

Original Research Article

Pattern of hepatobiliary involvement in HIV/AIDS patients: study in a tertiary care centre

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Received: 25 August 2018

Revised: 10 November 2018

Accepted: 13 November 2018

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ABSTRACT

Background: Diseases of hepatobiliary system is a major problem in patients with HIV infection. It has been estimated that approximately one third of the death of patients with HIV infection are in some way related to liver disease. While this is predominantly a reflection of the problems encountered in the setting of co-infection Hepatitis B or C, it is also a reflection of the hepatic injury in the form of hepatic steatosis, that can be due to antiretroviral therapy. There had been little work done on liver function tests in HIV patients without pre-existing liver disease like viral hepatitis, or alcoholic hepatitis. So, this study was designed to assess the pattern of liver function test derangement in HIV patients. Aims and objective was to study the different pattern of hepatobiliary involvement in HIV positive patients, and to gauge the extent of liver damage.

Methods: The study included 50 HIV positive patients coming to SMS hospital and Medical College, Jaipur, in medicine and HIV clinic of skin and VD department. Subjects having HIV test positive by ELISA, are included in this study. Other causes of liver function derangements were excluded from the study.

Results: Maximum number of the patients were in the age group of 23-32 years. Out of 50 cases studied, 41 (82 %) cases had abnormal liver function tests, while 9 (18%) had normal liver function tests. Most of the cases had liver function abnormalities, and most common abnormality was raised SGOT/SGPT.

Conclusions: Almost all types of liver function tests are found to be deranged in HIV patients. The pattern of hepatobiliary involvement varied from fatty liver, cholestasis to Toxic necrosis and granulomas.

Keywords: HIV positive patients, Liver function tests

INTRODUCTION

It has been estimated that approximately one third of the death of patients with HIV infection are in some way related to liver disease.¹ While this is predominantly a reflection of the problems encountered in the setting of co-infection Hepatitis B or C, it is also a reflection of the hepatic injury in the form of hepatic steatosis, that can be due to antiretroviral therapy.^{2,3}

The hallmark of HIV disease is a profound immunodeficiency, resulting primarily from a progressive quantitative and qualitative deficiency of helper T-cells. It is important to appreciate that pathogenic mechanism of HIV disease is multifactorial and multiphasic, with involvement of immune system, as well as neurological, cardiovascular, gastrointestinal and hepatobiliary system.⁴ Diseases of hepatobiliary system is a major problem in patients with HIV infection. It has been

estimated that approximately one third of the death of patients with HIV infection are in some way related to liver disease. While this is predominantly a reflection of the problems encountered in the setting of co-infection Hepatitis B or C, it is also a reflection of the hepatic injury in the form of hepatic steatosis that can be due to antiretroviral therapy.

Approximately 95% of HIV infected individuals have evidence of infection with HBV, 5-40% of patients are co-infected with HCV, co-infection with hepatitis D, E and G virus is also common.⁵ HIV infection has a significant impact on the course of hepatitis virus infection. It is associated with approximately a threefold increase in the development of persistent hepatitis B surface antigenemia. Patients infected with HBV and HIV have decreased evidence of inflammatory liver disease. Biliary tract disease, in the form of papillary stenosis or sclerosing cholangitis, has been reported in the context of cryptosporidiosis, CMV infection and Kaposi's sarcoma.⁶

Many of the drugs used to treat HIV infection, are metabolized by the liver and cause liver injury.⁷ Fatal hepatic reaction has been reported with a wide array of antiretroviral drugs including nucleoside analogue, non-analogue and protease inhibitor analogue resulting in toxicity to mitochondria which can lead to disturbances in oxidative metabolism. This may manifest as hepatic steatosis, and in severe cases, lactic acidosis and fulminant hepatic failure. It is reversible if diagnosed early, and the offending agent discontinued. Nevirapine has been associated at times with fatal, fulminant and cholestasis hepatitis, hepatic necrosis, and hepatic failure.⁸ Zidovudin, ritonavir, indinavir and atazanamavir cause mild to moderate deviation in serum bilirubin.

In addition to HIV and co-infection with HBV, HCV, Ebstein Bar virus, antiretroviral therapy, anti-tubercular drugs and chronic liver disease also contribute to liver dysfunction in HIV infected patients.

Basic pathogenic mechanism of liver injury

There are multiple mechanism which leads to liver injuries in HIV positive cases. These are- direct cytotoxic CD-8 T-cell mediated liver injury, macrophage/Kupffer cell activation, cell mediated immune injury, immune complex mediated injury, and increased secretion of IL-1, IL-6, TNF- α . While there are many contributory factors causing liver disease in HIV patients, they generally present clinically in a few distinct patterns, usually classified as hepatocellular, cholestatic (obstructive), or mixed.⁹

There had been little work done on liver function tests, in HIV patients without pre-existing liver disease like viral hepatitis, or alcoholic hepatitis. So, this study was designed to assess the spectrum of liver function test derangements in HIV patients.

