Does immunological status affect the prevalence of Hepatitis C virus infection among HIV/AIDS patients?

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Abstract

Background: Even though HIV-HCV co-infection rates vary widely according to western reports, not so much has been documented about the situation in our environment. We determined the prevalence of HCV among our HIV cohort as well as described the relationship between the immune and virological status of the patients in this report.

Methods: Data of 1044 consenting HIV infected patients (confirmed by Western blot assay) receiving treatment at our centre between Sep 2002 and Feb 2005 were analyzed using EpiInfo 2004 retrospectively. The sera of the patients were used to determine their anti-HCV status by third generation ELISA (DIA.PRO Diagnostic, Bioprobes srl, Italy).

HIV RNA levels and CD4 cell counts were also determined at recruitment by Roche Amplicor® 1.5 and Flow Cytometry (Partec, Germany).

Results: Ninety out of 1044 patients (8.6%) were positive for anti-HCV. The rate of co-infection was highest among the divorced (10.3%), followed by widows (9.9%) though this did not reach statistical significance. The odds of finding anti-HCV was more than twice with CD4 cell counts >600cells/microlitre compared to below 200cells/microlitre (p=0.026). The median HIV RNA levels of HCV co-infected individuals was 514copies/ml, while it was 200copies/ml for HIV monoinfected persons (p>0.05)

Conclusion: The prevalence of HCV among this HIV cohort is high. There is also an associated higher chance of detecting anti-HCV in sera of the HIV patients whose immunological status is better than severely immunocompromised individuals.

INTRODUCTION

Liver disease caused by chronic hepatitis C virus (HCV) is one of the leading causes of morbidity and mortality among Human Immunodeficiency Virus (HIV) infected patients in the developed world, where classic opportunistic complications of severe immunodeficiency have declined as a result of the widespread use of potent antiretroviral therapies. A variety of data indicate that coinfection of HIV with HCV results in increased HCV viral load and an accelerated HCV disease course. As immunodeficiency progresses, there is increased risk of perinatal and sexual transmission of HCV. Additionally, HCV negatively impacts HIV course by inhibiting immune reconstitution as well as impairs ability to use potent antiretroviral therapy and other HIV-related medications.

Several researchers worldwide have attempted to document the enormity of the problem of HCV among HIV patients. An estimated 200,000 persons out of 800,000 HIV/AIDS infected persons in the United States are co infected with HCV. Different research cohorts gave different rates of co-infection, ranging between 25 to 30%. Another group estimated the co-infection rate at 16.1%. The rate in Europe appears to be closer to 30%, 17.7% in Brazil and 7.27% in India. Agwale and co-workers in Abuja, Nigeria, documented a prevalence of HCV of 8.2% among their HIV cohort.

The prevalence of HCV is particularly important now that highly active antiretrovirals have profoundly altered the rates and types of HIV related morbidity. Additionally, with successful treatment of HIV, it is becoming clear that HCV may lead to early onset of advanced liver disease. We therefore, determined the prevalence of HCV among HIV/AIDS patients at our Centre, and related its epidemiological distribution with the immunological and virological status of the patients. This will equip clinicians in the sub-region with an action plan for afflicted patients.

PATIENTS, MATERIALS AND METHODS

The data of 1044 HIV infected patients including their age, gender, marital status, and investigations being treated at the ARV Centre of the Jos University Teaching Hospital between September 2002 and February 2005 were analyzed retrospectively. All the patients underwent serological tests to determine anti-HCV antibodies using third generation Enzyme Immunoassay (DIA.PRO Diagnostic, Bioprobes srl, Italy). Their HIV viral loads and CD4 cell counts were...
also determined using Amplicor HIV-1 Monitor® Test, version 1.5 and Flow cytometry (Partec Germany) respectively.

The data were analyzed using the Epi Info 2004 statistical software. Measures of central tendencies were determined for age and viral load of HIV RNA. The significance of observed differences were determined using Student's t test for continuous variables and Chi-squared test for differences of proportions and categorical variables. Simple proportion was used to describe prevalence. P values of <0.05 were considered statistically significant.

