Hepatotoxicity in HIV Patients, An Observational Study in Patients from Tertiary Care Centre of Western India

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Abstract

Objective: HIV AIDS has currently become a chronic manageable condition with HAART, but with its chronicity and lifelong therapy currently the adverse drug reactions to these drugs are the main concern for any treating physician. Hepatotoxicity is one of the prime concerns of any physician managing HIV patients. We observe a number of patients reporting hepatotoxicity in our cohort and this had great impact on the efficacy and intake of the HAART drugs, this led us to explore this area and to find out the prevalence and etiologies in our cohort.

Methods: Thus we conducted this observational study to determine the prevalence of hepatotoxicity, the various etiologies for hepatotoxicity and assess HAART as the etiology of hepatotoxicity. The study was conducted in the virology department after obtaining ethics committee approval and incompliance with ICH, GCP guidelines. The study was conducted over a span of 3 months and data was collected and analyzed.

Results: Data of 178 Subjects was considered for evaluation of which 10 were excluded due to incomplete information. 168 patients with hepatotoxicity were assessed in the study, the prevalence of hepatotoxicity in our cohort was around 2.25%. Of the 168 patients 111 were male and 57 were female. 52 patients were on Antituberculosis therapy (ATT) and thus 30.95% was the incidence rate of hepatotoxicity due to ATT. 23.80% (40 out of 168) were alcoholic and hence it was the etiological agent. HAART as the etiology was observed in 5 patients, 2.97% being the incidence. Hepatitis B as the causative agent for hepatotoxicity was observed in 3.57% patients.

Conclusion: We thus concluded that ATT and alcoholism are major areas of concern in HIV patients and thus a strict monitoring is warranted while prescribing ATT at the same time deaddiction is equally important. HAART induced hepatotoxicity is observed only in a small section of patients and thus these drugs need not be attributed as culprits blindly and put to disrepute.

Introduction

Hepatotoxicity means damage to the liver due to various causes. Clinically its spectrum is wide which could range from just mild asymptomatic derangements in transaminase levels (ALT, AST) to a full blown fulminant hepatitis. Hepatotoxicity in HIV patients is a commonly observed phenomenon but there is paucity of data regarding the same in Indian scenario. HAART has been the main stay of therapy in management of HIV patients, it is known that these drugs have hepatotoxic potential and thus most people think that any hepatotoxicity in HIV patients is due to these drugs. HIV patients are exposed to a number of drugs due to concomitant opportunistic infections of which Tuberculosis is commonest in India. Thus anti tuberculosis therapy is very common to the prescription of HIV patients. ATT has hepatotoxic potential more than HAART and hence is a factor to be considered. Co-infection with Hepatitis B and C in HIV Patients has been associated with reduced survival and increased risk of hepatotoxicity. Within India variable co-infection

Editorial Viewpoint

• As HIV becomes a chronic manageable condition with HAART more adverse drug reactions are coming to the fore.
• This study finds HAART induced hepatotoxicity in few patients; however, antitubercular therapy and alcoholism are the major causes of hepatotoxicity.

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rates have been reported from different regions 6% from Chennai to 7.5% in Chandigarh and 16% from Mumbai.3,5 Alcohol is another important etiological agent reported for hepatotoxicity. Several studies worldwide have reported alcohol abuse and addiction in HIV patients, heavy alcohol consumption with its associated adverse effects have been reported extensively in HIV patients. Compared to non HIV patients the exposure to alcohol is almost double.6,7 Thus adding to a potential etiological agent. These reports and paucity of evidence from Indian scenario made us perform this study to determine the etiologies in our cohort so as to act according with support from the evidence.

Methodology

The study was conducted at a teaching hospital of western India in the department of medicine, it was an observational study conducted after obtaining ethics committee approval. The study was done in compliance with ICH GCP guidelines. The inclusion criteria of our study were all consecutive HIV patients who consented to us with features of hepatotoxicity. Hepatotoxicity was defined as per AIDS clinical trial group definition, all patients who had moderate or severe hepatotoxicity i.e. in patients with a normal pretherapy ALT or AST, hepatic injury is graded as moderate or severe based on a 5-fold or 10-fold increase in aminotransferases, respectively.8 In patients with abnormal liver enzymes prior to therapy, a >3.5-fold or a 5-fold increase in ALT or AST is considered indicative of moderate or severe hepatotoxicity, respectively.9 were included in the study. The duration of the study was around 3 months. Strict confidentiality was maintained regarding the identity of patients during the study. The data was collected and later analyzed. Total data of 178 patients’ fulfilled the inclusion criteria but 10 patient’s data was incomplete so it was excluded and 168 were analyzed.

