

Study Design

It was an observational cross-sectional study, involving 30 people living with HIV/AIDS (PLHIV) co-infected with either hepatitis B or hepatitis C or both, presenting to the Anti-Retroviral Therapy Clinic, Department of Medicine at Maulana Azad Medical College and LokNayak Hospital, New Delhi.

Inclusion Criteria

- PLHIV with either Hepatitis B positivity (HBsAg positive)

- Hepatitis C positivity (Anti-HCV IgG positive)

Exclusion Criteria

- PLHIV with all other known causes of chronic liver disease (alcohol related, drug induced, autoimmune)
- Age less than 18years

Ethical Considerations

Informed consent was obtained from all the study subjects. Confidentiality was ensured.

Methodology

History and Examination

All the patients included in the study underwent a detailed history and clinical examination. Detailed history of presenting complaints, history of any liver disease such as jaundice, ascites, hematemesis, melena etc was taken. History of any significant past illnesses and possible mode of transmission of HIV and hepatitis such as intra venous drug abuse, needle sharing, blood transfusion and high risk sexual behaviour was also taken. Socioeconomic history was taken and modified Kuppuswamy scale was calculated.¹⁶ Detailed clinical examination was done to look especially for signs of liver disease such as icterus, gynecomastia, spider angiomas, ascites, dilated and torturous abdominal veins, splenomegaly, testicular atrophy etc. WHO clinical stage of every patient was determined at the time of inclusion into the study.

Laboratory Investigations

All the patients were subjected Complete blood count, Kidney function tests, Liver Function Tests, lipid profile and Serological tests for Hepatitis B {Hepatitis B surface antigen (HBsAg), Hepatitis B envelope antigen (HBeAg), Hepatitis B Viral DNA load}, Hepatitis C {Anti Hepatitis C viral antibody (Anti HCV) and Hepatitis C Viral RNA load (HCV RNA)} , cd4 count (by flow cytometer) Tests for toxoplasma, VDRL serology, ANA (Anti nuclear antibody), Chest X- Ray and Ultrasound abdomen were also done

Scoring System for Severity of Liver Disease (FIB-4)

It was calculated using the formula: age [year] × Aspartate aminotransferase(AST) [IU/L] / ((Platelet count [expressed as platelet $\times 10^9/L$]) × (Alanine aminotransferase(ALT) [IU/L]^{1/2})). FIB 4 score of <1.45 indicate moderate to no fibrosis and score of >3.25 indicate extensive fibrosis or cirrhosis.

Observation and Results

Of the 30 PLHIV subjects 9 subjects (30%) were co-infected with HCV (Anti HCV antibody positive) and 21 subjects (70%)

were co-infected with HBV (HBsAg positive). None of the subjects had co-infection with both HCV and HBV.(Figure 1)

Demographic Characteristics of Study Subjects

The mean age of the study population was 41.4 ± 11.11 years with a range from 19 – 66 years. The maximum number of patients was in the age group of 35- 45 years (50%). Most subjects enrolled in the study 26 of 30 (86.67%) were men. The gender distribution was similar in HCV and HBV co-infected groups with preponderance of males.

The major route for HIV acquisition in our subjects was heterosexual in 23 (76.67%) subjects. Intra venous drug use (IDU) was the cause of acquisition in 3 (10%) subjects. Blood transfusion was a suspected cause in 3 (10%) subjects and men who have sex with men (MSM) in 1(3.33%) subject. Similarly, among 9 subjects in HCV co-infected group 5(55.56%) were heterosexual, 3 (33.33%) were IDU and 1(11.1%) had history of blood transfusion. Among 21 HIV and HBV co-infected subjects 18 (85.72%) were heterosexual, 2 (9.52%) had history of blood transfusion and 1 (4.76%) subject was MSM. (figure 2)

The socio-economic status of subjects enrolled into the study based on education, occupation of the head of the household and per-capita income was assessed by the Modified Kuppuswamy Scale. By this scale 10% of the subjects belonged to the lower class, 66.67% belonged to upper lower class, 13.33% belonged to the lower middle class, 10% belonged to upper middle class and none in upper class.

Clinical Characteristics

The subjects presenting to the ART clinic were asymptomatic for their liver disease. There were no complaints of jaundice, melena, hematemesis etc. Pallor was seen in 5 of 30 (16.66%) subjects. Among the 5 subjects 3 also had both ascites and splenomegaly on examination. None of the study subject had jaundice and pedal oedema. The mean BMI of the subjects were 18.90 ± 2.14 kg/m² with 36.67% of subjects being undernourished (BMI < 18.5 kg/m²).

