

Significance of liver enzymes as a baseline investigation in recently diagnosed HIV positive patients

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Abstract

Back ground: Liver disease is a common feature in patients with Human Immunodeficiency Virus (HIV) infection and hence it is important to consider its involvement when treating HIV infected patients. In this study we analysed the liver functions by estimating the liver enzymes [Alanine amino transferases (ALT), Aspartate amino transferases (AST)] and bilirubin levels [total/unconjugated] at the time of diagnosis of HIV positive patients and compared it with healthy controls. This study aimed to determine the baseline values of liver enzymes and total and unconjugated bilirubin before the start of antiretroviral therapy.

Methods: Liver enzymes [ALT and AST] and Bilirubin [total and unconjugated bilirubin] were analysed in a total of 200 patients and compared with equal number of age and sex matched healthy controls.

Results: The mean age of healthy controls were 37.17±9.12 years and the mean age of the HIV positive cases were 43.14±11.09 years

In recently positive HIV patients the increase in liver enzymes [ALT and AST] and Bilirubin [total, unconjugated] was statistically significant ($P < 0.001$) when compared to the healthy controls

Conclusion: The involvement of liver as reflected by increase in enzymes and bilirubin at the time of diagnosis is significant as there is a time lag between the onset of infection to that of diagnosis. Therefore the baseline liver function tests at the time of diagnosis, before the start of antiretroviral therapy acts as a prognostic indicator and is useful in subsequent monitoring of the patient.

Keywords: Human Immunodeficiency virus, liver enzymes, bilirubin.

1.Introduction

Acquired immune deficiency syndrome (AIDS) is caused by human immunodeficiency virus (HIV) and was identified in 1983. About 70 million people have been infected, more than 42 million are still living with the virus and 15,000 people worldwide are infected each day [1,2]. Liver function tests help in monitoring patients with HIV infection. Elevated liver enzymes such as Alanine amino transferases (ALT) and Aspartate aminotransferases (AST) and Bilirubin [total and unconjugated] levels are common in HIV infected patients [3]. Patients infected with HIV can have liver involvement ranging from abnormal liver function tests, biliary diseases, and cirrhosis, with or without portal hypertension to hepatocellular carcinoma [4]. While antiretroviral therapy related toxicities are an obvious cause, there is emerging evidence that HIV infection itself may directly affect the liver, which may be evident at diagnosis and lead to subsequent progression to liver disease [5].

2. Materials and Methods

The current study was carried out in patients attending the outpatient department between January 2013 to January 2015 at A.J. Institute of Medical Sciences and Research Centre Hospital, Mangalore, Karnataka. The approval by the ethical committee of the institution and informed consent for the same was taken from all the patients who were recruited for the study. A total number of 200 HIV positive patients at diagnosis without evidence of any other coinfection and equal number of age and sex matched healthy controls were included in the study. Patients already on antiretroviral therapy, with other coinfection, and alcoholics were excluded from the study. The diagnosis and confirmation of HIV infection was as per the National AIDS Control Organization (NACO 2012) recommendations. Samples were analysed by a fully automated analyser (Biolis).

Liver enzymes such as Alanine amino transferases (ALT) and Aspartate amino transferases (AST) were estimated by IFCC, UV kinetic method [6]. Bilirubin was determined by the VanDenBergh method [7] based on the diazo reaction.

2.1 Statistical methods

The data was analysed using SPSS v 17.

Independent sample t test was applied to compare the variables of the two group 't' test. Results were represented as mean and standard deviation

Pearson's correlation analysis was done to know the association of the enzymes (ALT, AST) with bilirubin in cases.

3. Results

The mean age was 43.14±11.09 and 37.179. ±12 years in the study and control group respectively. Males and females in the control groups were 100(50%) and 100 (50%) respectively and in the cases group males and females were 118 (59%) and 82 (41%) respectively. The mean SD± of ALT of controls and cases were 17.175.3±4IU/L and ±33.0612.33 IU/L respectively. The mean ±SD of AST of controls and cases were ±20.556.35 IU/L and 30.74±10.95 IU/L respectively. The mean ± SD of total bilirubin of the control and cases group was 0.43±0.12 mg/dl and 0.61± 0.36 mg/dl respectively. The mean SD of unconjugated bilirubin of the control and cases group was 0.29±0.10mg/dl and 0.36 ±0.21 mg/dl respectively.

Comparison of the liver enzymes (AST and ALT) and bilirubin (total/unconjugated) between the study and control group [Table 1] revealed significant elevations of the same in the study group (p values 0.001).