RESULTS

The mean age of the HIV population was 38.1±8.4SD years. Ninety out of 1044 patients (8.6%) had associated hepatitis C (HCV) co infection. The mean age of the co-infected individuals was 39.4±8.2SD years while that for monoinfected HIV patients was 38.0±8.4SD years. There was no statistically significant difference between the mean ages of the two groups (t=1.54, p=0.12).

Two (5.3%) of 38 patients in the age-group 15-25, had associated HCV co-infection, 30 (7.5%) in the 26-35 age-group and 39(9.7%) of the 36-45 age-group had anti-HCV antibodies (Fig. 1). Fifteen (8.7%) of the 46-55 age-group had HCV co-infection while 4 (12.9%) people within the age category 56-75 had the co-infection. There was no statistically significant relationship between the age-group of the population and HCV co-infection (p=0.64).

Sixty-two (9.1%) out of 682 females had reactive anti-HCV detected in their sera while only 28(7.7%) of the males had it (Table I). The male to female ratio of HCV co-infection is 1:1.2. There was no significant association between the gender of an individual and HCV co-infection (p=0.46).

While the divorced people had the highest rate of infection (10.3%), the widows had 9.9% (see Table II). This was followed by singles (9.0%) and then the married (7.7%). There was no significant difference between marital status and HCV co-infection however ($X^2=1.28$, $p=0.73$).

The relationship between CD4 count group and co-infection by HCV is described in table III. While patients with the lowest CD4+ group had the lowest rate of HCV co-infection, patients with the highest CD4+ group had the highest co-infection rate (6.8% vs. 15.4% for <201 and >800 respectively). Considered as a whole, there is a progressive increase in the rate of HCV co-infection from the lower CD4+ count group to the higher one ($p=0.026$). The odds of finding co-infection are more than twice with CD4+ counts above 600 compared to CD4+ count below 201.

The median HIV viral load of HCV co-infected individuals was 514/mm³ while it was 200/mm³ for non-HCV infected persons. There was no statistically significant association between the HIV viral load and the HCV co-infection ($t=1.29$, $p=0.17$).

Table I: Distribution of Gender with HCV co-infection

<table>
<thead>
<tr>
<th>GENDER</th>
<th>HCV+(%)</th>
<th>HCV-(%)</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>62(9.1)</td>
<td>620(90.9)</td>
<td>682</td>
</tr>
<tr>
<td>Male</td>
<td>28(7.7)</td>
<td>334(92.3)</td>
<td>362</td>
</tr>
<tr>
<td>Total</td>
<td>90(8.6)</td>
<td>954(91.4)</td>
<td>1044</td>
</tr>
</tbody>
</table>

Table II: Distribution of the HIV population by marital status and HCV co-infection

<table>
<thead>
<tr>
<th>MARITAL STATUS</th>
<th>HCV+(%)</th>
<th>HCV-(%)</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Divorced</td>
<td>6(10.3)</td>
<td>52(89.7)</td>
<td>58</td>
</tr>
<tr>
<td>Married</td>
<td>42(7.7)</td>
<td>501(92.3)</td>
<td>543</td>
</tr>
<tr>
<td>Single</td>
<td>18(9.0)</td>
<td>182(91.0)</td>
<td>200</td>
</tr>
<tr>
<td>Widowed</td>
<td>24(9.9)</td>
<td>219(90.1)</td>
<td>243</td>
</tr>
<tr>
<td>Total</td>
<td>90(8.6)</td>
<td>954(91.4)</td>
<td>1044</td>
</tr>
</tbody>
</table>

Table III: Distribution of the population by CD4 count group and HCV co-infection