All the subjects were on Anti- Retroviral Therapy (ART) and were classified clinically into 4 different stages according to WHO classification. 21 of 30 subjects (70%) were in T1 stage, 3 of 30 subjects (10%) were in T2 stage, 4 of 30 subjects (13.33%) were in T3 stage, and 2 of 30 (6.67%) were in T4 stage.

Patients were further grouped into Early WHO stage (T1&T2 stage) and Advanced WHO stage (T3 and T4 stage). In our study population 80% of subjects were in Early WHO stage and 20% were in Advanced WHO stage. Among the 9 subjects in HCV co-infected group 7 (77.78%) were in early WHO stage (T1&T2 stage) and 2 (22.22%) were in

advanced WHO stage (T3 and T4 stage). Similarly in the HBV co-infected group 17 of 21 (81%) were in early WHO stage and 4 of 21 (19%) were in advanced WHO stage (Table 1). Seven of 30 (23.33%) patients had the evidence of opportunistic infection. Of these 4 had tuberculosis (2 pulmonary + 2 extra pulmonary), 2 had oral candida and 1 had herpes zoster.

Immunological Status by CD4 Counts

Assessment of immune status of the subjects was done by estimating their CD4 counts. The mean CD4 count of the subjects was 416.70 ± 189.50 cells/mm³ with the range of 69 – 909 cells/mm³. 5 (16.67%) had a CD4 count <200 cells/mm³, 17 (56.67%) had a CD4 count between 200 to 500 cells/mm³ and 8 (26.66%) had CD4 count >500 cells/mm³.

Among 9 patients of HCV group CD4 count ranged between 101 – 537 cells/mm³ (mean 353 ± 114.94 cells/mm³). In 7 of 9 (77.77%) patients the range was 200 – 500. In the HBV group CD4 range was 69 – 909 (mean 444 ± 207.76 cells/mm³). In these subjects 10 of 21 (47.62%) had CD4 between 200 – 500 cells/mm³ and 7 of 21 (33.33%) had CD4 count above 500 cells/mm³ (Table 2).

Laboratory Parameters

The mean haemoglobin (Hb) of the subjects were 12.05 ± 2.28 g/dl with a range of (5.5 – 15.1) g/dl. There were 4 female subjects in the study group in which 3 subjects (75%) had haemoglobin <12 g/dl and 1 subject had haemoglobin >13 g/dl. Using haemoglobin less than 12 mg/dl for women and less than 13 mg/dl for men as cut off value, 56.66% of subjects had anaemia. The mean platelet count of the subjects were 1.92 ± 0.67 lakh/mm³ with a range of (0.6 – 3.58) lakh/mm³. 20% of subjects had a platelet count less than 1.5 lakhs/mm³.

The mean serum bilirubin in our subjects was 0.64 ± 0.27 mg/dl. None of the subject had serum bilirubin more than 1.2 mg/dl. The mean Alanine transaminase (ALT) levels of the subjects were 59 ± 44.40 IU/ml with a range of 14 – 212 IU/ml. 56.67% subjects had ALT >40 IU/ml. Only 5 of 30 (16.67%) subjects had ALT > 80 IU/ml of which 3 belong to HCV co-infected group and 2 belong to HBV co-infected group. The mean Aspartate transaminase (AST) levels of the subjects were 54.2 ± 36.67 IU/ml with a range of 17 – 175 IU/ml. AST levels more than 40 IU/ml was also seen in 17 of 30 (56.67%) subjects. The mean serum albumin levels were 3.46 ± 0.36 g/dl. 13 of 30 (43.33%) subjects had serum albumin less than 3.5 g/dl.

FIB 4 SCORE and VIRAL LOAD

Among the 30 subjects, 17 (56.7%) had no fibrosis or moderate fibrosis (FIB 4 < 1.45), 4 (13.3%) subjects had extensive fibrosis or cirrhosis (FIB 4 > 3.25) and 9 (30%)

had FIB 4 score between 1.45-3.25. In the 4 subjects with extensive fibrosis 3 patients had ALT levels >2.5 times normal (212, 150, 115) and 1 patient had normal ALT level of 38 IU/ml. In HCV co-infected subjects 33.34% had extensive fibrosis or cirrhosis (FIB > 3.25) and in HBV co-infected subjects 4.7% had extensive fibrosis or cirrhosis. The liver disease was more severe in HIV and Hepatitis C co-infected as compared to subjects with HIV and Hepatitis B co-infection (figure 3).