METHODS

The present study is an observational type of study, done at a tertiary care Centre. It included 50 patients, tested positive for HIV by ELISA test, admitted in the wards, or attending medical outdoor, and HIV clinic in SMS medical college and associated hospitals. Institutional ethical committee clearance was taken and written consent of the patients were obtained. All those patients who were alcoholic, on prolonged hepatotoxic drugs, had acute or chronic viral hepatitis, chronic congestive heart failure, extra- hepatic biliary obstructive disease, or any evidence of chronic liver disease, were excluded from the study. In addition to detailed interrogation, thorough clinical examination and relevant routine investigations, along with liver function tests were done. Specific evaluation was done to assess the presence of any chronic liver disease, or any other systemic disease, which may alter liver function tests. It included Chest X-ray, PA view, ECG, 2D echo, USG whole abdomen, viral hepatitis markers, TORCH test. ELISA test was done for the screening of HIV patients, later confirmed by Western blot method. Further, HIV viral load test, P 24 antigen, CD-4 count was also done.

RESULTS

Out of 50 patients studied, 37 were males and 13 were females. In the age group of 3-12 years and 13- 22 years, only 1 male was affected while no female was found to be affected in each group respectively. Maximum number of the patients were in the age group of 23-32 years involving 16 males and 11 females. In the age group 33-42, out of 18 patients only 2 were females. In the age group of more than 43 years, all the 3 patients enrolled were male (Figure 1).

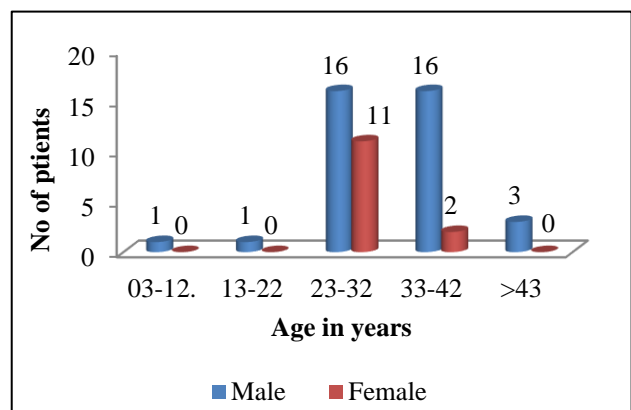


Figure 1: Age and sex distribution of patients.

Regarding symptomatology, out of 50 cases, 40 cases were presented with cough (80%), 39 patients with weight loss (78%), 36 patients with fever (36%), only 13 (26%) cases had jaundice as a presenting complain. Jaundice was the least common mode of presentation (Table 1).

Table 1: Symptomatology of presenting illness in patients.

Presenting illness	No. of patients	Percentage (%)
Cough	40	80.00
Fever	36	72.00
Weight loss	39	78.00
Diarrhoea	18	36.00
Anorexia	32	64.00
Jaundice	13	26.00

Out of 50 cases studied, 41 (82 %) cases had abnormal liver function tests, while 9 (18%) had normal liver function tests (Figure 2) Most of the cases had liver function abnormalities, and most common abnormality was raised SGOT/SGPT found in 41 patients. Out of 50 cases, 33 had hyperglobulinemia. Hypoalbuminemia (serum albumin <3gm/dl) was found in 10 cases. Hyperbilirubinemia (bilirubin >1mg/dl) was found in 15 cases out of 50 cases. Alkaline phosphatase was marginally (300-1000U/L) raised in 21 patients, and only 7 patients had alkaline phosphatase more than 1000U/L (Figure 3).

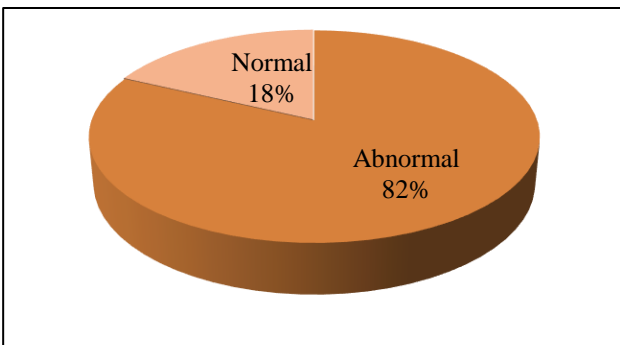


Figure 2: Liver function test profile in study group.

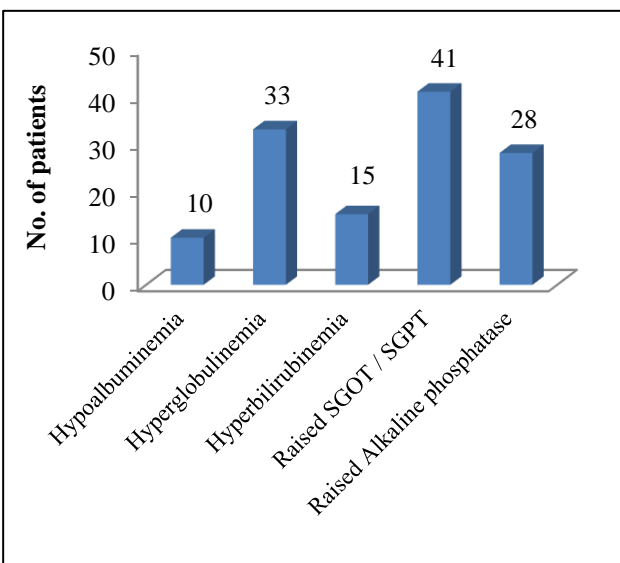


Figure 3: Distribution of liver function abnormalities.

