International Journal of Research in Medical Sciences
Suman S. Int J Res Med Sci. 2020 Nov;8(11):3955-3961
www.msjonline.org
pISSN 2320-6071 | eISSN 2320-6012

DOI: https://dx.doi.org/10.18203/2320-6012.ijrms20204885

Original Research Article

Clinical, haematological, and biochemical profile of HIV patient co-infected with hepatitis B and /or C

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Received: 24 August 2020
Revised: 30 September 2020
Accepted: 01 October 2020

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ABSTRACT

Background: Human immunodeficiency virus (HIV) positive population is at higher risk of getting infected with hepatitis B virus (HBV) or hepatitis C virus (HCV) or both. Co-infection with HBV/HCV may possibly complicate the clinical course of HIV in infected patients. Aim and objectives of the study were intended to determine clinical, haematological and biochemical profile of HIV patients co infected with hepatitis B and/or C.
Methods: All consecutive patients presented with HIV infection who were coinfected with either Hepatitis B, C or both presenting to immunodeficiency or Gastroenterology OPD Base Hospital Delhi, were included in the study. It was a prospective, observational study.
Results: HIV impacts the progression of HCV and increases the likelihood of subsequent liver damage as it is apparent in study by significant raised liver enzymes and hypoalbuminemia in HIV-HCV co infection compare to HIV–HBV.
Conclusions: These coinfections are more common in younger and lesser educated people. Biochemical parameters could serve as pointers for early detection of liver disease as result of hepatitis co infections in HIV patients. Prompt diagnosis of HCV and HBV co-infection in HIV patients has both individual and public health benefits.

Keywords: Hepatitis B, Hepatitis C, Human immunodeficiency virus, Coinfection of HIV

INTRODUCTION

Human immunodeficiency virus (HIV) positive population is at higher risk of getting infected with hepatitis B virus (HBV) or hepatitis C virus (HCV) or both. HBV, HCV and HIV share common routes of transmission, but the differential efficiency of these viruses to the types of exposures underlies difference in their prevalence by geographic region. Since 1996, when the highly active antiretroviral therapy (HAART) was first used in AIDS patients, HBV/HCV have emerged as a major viral pathogen associated with morbidity and mortality in these patients.[1,2,3] HBV and HCV co-infections in HIV positive individuals is of utmost importance due to the underlying consequences such as the hepatological problems associated with these viruses, which have been shown to decrease the life expectancy in the HIV-infected patients.[4]

According to WHO data, infection with hepatitis C virus is estimated to affect 2-4% of the world population, approximately 170 million people. This population is also at risk for progression to hepatocellular carcinoma.[5] HBV infection accounts for an estimated 370 million chronic infections and HIV infection for an estimated 40 million. Among the estimated 40 million persons infected with HIV worldwide, an estimated 2–4 million are chronically infected with HBV and an estimated 4–5 million are

chronically infected with HCV.[6,7] It is not surprising that markers of past HBV infections namely hepatitis B surface antibody (anti-HBs) or hepatitis B surface antigen (HBsAg) positivity, as the reported evidence of past HBV infection among people living with AIDS is about 10%.[8,9]

Aims and objective

Aim of this study was intended to determine clinical, haematological and biochemical characteristics of HIV patients co infected with hepatitis B and/or C.

Objectives were to study the clinical profile of HIV patients who are co-infected with HCV and/ or HBV and to study the effect of co-infections with HCV and/ or HBV on biochemical profile like renal function tests (RFT), liver function tests (LFT) and Haemogram of HIV patients.

METHODS

It was observational and prospective study conducted at Base Hospital Delhi Cantt, New Delhi between Jan 15 to Jun 16.