Among the 9 HCV co-infected subjects, 3 (33.33%) had undetectable HCV RNA. Of the 6 subjects the mean HCV RNA load was $6378768.66 \pm 10851308.08$ IU/ml with range of (2361 – 29866705 IU/ml). In the subject with lowest detectable HCV RNA load (2361 IU/ml) the FIB 4 score was lowest (1.2). With increasing viral loads the severity of liver disease increased with a maximum FIB 4 score of 8.2 (figure 4). All 3 subjects with undetectable HCV RNA load had no or moderate fibrosis (FIB 4 < 1.45) while 50% of subjects with HCV RNA load >250 IU/ml had extensive fibrosis or cirrhosis (FIB 4 > 3.25). The subjects with detectable hepatitis C viral load have higher prevalence of severe liver disease as compared to undetectable viral load.

Hepatitis B and HIV

Among the 21 HIV and HBV co-infected subjects the HBeAg positivity was seen in 9 subjects (42.86%) while 12 subjects (57.14%) were HBeAg negative. 13 (61.9%) had undetectable HBV DNA levels. Among the rest, mean HBV DNA load was 3899190 ± 4035389.89 copies/ml with range of (4157 – 11311334 copies/ml). HBeAg positivity was seen in 6 of 8 (75%) with detectable HBV DNA as compared to 3 of 13 (23.07%) with undetectable HBV DNA. The p value is significant 0.03 (fisher t test).

No correlation could be found between FIB 4 score and hepatitis B envelope antigen (HBeAg) positivity with p value- 0.48. No correlation could be found between FIB 4 score and HBV DNA load with p value- 0.53. No correlation between FIB 4 score and WHO staging could be seen. In subjects with advanced WHO stage (T3 and T4), 1 of 6 (16.67%) had extensive fibrosis (FIB 4 > 3.25) and in early WHO stage (T1 and T2), 3 of 24 had extensive fibrosis or cirrhosis with p value - 0.41.

Hepatitis C and HIV

No correlation was found between HCV RNA levels and WHO stage. In subjects with early stage (T1 and T2) 5 of 7 (71.4%) had detectable HCV RNA and in advanced stage (T3 and T4) 1 of 2 (50%) had detectable HCV RNA. The p value was 1.0.

In 4 subjects with advanced WHO stage 3 (75%) had HBeAg positive and in 17 with early WHO stage 6 (35.2%) were HBeAg positive. However no statistically significant

difference could be seen. (p value 0.27). In 4 subjects with advanced WHO stage 2 (50%) had HBV DNA detected and in 17 with early WHO stage 6 (35.2%) had HBV DNA detected. However no statistically significant difference could be seen. (p value 0.617)

No significant correlation could be found between CD4 count and FIB 4 score. Extensive fibrosis or cirrhosis (FIB 4 > 3.25) was seen in 1 (20%) of 5 subjects with severe immunosuppression (CD4 <200 cells/mm³), and in 3 (12%) of 25 with CD4 >200 cells/mm³. The p value was 0.96. Subjects with undetectable HCV RNA load did not have severe immunosuppression. In 5 of 6 (83.33%) subjects with detectable HCV RNA had CD4 between 200 – 500 and only 1 (16.67%) had CD4 <200 cells/mm³. The p value was 0.27

In subjects with severe immunosuppression (CD4 <200 cells/mm³) 3 (75%) of 4 were HBeAg positive and in subjects with CD4 > 200 cells/mm³ 6 (35.2%) of 17 were HBeAg positive. But no statistically significant difference could be seen. (p value 0.27). Similarly in these patients, 2 (50%) of 4 had detectable HBV DNA and in subjects with CD4 > 200 cells/mm³ 6 (35.2%) of 17 had detectable HBV DNA. But no statistically significant difference could be seen. (p value 0.28).

