

Original article

Clinicopathological correlation of liver disorders in HIV positive/ AIDS patients

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Abstract

Introduction: Human immunodeficiency virus (HIV) infection resulted in more than 25 million deaths worldwide in last 2 decades. High prevalence of hepatic abnormalities is found in HIV infected patients. Liver disease in HIV infected patients may result from the infection itself, antiretroviral treatment or co-morbidities.

Objectives: The study was carried out to evaluate the spectrum of hepatic manifestation in HIV/ AIDS patients and attempt was made to correlate clinicopathological findings with other investigations.

Materials and methods : Patients reactive for HIV by ELISA method abnormal liver function tests and clinical or radiological evidence of hepatomegaly were included in the study over the period of two years. Liver biopsy/ necropsy done in such patients. Histopathological findings were correlated with clinical findings and other investigations.

Observations and conclusion: 70 patients were included in the study period with age range of 13-52 years. There was preponderance of males 44 (62.86%) as compared to females 26 (37.14 %). A total of 31 of 70 biopsies (44%) showed significant pathologic lesions including mycobacteria in 21 (37%) cases, cryptococosis in 5 (7%) cases and cirrhosis in 3 (4%) cases.

Conclusion: Liver biopsy is useful tool in HIV patients with abnormal LFTs and hepatomegaly.

Keywords: Human Immunodeficiency Virus, Liver disorders, Clinicopathological correlation\

Introduction:

HIV/ AIDS is still the major public health problem worldwide. Globally in 2016, there were about 37 million people living with HIV, about 1 million AIDS related death and 1.8 million new HIV infections.¹ AIDS patients are found to have high prevalence of underlying hepatic abnormality. Morphological abnormalities range from non-specific changes, opportunistic infections to malignancy.² Liver disease in HIV infected patients may result from infection itself, antiretroviral treatment or comorbidities including coinfection with hepatitis B and C viruses.³

With the help of histopathological patterns in liver along with liver function tests and clinical presentation one can follow progression of HIV/AIDS and its impact on the survival of patients. In Indian literature very few studies of hepatic involvement in HIV/AIDS have been published. ^{2,4,5} The present study was therefore undertaken to study spectrum of liver disorders and its clinicopathologic correlation in HIV positive/ AIDS patients.

Materials and methods:

Prospective study was carried out in the Dept. of pathology, B.J.G.M.C Pune over a period of 2 years. The patients included in the study were patients admitted in Sassoon General Hospital, Pune who were reactive for HIV by ELISA method and having hepatic involvement in the form of following:

1. Abnormal liver function tests and / or
2. Clinical or radiological evidence of hepatomegaly.

Patients fulfilling above mentioned criteria were included in the present study.

None of the patients in the study period was on antiretroviral therapy. CD4 count were available in few cases. Liver biopsy/ necropsy done in selected patients sent by clinicians were included in the present study. Sections from tissue were stained with hematoxylin & eosin. Special stains like Ziehl Nielson (ZN stain), reticulin stain, Periodic acid Schiff (PAS), Silver Methenamine (SM), Mucicarmine were done wherever required. Histopathological findings were correlated with clinical findings & other investigations.

Observations:

70 cases of liver biopsy were included in the study period. Patients age ranged from 13-52 years with maximum number of cases in age group of 23 to 32 years accounting for 61 of 70 cases (87.14%). Male to female ratio was 1.7:1. (Table no.1) The most common clinical presentation was hepatomegaly evident in 54 out of 70 cases (77%) followed by fever (71%) and cough (51%). Generalised lymphadenopathy was observed in 26 cases (37%). Only 3 patients (4%) were presented with jaundice. Patients presented with gastrointestinal symptoms like vomiting and oral candidiasis in 33 cases each (47%) pain in abdomen & distension of abdomen in 22 cases each (31%) and loose motions in 17 cases (24%).