Table 1: Comparison of the liver enzymes and bilirubin in cases and controls

Parameter	Controls n=200	Cases n=200	P* value
Age(in years)	37.17± 9.12	43.14±11.09	<0.001
Females(n)	100(50%)	82(41%)	
Males (n)	100(50%)	118(59%)	
Serum ALT	17.17 ±5.34IU/L	33.06±12.33 IU/L	<0.001
Serum AST	20.55±6.35 IU/L	30.74±10.95 IU/L	<0.001
Total bilirubin	0.43±0.12mg/dl	0.61±0.36 mg/dl	<0.001
Unconjugated bilirubin	0.29±0.10 mg/dl	0.36± 0.21mg/dl	<0.001

*P value <0.001 is considered significant.

Table 2 shows the Pearson's correlation analysis, showing correlation of ALT with bilirubin (total and unconjugated) in HIV positive patients.

Table 3 shows the Pearson's correlation analysis, showing correlation of AST with bilirubin(total and unconjugated) in HIV positive patients .

Table 2: Correlation of ALT with Bilirubin amongst cases of HIV

Parameter	R value	p-value*
Total Bilirubin	0.261	<0.001
Unconjugated Bilirubin	0.216	<0.002

*p value <0.05 is considered significant

Table 3: Correlation of AST with Bilirubin amongst Cases of HIV

Parameter	R value	p-value*
Total Bilirubin	0.288	<0.001
Unconjugated Bilirubin	0.327	<0.001

*p value <0.001 is considered significant

4. Discussion

HIV infection can affect liver and can be reflected by elevated enzymes and bilirubin at diagnosis although the disease spectrum can vary from abnormal liver function tests to cirrhosis, portal hypertension and hepatocellular carcinoma. In addition opportunistic infection like cytomegalovirus, mycobacteria, parasitic infection, viral infections, tumours or drug related hepatitis may also have a role in involvement of the liver [8].

Our study revealed a significant increase in serum liver enzymes (ALT 33.06±12.33 IU/L and AST 30.74± 10.9 5IU/L) in the cases compared with the control group (ALT 17.17±5.34 IU/L and AST 20.55± 6.35 IU/L) which is statistically significant (P <0.001). This is in accordance with the study by Pakhale *et al* [9]. Our study is also consistent with the findings of Oluwafem *et al* [10], Sterling RK, Chiu S, Snider K *et al* [11] and Ejilmele *et al* [12] at the time of diagnosis of HIV infection. Further analysis of our study showed that the concentrations of the total bilirubin (0.61±0.36 mg/dl) and unconjugated bilirubin (0.36±0.21mg/dl) in the study group were significantly increased (p<0.001) from that of the control group (total bilirubin 0.43±0.12mg/dl, unconjugated bilirubin 0.29±0.10 mg/dl).

The reasons for the increase in liver enzymes and bilirubin could be by both direct and indirect means. Directly the Kupffer cells and sinusoidal cells are infected by HIV [13-14]. HIV RNA has been detected in sinusoidal cells and hepatocytes [13,14]. Infection of hepatocyte cell lines is CD4 independent and do not express CD4 [14]. Hepatocytes may act as a transient HIV reservoir and promote CD4+ T cell infection by cell to cell contact [15]. HIV can also induce hepatocyte apoptosis by gp120 signalling [16]. Hepatocyte apoptosis can trigger pro-fibrotic activity of hepatic stellate cells (HSC) [17,18]. Indirectly, the HIV infection of Gastrointestinal tract is associated with CD4+ T-cells which leads to increased permeability to bacterial endotoxin - lipopolysaccharide (LPS) and cause chronic immune activation in HIV-infected patients [19,20].Kupffer cells are the main cell type in the liver that responds to LPS. Under physiological conditions, Kupffer cells remain tolerant to repeated LPS stimulation but increased LPS contributes to progression of liver disease in HIV-infected patients [21,22].

The presence of a marked elevation of serum total bilirubin & and liver enzymes at diagnosis helps to identify patients requiring further investigations such as USG, liver biopsy, & ERCP and may serve as a prognostic indicator, since HIV positive patients with elevated levels of these parameters had a poor prognosis [23].

5. Conclusion

Liver disease in HIV-infected individuals at diagnosis, in the absence of co-infection with HBV or HCV, is an emerging issue. The current study reveals that liver is affected in a significant number of patients at diagnosis because of HIV infection. Thus liver enzymes estimated at diagnosis gives us information about the baseline hepatic status of the patients and could help in prognosis as well. This will help in modifying the prescription of a safer combination of antiretroviral therapy, thereby improving the morbidity and mortality of the patients. Further research is needed to determine the causal link between HIV infection and liver disease progression.

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