Discussion

HIV and hepatitis virus co-infection occur very commonly due to their similar routes of transmission. HIV infection leads to depressed cellular immunity of the body which can lead to persistence of hepatitis infection and increased chronicity of the disease.⁸ Co-infection of HIV and hepatitis are of great concern due to their possible association with unfavourable outcomes and increased risk of anti-retroviral therapy (ART) related hepatotoxicity. HIV co-infection negatively impacts the course of hepatitis with increased risk of cirrhosis and increased viral loads in the patients⁸ whereas the effect of hepatitis virus co-infection on HIV disease course is very uncertain with some studies showing an accelerated progression to AIDS, but other studies showing no effect on the risk of acquiring an AIDS-defining condition or on overall mortality.^{3,11-13}

The prevalence of co-infection of HIV with hepatitis B or hepatitis C varies in different geographical areas depending upon the risk groups involved, type of exposure etc. In this study also hepatitis B co-infection was more common with 70% subjects co-infected with HIV and Hepatitis B and only 30% subjects co-infected with HIV and Hepatitis C. Other studies from India have also reported HIV/HBV coinfection being more common. In a study by Saravanan et al HIV and HBV co-infection was seen in 9% of population and HIV and HCV co-infection was seen in 2.2% of population.¹⁷ Manishajain et al have shown HIV/ HBV co-infection to be 9.9% and prevalence of HIV/HCV co-infection to be 6.3%.⁵

HIV infection generally occurs among the young and sexually active age group. The mean age of the study population was 41.4 ± 11.11 years of which 86.67% men. According to National AIDS Control Organisation (NACO), 90% of HIV infections in India occur in 15 to 44 years of age group, with men being more commonly infected than women.¹⁸ Male subjects are at a significantly higher risk of acquiring HIV and hepatitis co-infection, has been observed in studies all over the world.^{3,5,17}

The routes of acquisition of HIV and hepatitis virus are similar which includes, sexual contact, intra venous drug use (IDU), blood transfusion, mother to child during pregnancy or birth. The major route of HIV and hepatitis transmission was heterosexual in the present study, as has also been reported from India by others.^{5,99} There were 33.33% subjects with history of intra venous drug use in HIV/ HCV co-infected group but none in HIV/ HBV co-infected group. Studies conducted in the Indian population have reported that most HIV positive people belong to lower socioeconomic status.^{19,20} In our study 76.67% subjects were in lower and upper lower socioeconomic class (10% belonging to lower and 66.67% belonging to upper lower) as per modified Kuppaswamy classification.

Anaemia is very commonly seen in HIV patients and has a multifactorial cause. It is related to the HIV disease, opportunistic infections occurring in HIV, ART such as Zidovudine etc, lower socioeconomic status etc.²¹ The mean haemoglobin (Hb) of the subjects were 12.05 ± 2.28 g/dl with 17 (56.66%) of 30 subjects having anaemia. Of the anaemic subjects most of them 10 of 17 (58.82%) had mild anaemia (11-13g/dl), and only 3 of 17 (17.6%) had severe anaemia (<8 g/dl). Anaemia in HIV patients has also been reported across India in different studies.^{22,23} Body Mass Index is a marker for assessment of nutritional status of an individual. Low BMI is related to lower socioeconomic status, concurrent opportunistic infections, advanced immunosuppression etc.²⁴ The mean BMI of the subjects were 18.90 ± 2.14 kg/m² with 36.67% of subjects being undernourished (BMI < 18.5 kg/m²). The low BMI could be possibly related to the low socioeconomic status.

Tuberculosis was the most common opportunistic infection observed in our study subjects followed by oral candidiasis. Studies done in India by Bachani et al and Ghatge et al, also reported that tuberculosis and oral candidiasis were the most common opportunistic infections in PLHIV in India.^{25,26}

Hepatitis virus co-infection can have a significant impact on HIV disease course. Increased risk of AIDS defining illnesses and increased mortality in HIV and hepatitis virus co-infection have been observed in various studies most of which belong to pre HAART (Highly active antiretroviral therapy) era.^{11,12} In spite of being co-infected with hepatitis B or hepatitis C majority of the PLHIV in our study were

in early WHO stage (80%). Similarly the mean CD4 count of the subjects was 416.70 ± 189.50 cells/mm³ with only 16.67% having a CD4 less than 200 cells/mm³. Recent studies of HAART era done in North America and Brazil has also observed that the median CD4 cell count was 415 cells/mm³ and 545 ± 250 cells/mm³ respectively in a group of HIV and hepatitis B co-infected patients on HAART.^{27,28} A study by Konopnicki et al in EUROSIDA cohort showed no difference in occurrence of AIDS defining illness in HBsAg positive and HBsAg negative group on HAART.³ Thus hepatitis virus co-infection does not affect the response of HAART in HIV patients and since all our subjects were on ART there was no significant impact on WHO staging or CD4 count of the subjects. No correlation was found between CD4 count or WHO stage with severity of liver disease and hepatitis viral loads.