All consecutive patients presented with HIV infection who were coinfected with either Hepatitis B, C or both presenting to immunodeficiency or Gastroenterology OPD Base Hospital Delhi, were included in the study. The sample size was calculated and 30 subjects were included for study. Written informed consent was taken from all the subjects. The study protocol was approved by the Institutional Ethics Committee Base Hospital. It was a prospective, observational study. Patients' demographic data such as gender, age, job, alcohol consumption, use of hepatotoxic drugs, concomitant diseases were recorded. Detailed history regarding symptoms suggestive of hepatic disease (such as loss of appetite, jaundice, abdominal distention, blood in vomiting, black stool), potential source of HIV, HCV or/and HBV infection (such as sexual activity, status of spouse, blood transfusion, use of intravenous drug or potentially infected material), and adherence to the antiretroviral regimens used, were recorded. All patients were subjected to detailed clinical examination and findings pertaining to weight, icterus, organomegaly, ascites, sign of hepatic encephalopathy and opportunistic infections were recorded. All patients enrolled in study underwent complete blood counts, liver function tests (LFT), prothrombin time, and chest X-ray. All subjects were also tested for HBsAg (hepanostica HBsAg, biomerieux, netherland) and anti-HCV antibodies (general biologicals Corporation Taiwan) by enzyme linked immunosorbent assay (ELISA) as per the manufacturer's instructions. Ultra-sonography of the abdomen, serum alpha fetoprotein, endoscopy was done in all HBV, HCV positive patients.

Inclusion criteria

All co infected patients of HIV with HBV and/ or HCV

Exclusion criteria

All patients with pre-existing chronic liver disease in form of cirrhosis (other than HBV/HCV) and alcohol intake (daily intake of alcohol more than 60 gm in male and 20 gm in female for 10 years)

Sample size calculation

Sample size was calculated keeping in view at the most 5% risk, with minimum 80% power and 5% significance level (significant at 95% confidence level). However, consider the past data, which gives idea of variation in the variables, play important role in calculating the sample size. However, cost involvement in collecting sample, observation, availability of patients were the points to consider in calculating sample size.

Statistical analysis

Being an observational study, all parameters were analyzed three-monthly over a period of eighteen month. The improvement or deterioration in clinical, biochemical or hematological profile and significance of the same was analyzed using chi-square, student t test or logistic regression as applicable. The distribution of variables like ALT and serum albumin were used as continuous variables. The mean, median and distribution of these variables between the two groups, i.e. HIV plus HBV; HIV plus HCV were studied using t test and p value <0.05 was considered significant.

RESULTS

All consecutive patients presenting with HIV and co-infected with hepatitis (HCV/HBV) at immunodeficiency or gastroenterology OPD Base hospital Delhi were included in the study.

Total 30 patients were included in the study for further evaluation.

Demographical data

One out of thirty patients were female. Out of 30 patients included in the study, 4 (13%) were less than or equal to 30 years of age, 9 (30%) more than 40 years while the largest segment 17 (57%) came from between 31-to 40 years of age group. The mean age for the all study participants was 36.93±5.27.

Mean height recorded was 167.47±5.8 cm and mean weight was 68.1±6.05 kg.

Nineteen patients, 63.3%, were high school passed while 11(36%) had their education up to higher secondary level (Table 1).

Table 1: Demographic data.

Baseline Characteristics	Mean±SD
Age (years)	36.93±5.27
Weight	68.10±6.05 kg
Height	167.47±5.81
Sex	
Male	29 (96.6%)
Female	1 (3.3%)
HIV/ HBV	21
HIV/HCV	9

High risk behaviour was recorded only in 3 (9.9%) patients and 90% no behavioural risk indicators could be identified (Figure 1).

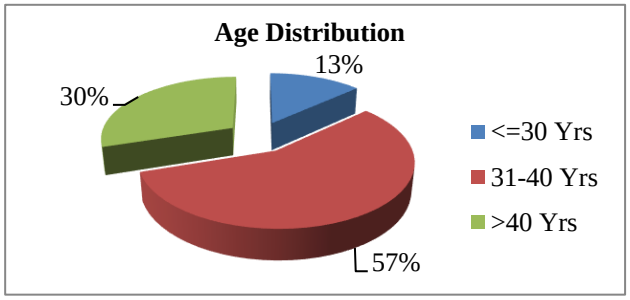

Figure 1: Age distribution.

All patients were evaluated for baseline laboratory characteristics. All assessed baseline characteristics are given in (Table 2).

Table 2: Baseline laboratory evaluation.