<table>
<thead>
<tr>
<th>CD4+ GROUP</th>
<th>HCV+(%)</th>
<th>HCV-(%)</th>
<th>TOTAL</th>
<th>ODDS</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-200</td>
<td>32(6.8)</td>
<td>439(93.2)</td>
<td>471</td>
<td>1.00</td>
</tr>
<tr>
<td>201-400</td>
<td>33(9.4)</td>
<td>318(90.6)</td>
<td>351</td>
<td>1.42</td>
</tr>
<tr>
<td>401-600</td>
<td>14(9.5)</td>
<td>133(90.5)</td>
<td>147</td>
<td>1.44</td>
</tr>
<tr>
<td>601-800</td>
<td>8(14.5)</td>
<td>47(85.5)</td>
<td>55</td>
<td>2.34</td>
</tr>
<tr>
<td>801-1000</td>
<td>2(15.4)</td>
<td>11(84.6)</td>
<td>13</td>
<td>2.49</td>
</tr>
<tr>
<td>Total</td>
<td>89(8.6)</td>
<td>948(91.4)</td>
<td>1037</td>
<td></td>
</tr>
</tbody>
</table>

$X^2$ for trend =4.98, $p=0.026$.

NB. 7 patients did not have CD4 count results.
DISCUSSION

Ninety (8.6%) of the 1044 patients were reactive to anti-HCV antibodies. Even though, the male to female ratio of HCV co-infection was 1.2:1, there was no statistically significant relationship between the gender or marital status of the population and co-infection by HCV. The observed mild differences might be reflecting the health-care seeking behaviour of the population. This prevalence of 8.6% is low compared to other reports, particularly from the industrialized nations. Researchers from Europe reported prevalence of 41.33% while American writers found a rate of between 25-30% and Brazil at 17.7%. The prevalence is however, comparable to an earlier study at Abuja, of 8.2%, India of 7.27% as well as the prevalence of the disease among blood donors from Benin, Nigeria (12.3%)11. The latter report however, did not include information on the HIV status of the blood donors. It is however apparent that the prevalence of this disease varies widely depending on the HIV population studied and the risk factors associated with HCV transmission in these settings. The risk factor for possible transmission of HCV in this population was heterosexual intercourse; suggesting that it is indeed, a less efficient route of its transmission.

The reason for the comparatively low prevalence of HCV infection among our patients is a subject for further study. The significant relationship between progressive increase in the rate of HCV co-infection with CD4 group may suggest the influence of the sensitivity of the assay method relative to the immunological status of the individuals. It has been documented that the ability of Enzyme Immunoassay (EIA) to detect anti-HCV antibodies decreases as the CD4 count falls below 200cells/mm3. False negative results therefore are highest in populations with low CD4 counts. This further strengthens the point as most of our patients had their CD4 counts below 400 (table III). However, it is important to note that the CD4 count may be affected by the presence of HCV-associated portal hypertension with concomitant splenomegaly, giving the appearance of a more severe immune deficiency state than is actually present.

This increased rate of false negative antibody testing in the presence of HIV has been attributed to several factors, including a possible lack of HCV antibody production with immunosuppression, more rapid decline in HCV antibody titer, possible interaction between the two viruses, and an anti-HCV seroreversion into a negative state. This can under-report the prevalence of HCV infection by 10-30%. It is also important to note that the hypergammaglobulinaemia reported in HIV can lead to false positive anti-HCV EIA results. The foregoing therefore suggests that the measurement of serum HCV RNA by highly sensitive reverse transcriptase PCR may be required for detection of HCV in individuals with undetectable antibodies (depressed T-cell function) and other evidence of chronic liver disease.

Additionally, researchers have demonstrated that the prevalence of HCV is lower among patients whose risk behaviour is heterosexual intercourse compared to those whose is by parenteral means. A compelling postulation is the fact that most of the co-infected persons might have died earlier than they could have presented to our facility, hence evaluation. Several researchers have documented more mortality among HCV/HIV co-infected persons compared to HIV monoinfected individuals. This mortality is expectedly more among our population due to poor health resources.

Conclusion

HCV co-infection in HIV is prevalent and is becoming a significant co-morbidity that requires further evaluation among our population. This may involve the use of PCR to properly characterize false negative cases. The influences of HCV on the response of HIV patients to HAART, its effect on liver toxicity of ARVs as well as CD4 recovery are subjects of further study.

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