Abnormal liver functions are commonly seen in HIV and hepatitis co-infection both due to virus mediated injury and ART hepatotoxicity. Solomon Taye et al from Ethiopia have shown that 75% of HIV and HCV co-infected subjects had deranged LFT.²⁹ Mendes-Correa et al from Brazil have reported that in HBV co-infected subjects, 37.2% had ALT levels > 1.5 times normal limit.²⁷ In the present study 17 (56.67%) subjects had deranged ALT and AST levels (>40 IU/ml). Among them 5 subjects had ALT more than 80 IU/ml, 3 (60%) were in HCV co-infected group and 2 (40%) were in HBV co-infected group.

Severity of liver disease was assessed by FIB 4 score. Only 4 subjects had extensive fibrosis or cirrhosis (FIB 4>3.25) and majority of them, 3 of 4 were co-infected with HCV. These 3 HCV co-infected subjects with extensive liver fibrosis also had increased HCV RNA levels, whereas a single patient in the HBV group with severe liver fibrosis had undetectable hepatitis B viral load. Irrespective of the HIV status, hepatitis C is known to be associated with chronic liver disease in as high as 80% as compared to about 30% in hepatitis B.

In the present study HBV DNA was undetectable in 13 of 21 HBV co-infected subjects and only one subject had severe liver disease according to FIB 4 score, therefore a therapeutic role of tenofovir + lamivudine based ART regimen could not be ruled out. HBV DNA load and HBeAg positivity are markers of increased viral replication and infectivity in a subject. In 8 subjects with detectable HBV DNA, viral load ranged between 4157 – 11311334 copies/ml and 6 of these also had HBeAg positivity. There was a significant correlation between HBV DNA load and HBeAg positivity (p value 0.03).

HIV infection may alter the natural course of hepatitis B virus. The rate of progression and complications from viral hepatitis are accelerated in these patients.³⁰ There is decreased clearance of HBeAg and increased HBV replication with higher HBV DNA viral load.³¹⁻³³ HBeAg

positivity in the present study was seen in 9 of 21 (42.86%) subjects in the HBV co-infected group. Chandra et al from India and Mendes-Correa et al from Brazil have reported HBeAg positivity of 33.3% and 48.9% respectively in HIV and HBV co-infected subjects.^{27,34} Immune suppression in HIV patients prevents seroconversion of HBeAg status in these patients. It also favours HBV re-activation, which would make individuals who had previously experienced HBeAg seroconversion (i.e., had developed anti-HBe antibody and lost HBeAg) to become HBeAg seropositive again.^{35,36}

No statistically significant correlation was seen between HBeAg positivity and CD4 count or WHO staging in the study. 75% study subjects with CD4 less than 200 cells/mm³ had HBeAg positivity as compared to 37.2% in those with CD4 >200 cells/mm³ but the difference was not statistically significant. Only a further follow up of these HBeAg positive patients will show how fast do they progress to a stage of severe liver fibrosis. No correlation was seen between CD4 count and severity of liver disease or viral loads. There was a robust response to HAART in all our subjects and the mean CD4 was also high.

Deranged liver enzymes was seen in more than 50% of the co-infected subjects. Liver disease was more severe in hepatitis C. even when no statistically significant correlation was found there was a trend towards higher HCV RNA load in those with severe liver disease. No correlation was found between liver disease severity and HBV DNA load because there was only one subject with severe liver disease in HBV co-infected group in whom HBV DNA was undetectable. There was high prevalence of HBeAg positivity in HBV co-infected subjects and HBeAg positivity has a significant correlation with HBV DNA load.

Conclusion and Recommendations

This observational study shows that hepatitis B co-infection is more common than hepatitis C in PLHIV also. In IDU, an aggressive search for hepatitis virus co-infection should be made especially for hepatitis C.

Liver enzyme derangement is very common in HIV and hepatitis virus co-infection therefore regular monitoring of liver function test and avoidance of hepatotoxic drugs should be ensured. Hepatitis C co-infected subjects are more likely to have severe liver disease inspite of good CD4 count, so specific treatment for hepatitis C virus should be considered.

There is no correlation of CD4 count and WHO stage with liver disease severity or hepatitis viral load in patients on HAART. In HIV and HBV co-infected patients high prevalence of HBeAg positivity is seen. Thus it becomes important to look for deranged liver enzymes and HBeAg positivity in PLHIV co-infected with hepatitis B so that ART can be initiated in these patients irrespective of CD4 count.

Conflict of Interest: None

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