Lab Parameters	Mean ± SD
Hb	13.65±1.32
TLC	6913.33±2043.11
Hct	43.83±1.32
S. Bill	0.77±0.17
SGOT/AST	41.07±14.77
SGPT/ALT	35.23±8.6
TP	7.17±0.72
ALB	3.45±0.82
ALP	49.73±12.09

Diagnosis

Out of 30 HIV patients in this study, 21 (70%) patients were co-infected with hepatitis B virus, 9 (30%) were co-infected with hepatitis C virus.

Disease progression

Hemoglobulin (Hb) showed falling trends with the disease progression over a period of 18 months with an overall decrease of 0.31 g/dl. Despite of downward trend, the mean Hb levels remained within normal range during 18 months follow-up period. There was no significant difference recorded in mean Hb within the visits (Figure 2).

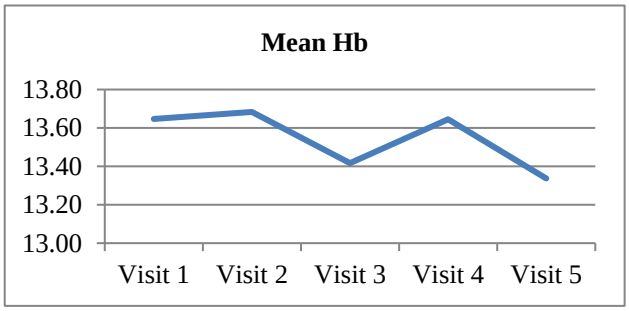

Figure 2: Mean Hb.

Total leukocyte counts

An overall upward trend was noticed in TLC during 18 months follow-up period. The mean TLC levels never seemed crossing normal range (Figure 3).

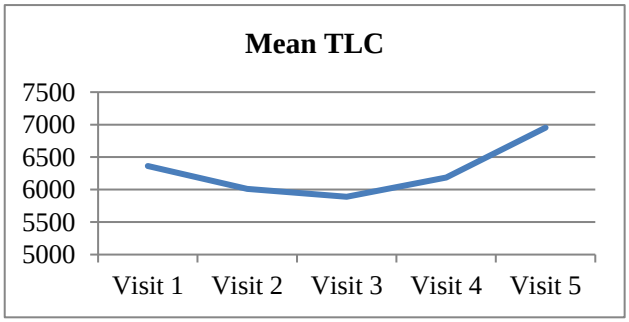

Figure 3: Mean TLC.

Hematocrit

Hematocrit with a rather fluctuating upward trend remained within normal range but on lower side. The mean hct calculated was 44.25±1.04 u/l (Figure 4).

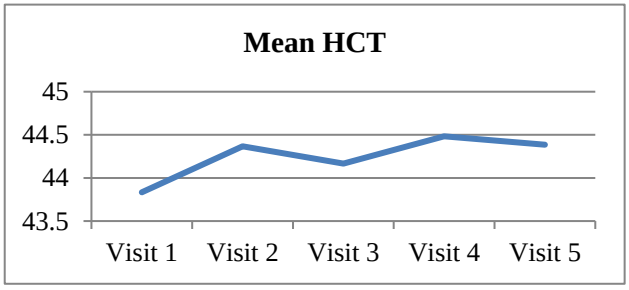

Figure 4: Mean HCT.

Aspartate aminotransferase (AST) and alanine aminotransferase (ALT)

Both SGOT/AST and SGPT/ALT both had an upward trend over follow-up period of during 18 months. No statistically significant increment was recorded for ALT or AST within different visits despite continuous up-ward trends (Figure 5).

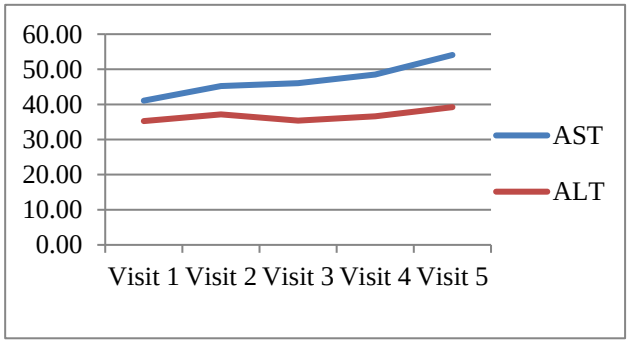

Figure 5: Mean AST and ALT.