DISCUSSION

The acquired immunodeficiency syndrome is a fatal illness, caused by retrovirus HIV, which break down the body’s immune system, which leads the victim vulnerable to a host of life-threatening opportunistic infections.^{10,11}

There is a growing evidence to suggest that the hepatobiliary system is also affected in HIV patients.^{12,13} It has been estimated that approximately one third of the death of patients with HIV infection are in some way related to liver disease.¹⁴ While this is predominantly a reflection of the problem encountered in the setting of co-infection with hepatitis B or C.^{15,16} It is also a reflection of hepatic injury caused by anti-retroviral drugs, or by disease itself.¹⁷ It is very difficult to differentiate, which factor is predominantly involved in causing these liver function abnormalities, either HIV disease itself, or associated factors like viral hepatitis, or chronic alcoholic disease. So, our aim of the study was to assess liver function tests in HIV positive patients, without having any co-existing liver disease. All major factors, which can cause liver function abnormalities individually, were excluded from this study.

In our study, we found that only 13 (26%) cases had jaundice as a presenting complain. Majority (74%) presented with chronic cough, fever, weight loss and diarrhea. Hypoalbuminemia (serum albumin <3gm/dl) was found in 10 (20%) cases. As serum albumin is exclusively synthesized in hepatocytes and has a long half-life (15-20 days) and slow turn over, serum albumin is not a good indicator of the acute or mild hepatic injury. Still, low serum albumin levels should raise the possibility of chronic liver disease and reflect severe liver damage resulting in decreased albumin synthesis.¹⁸

Serum globulin are a group of proteins made up of gamma globulins (immunoglobulins), produced by B lymphocytes, and alpha and beta globulins produced primarily in hepatocytes. In our study we found that out of 50 cases, 33 (66%) had hyperglobulinemia. Serum globulin levels are increased in chronic liver disease and cirrhosis. Most of the HIV patients have absolute increase in serum globulin levels. In such patients, increased serum globulin concentration is due to the increased synthesis of antibodies, some of which are directed against intestinal bacteria. This occurs because the cirrhotic liver fails to clear bacterial antigens that normally reach the liver through the hepatic circulation. It is an indirect evidence of chronic liver disease in HIV patients and found in about 66% cases in our study.

In this study, hyperbilirubinemia (bilirubin >1mg/gl) was found in 15 (30%) cases out of 50 cases studied. 13 cases (26%) had icterus on physical examination. It was found that most of the patients with hyperbilirubinemia have increased level of direct and indirect bilirubin both, which is indicative of hepatocellular injury and

cholestasis. It is similar to the observations of Myer RP et al, who studied 130 HIV patients and found significant hyperbilirubinemia in most of the HIV patients.¹⁹ He also state that hyperbilirubinemia with GGT and haptoglobin accurately predicts chronic liver disease and fibrosis. Rathi et al, studied 74 HIV patients, hyperbilirubinemia was found in 13% cases. It shows that hyperbilirubinemia is a major liver function abnormality in HIV patients.²⁰

Raised liver enzymes, like SGOT/SGPT were found in 41 (82%) cases out of 50. As we know SGOT is found in liver, cardiac muscle, kidney, brain, pancreas and lungs, SGPT is found primarily in liver. These enzymes are released in the blood in greater amount whenever there is damage to the liver cell membrane. Any type of hepatic injury can cause elevation of these enzymes. It is in consistent with the previous studies done by Wunk AM et al, where increased levels of SGOT/PT was found in 110 (88%) cases out of 125 cases studied.¹⁰

Similarly, alkaline phosphatase was found to be raised in 28 (56%) cases. Less than threefold elevation can be found in any type of hepatic disease, but greater than four times of normal occurs primarily in cholestatic hepatic disorders and infiltrative liver disease. From our data, raised alkaline phosphatase levels are found in significant number of HIV patients, which is indicative of presence of cholestasis disorders in such patients.

CONCLUSION

Disease of hepatobiliary system is a major problem with HIV infection, and about one third of the death of patients are in some way related to the liver disease. Liver function abnormalities like hyperbilirubinemia, hypoalbuminemia, hyperglobulinemia, raised SGOT/SGPT and alkaline phosphatase levels, were common even in those HIV infected patients, who did not have any underlying liver pathology previously.

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: Sharma K, Sharma V, Singh A, Ketki. Pattern of hepatobiliary involvement in HIV/AIDS patients: study in a tertiary care centre. *Int J Res Med Sci* 2019;7:146-50.