Hepatomegaly was the commonest presentation in USG abdomen seen in 62 cases (88.57%) followed by abdominal lymphadenopathy seen in 23 cases (32.86%). Hepatosplenomegaly was seen in 27 cases (38.57%). The derangement in liver function tests were seen in 62 out of 70 cases (88.57%). Most frequently altered parameter was raised alkaline phosphatase observed in 43 cases (61.43%). Raised SGPT was seen in 20 cases (28.57%), hypoproteinemia in 12 cases (17.14%) and reversal of A:G ratio in 38 cases (54.29%).

Assessment of liver biopsies showed different alterations ranging from normal liver 8 cases (11.59%) , cholestasis 25 cases (36.23%), Kupffer cell hyperplasia in 12 cases (17.39%). Hepatic steatosis was most common histopathological finding seen in 41 cases (59%). Of 41 cases, 28 patients were non alcoholic. Hepatic steatosis was associated with other changes like lobular inflammation, perisinusoidal and periportal fibrosis.

Opportunistic infections were detected in 26 cases (37.14%). Amongst these mycobacteria with granuloma were present in 20 cases (Figure no.1) , atypical mycobacteria in one patient and cryptococcosis in 5 patients (Table no. 2 anf Figure no, 2). The granuloma in atypical mycobacteria was without caseous necrosis. ZN stain demonstrated acid fast bacilli with angulations. Sputum culture was suggestive of atypical mycobacteria. CD4 count in this case was <50/ul. These infections had been detected at an extrahepatic sites prior to liver biopsy in 11 cases; 8 patients had mycobacterium tuberculosis and 3 had cryptococcosis demonstrated by X ray chest, Sputum positive AFB, FNAC or biopsy of lymph node & CSF examination.

Table no. 1: Age and sex distribution

Age (Yrs)	Sex		Total
	Male	Female	
13-22	2 (2.86)	0 (0)	2(2.86)
23-32	10 (14.28)	17(24.29)	27(38.57)
33-42	27(38.57)	7(10)	34(48.57)
43-52	5 (7.14)	2(2.86)	7(10)
Total	44	26	70(100)

Figures in brackets indicate percentage.

Table no. 2 Histopathological findings in the study group

Histopathological Lesions	No. of cases	Percentage
Normal	8	11.59
Kupffer cell Hyperplasia	12	17.39
Fatty change	41	59
Cholestasis	25	36.23
TB granuloma	20	28.98
Cryptococcosis	05	7.25
Cirrhosis	03	4.35

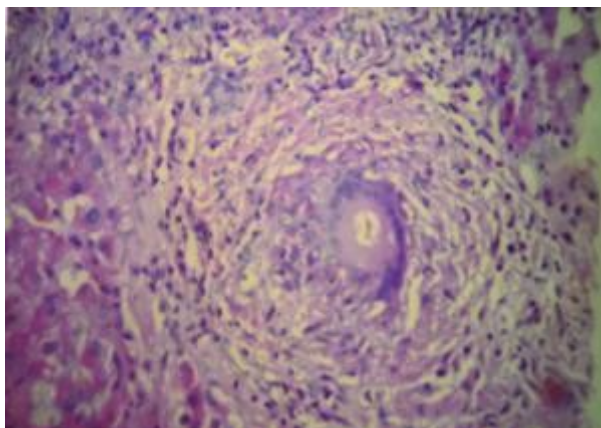


Figure No. 1: Granuloma in liver biopsy (H & E stain 40X)

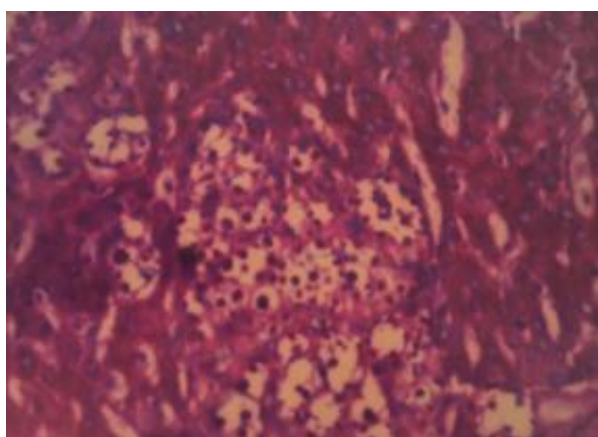


Figure No. 2: Cryptococcal infection in liver biopsy (H & E stain 40X)