Total protein (TP)

It too had a downward trend but remained within normal range during one and half year follow-up. There was no statistically significant reduction noticed in total protein within visits. The mean TP recorded was 7.17±0.72 g/dl (Figure 6).

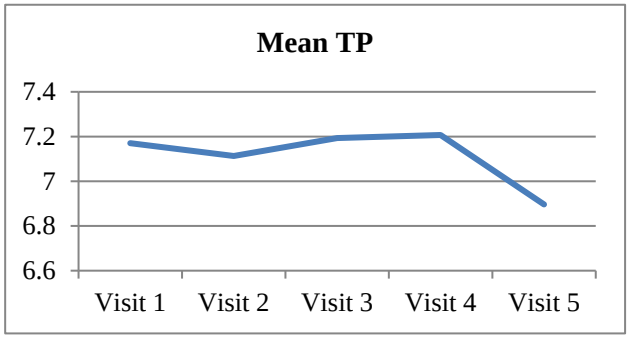

Figure 6: Mean TP.

Serum albumin

The mean serum albumin levels were recorded within normal range having minimal downward movement but there was no significant reduction noticed. The mean serum albumin was 3.45±0.82 g/dl (Figure 7).

Alkaline phosphate (ALP)

The mean ALP recorded was 49.73±12.09 IU/l on the lower side of normal range with slow increase in subsequent visits. No statistically significant increase in ALP was noticed within visits (Figure 8).

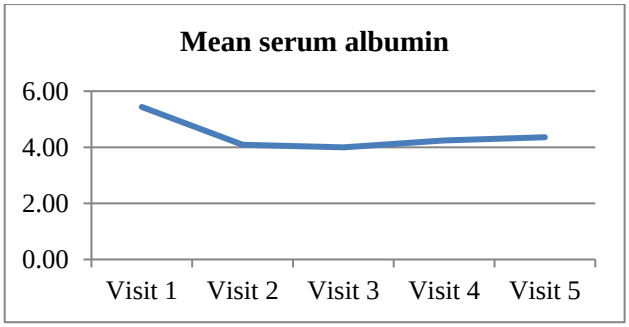

Figure 7: Mean serum albumin.

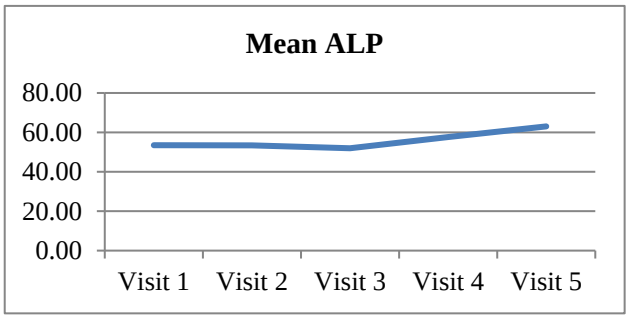

Figure 8: Mean ALP.

HBV versus HCV /HIV coinfection

We further divided the study population into two groups; HIV patients infected with HBV and the other group consisting patients coinfected with HCV. There were 56.7% HIV patients infected with HBV while 33.3% infected with HCV. The mean age for HBV coinfected group was 36.10±5.1 and for HCV it was 38.9±5.5

The mean height was 167.6 cm, 167.1 cm, and mean weight was 68.95 kg, 66.1 kg, respectively for HBV and HCV confected patients. There was no significant difference recorded in baseline characteristics of two group (Table 3).

Table 3: Mean Age, Height and Weight.