Results

In our study cohort of all the HIV patients 178 patients developed hepatotoxicity, thus a prevalence of around 2.25% was observed. Of the total 168 patients analyzed around 111 were male and 57 were female patients (Table 1). The mean age of patients was 37.33 (± 7 years) majority of our patients were in the age group of 30-39 years (Table 2). Among the etiological agents for hepatotoxicity, ATT was the causative agent in 52 (30.95%) of patients, Hepatitis B as the coinfection was observed in 6 (3.57%) patients. None of the patients in our study were co-infected with hepatitis C, Alcoholism was noted in 40 (23.8%) patients. HAART alone causing hepatotoxicity was observed in 5 (2.97%) patients. Around 32 (19.04%) patients had multiple factors contributing to hepatotoxicity. While in 33 (19.64%) patients’ etiology could not be definitely ascertained (Table 3).

Discussion

Prevalence of Hepatotoxicity in HIV patients has not been reported from Indian literature but we in our cohort observed a prevalence of around 2.25%. In our study there was male preponderance of patients. Majority of our patients were in the age group of 30-39 years which is similar to the study of Shamanna et al from JIPMER, in their study as well they observed a male preponderance and median age was 40 years.10 Before the wide adoption of HAART opportunistic infections and lymphomas were the most common causes of liver injury in HIV patients.11,12 After the HAART era the spectrum has shifted to coinfection with chronic hepatitis C virus (HCV), chronic hepatitis B virus (HBV), medication-related hepatotoxicity, alcohol abuse, and nonalcoholic fatty liver disease (NAFLD).13-15 In our study we observed that Antituberculosis therapy induced hepatotoxicity was the commonest cause, observed in 30.95% of the patients. A study from Brazil by Tomich LG et al on HIV patients have reported 22% incidence of Drug induced liver injury of which antituberculosis drugs being the main cause.16 In our study 23.8% patients had alcohol as the cause of liver damage which is a little lower to what has been reported by another Indian study by Rathie et al wherein around 45% of their patients were alcoholic.17 This difference could be attributed to the difference in the cohort, their study predominantly being from patients in gastroenterology department whereas our study was from the patients in general medicine department. The prevalence of hepatitis B coinfection in our study was 3.57%. The report from AzamAskari states the hepatitis B and HIV co-infection prevalence

<table>
<thead>
<tr>
<th>Table 1: Gender distribution of study population</th>
<th>Table 2: Age distribution of study population</th>
<th>Table 3: Probable etiologies of hepatotoxicity in study population</th>
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<tbody>
<tr>
<td>N %</td>
<td>Age group N %</td>
<td>Etiology N %</td>
</tr>
<tr>
<td>Male 111 66</td>
<td>18-29 years 17 10.11%</td>
<td>Alcoholism 40 23.80%</td>
</tr>
<tr>
<td>Female 57 34</td>
<td>30-39 years 91 54.16%</td>
<td>Antituberculosis therapy (ATT) 52 30.95%</td>
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<td>Total 168 100</td>
<td>40-49 years 49 29.16%</td>
<td>Hepatitis B coinfection 6 3.57%</td>
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<tr>
<td></td>
<td>50-60 years 11 6.54%</td>
<td>Hepatitis C coinfection 0 0</td>
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<tr>
<td></td>
<td>Total 168 100%</td>
<td>HAART 5 2.97%</td>
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<td>Multiple factors 32 19.04%</td>
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<td></td>
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<td>(ATT, ART, Alcohol)</td>
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<td></td>
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<td>Uncertain 33 19.64%</td>
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<td>Total 168</td>
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of around 7-10% in India. This difference is due to the fact that our study focused on patients with moderate and severe hepatotoxicity whereas these studies have included asymptomatic patients as well, thus the increase in the prevalence. Our cohort of patients did not have any patient with HCV co infection, the prevalence reported from Mumbai in other study has also been relatively low to around 2.2% or so, although it is varied in different studies from India. We observed that HAART was the etiology of Hepatotoxicity in 2.97% of the patients; other studies have reported an incidence ranging from 2-18% similar to our cohort. In around 19% patients there were multiple cause for hepatotoxicity and in a similar number of patients no definitive cause could be ascertained as the etiology for hepatotoxicity.

Conclusion

On the basis of our observations we thus conclude that Antituberculosis drugs and alcoholism are the main agents responsible for liver damage in HIV patients, only after ruling them out should one consider the possibility of HAART as the causative agent, the incidence of Hepatitis B and HCV although are low but one should not miss these treatable cause as they have impact on the liver pathology Thus a physician treating an HIV patient should be vigilant to these etiologies always.

References