Discussion:

The mortality scenario of HIV/AIDS in India is different from Western countries. Indian population is at risk of opportunistic infections in HIV/AIDS.² Liver affection in HIV remains unaddressed in INDIA and little data is available for review.^{2,3,4} Increased awareness is warranted to diagnose liver abnormalities as well as opportunistic infections which can be detected effectively with appropriate investigations and can be treated effectively. For this one must know the range of liver abnormalities which can occur in the course of HIV/AIDS and should have insight into its pathogenesis. With this purpose the present study was undertaken.

The age range in the present study was 13 years to 52 years. Findings in the present study are comparable with other published studies in relation to age and sex.^{6,7} Most of the patients were in the 3rd and 4th decade of their lives. The involvement of younger age group in the present study and most of the other studies is due to high risk behaviour and sexual promiscuity associated with this age group of population. Male predominance was seen in the present study with male to female ratio was 1.7:1. Similarly male preponderance was seen in other series in India as well as from Western countries.^{2,6,7}

In the present study hepatomegaly was the commonest clinical finding expected because patients included in the study were having clinical or radiological evidence of hepatomegaly as inclusion criteria. Fever

was the next common presenting feature (71.3%). Bhattacharya N et al also reported fever as the most common presenting symptom.⁸

Liver function tests were abnormal in 88.57% cases in the present study. Bhattacharya N et al, Ejilemele et al reported abnormal liver function tests in 90%, and 87.6% cases^{8,9} Serum alkaline phosphatase was the commonest parameter altered among the liver function tests, seen in 43 cases (61.43%) followed by reversal of A:G ratio in 38 cases (54.27%). The standard deviation of serum alkaline phosphatase was 170.53 U/L which indicate wide range of serum alkaline phosphatase in the study group. Roger PM et al also reported similar results with standard deviation of serum alkaline phosphatase 276 U/L in non diagnostic group and 157 U/L in diagnostic group in their study.¹⁰

The definitive diagnosis on liver histopathology in our study were present in 42% cases. Similarly Wiboonthukul S et al documented liver biopsy was diagnostic in 50.5% of patients.¹¹ Garcia-Ordonez MA et al also documented usefulness of liver biopsy in 43.1% of HIV positive patients.¹² Fatty change was nonspecific but the commonest finding in present study, seen cases (67.14%). Lanjewar DN et al and Sterling RK et al documented fatty change as non specific change in 34% and 65% cases respectively.^{2,13} Fatty change in patients of HIV/AIDS most likely to be caused by malnutrition, weight loss and chronic debilitating conditions caused by various opportunistic conditions.³

Tuberculosis is the commonest opportunistic infection in the present study, seen in 20 cases (28.57%). Different previously published studies have shown incidence of 24-41% of hepatic tuberculosis in patients with HIV/AIDS.^{2,5,14} Lanjewar DN et al pointed out high incidence of disseminated tuberculosis in India due to endemicity, lack of patient compliance and development of resistance. High incidence of tuberculosis in present study indicates that one must have high index of suspicion for tuberculosis in HIV/AIDS patients.

The other commonly detected opportunistic infection in the present study was cryptococcus neoformans seen in 5 cases (7.14%). Various studies in the literature have described cryptococcus neoformans infection in 2.3% to 10% cases of HIV/AIDS.^{2,5,15} Cirrhosis was seen in 3 cases (4.29%) in the present study. Two of these patients gave history of chronic alcoholism but in one female patient cause remained undetermined. Castellares C et al documented 8.3% of liver cirrhosis in HIV infected patients.¹⁶

Conclusion:

Liver disease is known to occur in HIV/AIDS patients. Mycobacterium tuberculosis was the most common histological finding in HIV patients with abnormal LFTs. Liver biopsy is useful procedure in evaluating abnormal LFT in HIV patients and its impact on survival of patients.

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