Characteristics	HBV/HIV (21)	HCV/HIV (9)	P value
Age (years)	36.10±5.1	38.9±5.5	0.18
Height (cm)	167.6 ± 5.4	167.1 ±7.1	0.8
Weight (kg)	68.95 ± 5.95	66.1 ± 6.2	0.2

Clinical Parameters

Haemoglobin levels were equally distributed between both groups with HBV/HIV 13.46 gm% and HCV/HIV 14.08 gm%, statistically insignificant (p=0.2). The mean TLC in HBV/ HIV group (7785 cu/mm) were higher than TLC in HCV/HIV (4877±1437 cu/mm) group and the difference between the groups was highly significant ($p<0.05$). The mean Hct in HBV/ HIV group (44.137±1.3 cu/mm) was same as HIV/HCV (43±1.1 cu/mm) group.

The total mean protein was 7.1±0.70 in HBV/HIV group and 7.3±0.76 in HIV group. Table: The mean values for different lab parameters for HIV patients co-infected with HBV/HCV (Table 4).

Table 4: Mean hematological value of two group.

Characteristics	HBV/HIV	HCV/HIV	P Value
Hb	13.46±1.3	14.08±1.5	0.2
TLC	7785±1563	4877±1437	0.00
HCT	44.137±1.3	43±1.1	0.2
TP	7.1±0.70	7.3±0.76	0.4

The mean ALT and serum albumin levels etc. in the two groups are shown in (Table 5) mean values of liver function test.

Table 5: Mean values of liver function test

Characteristics	HBV/HIV	HCV/HIV	P values
S Bil	0.75±0.17	0.81±0.16	0.3
AST	34.3±5.9	56.9±17.3	0.000
ALT	31.5±5.4	43.9±8.7	0.002
ALP	45.5±10.5	59.5±9.9	0.002
Albumin	3.9±0.6	2.5±0.5	0.000

The mean ALT was high in HCV/HIV infection in comparison to HBV/HIV and it was also significant ($p<0.05$). Albumin levels were also, higher in HBV/HIV (3.9±0.6) patients then in HCV/HIV patients and it was also significant ($p<0.05$).

The mean AST levels were high in HCV/HIV infected patients in comparison to HBV/HIV coinfected patients and the difference was statically significant ($p<0.05$).

DISCUSSION

Co-infection with HBV/HCV may possibly complicate the clinical course of HIV in infected patients. The prevalence of HBV and HCV co-infection in HIV has been variably reported in different studies.[10,11,12] The reported prevalence of hepatitis B and hepatitis C with HIV co infection is approximately 50%, of which HBV/HIV co infection contributes to 8 to 10%, while HCV/HIV comprises of 35 to 40%. Co-existence of both infections in HIV patients was found 5 to 10% by many studies.[13,14,15] Therefore, overall reported prevalence of HCV/HIV co infection has been considerably higher than HBV/HIV.[16] TREAT Asia HIV Observational Database study from Taiwan has reported HBV-HCV co-infection to be approximately 10 per cent each.[17]

In our study, out of 30 coinfected patient, 21(70%) were co-infected with hepatitis B virus while HCV were detected in 9 (30%) patients.[18]

In another study conducted at Nizam Institute of Medical Science (Hyderabad, India), HBV coinfection was found in 15% and HCV in 8.3% patients.

Co-infection rates in our study differs from some cross-sectional studies in Vietnam which have reported the prevalence of HCV/HIV that ranges from 74% to 100% findings that are similar to those reported from China which range from 62.4 to 93.6%.[19,20]

In another report in Vietnam, the authors showed that the prevalence of hepatitis B (HBsAg) ranged from 5.7% to 24.7% and anti-HCV ranged from 0.38% to 4.3% in the general population, while anti-HCV among IDUs ranged from 31% to 97.2%. The HBV prevalence among HIV population was similar to the general population, while HCV/HIV coinfection was concentrated in some groups and it can be as high as 98.5% among HIV-infected patients.[21]

Frequency of HBV infection is higher as compared to other study because of less vaccination against HBV in our country, especially in rural population. Majority of patients in our study hail from rural background.[22]

The frequency of anti-HCV positivity among our HIV subjects is lower than that reported in previously similar study amongst HIV/HCV co-infected Indian subjects and much higher than from the general Indian community.

The low frequency of HCV could be due to the low incidence of IVD use and infrequent transfusion in our study groups, which are relatively different from that reported from other parts of India where IVDs and transfusion history were the main risk factors identified for HCV infection among HIV patients

In this study, rates of HBV/HIV co infection and HCV/HIV co infection did not differ significantly in the age groups. However, rate of coinfection was significantly higher in the group aged 30–39 years. The rate of hepatitis and HIV coinfection across different age groups has been reported to be widely different across studies and countries. As we found, reported rates of coinfection are considerably higher in the age group of 30–40 years in some studies from developing countries, while rates in industrialized countries were the highest in the age group aged over 40 years. Lower rates of hepatitis/HIV coinfection in the age group over 40 years may be related to loss to follow-up, mostly due to end-stage liver disease complication.

The mean ALT levels were high in HCV/HIV co-infections than in HBV/HIV co infected patients. ALT levels more than 1.5 times normal are an indicator of liver damage, and serum albumin levels less than 3.0 g/dl should raise the possibility of chronic liver disease. The overall mean ALT levels were within normal range and a marked decrease in ALT was seen over one and half year follow-up.

Significantly higher mean value of AST was obtained in the HCV/HIV co-infected than the HBV/HIV coinfected patients. Overall, AST values remained within normal range despite of a continuous upward trend throughout the follow up period.

In our study, albumins level in HBV/HIV coinfected patients were significantly higher than HCV/HIV coinfected patients ($p<0.05$) while the mean albumin levels of HCV/HIV group (2.5±0.5 g/dl) were less than 3.0 g/dl indicating a hypoalbuminemia state.

Hypoalbuminemia is more common condition in chronic liver diseases and usually indicates severe liver damage and poor albumin synthesis. However, hypoalbuminemia is not always specific to liver diseases and may occur in other conditions such as protein malnutrition and protein losing enteropathies associated with HIV.[23]

HIV impacts the progression of HCV and increases the likelihood of subsequent liver damage (Benhamou, Bochet and Di Martino et al, Greub et al Rossi et al noted a more rapid progression to cirrhosis in individuals with HCV/HIV co-infection who have a low CD4+ count.

Biochemical parameters could serve as pointers for early detection of liver disease as result of hepatitis confections in HIV patients. Biochemical parameters such as ALT, AST, alkaline phosphatase, creatinine, and urea should be monitored closely. Most liver diseases cause only mild symptoms initially, but it is vital that these diseases be detected early.[24] Prompt diagnosis of HCV and HBV co-infection in HIV patients has both individual and public health benefits.

A raised mean serum ALT concentration above the acceptable range is a strong predictor of insulin resistance and principally reflects direct hepatocellular damage or liver dysfunction.[25]

The mean levels of Hb remained within normal range during one-year follow-up period and there was no significant difference recorded in mean Hb within the visits. Despite of an overall upward trend noticed in TLC; the mean TLC levels never seemed crossing the normal range.

Hematocrit with a rather fluctuating upward trend remained within normal range but on lower side as all the participants were men. The mean HCT calculated was 44.25±1.04 U/L.

No statistically significant reduction was recorded for ALT/AST within different visits despite continuous downward trends.

Total protein too had a downward trend but remained within normal range during one-year follow-up. There was no statistically significant reduction noticed in total protein within visits. The mean TP recorded was 7.12±0.8 g/dl. The mean serum albumin levels were recorded within normal range having minimal downward movement but there was no significant reduction noticed. The mean serum albumin was 4.42±1.8 g/dl

The mean ALP recorded was 55.9±13.7 IU/l on the lower side of normal range with slow increase in subsequent visits. No statistically significant increase in ALP was noted.

CONCLUSION

A total of 30 HIV patients co infected with HBV or HCV were studied over period of one and half years Prevalence of HBV-HCB coinfection with HIV varies among different studies because of difference in population being studied. This coinfection is more common in younger and lesser educated people. HIV impacts the progression of HCV and increases the likelihood of subsequent liver damage. Biochemical parameters could serve as pointers for early detection of liver disease as result of hepatitis co infections in HIV patients. Prompt diagnosis of HCV and HBV co-infection in HIV patients has both individual and public health benefits.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Suman S Clinical, haematological, and biochemical profile of HIV patient co-infected with hepatitis B and /or C. Int J Res Med Sci 2020;8:3955-61.