Is the Prevalence of Hepatitis C Virus (HCV) RNA in Anti-HCV–Positive Injection Drug Users Positively Correlated with Age?

To the Editor—Thomas et al. [1] observed higher levels of hepatitis C virus (HCV) RNA in older and human immunodeficiency virus (HIV)–infected women among a group of female injection drug users (IDUs) with detectable HCV RNA. In their analysis, HCV-infected persons with levels of HCV RNA below the limit of detection were excluded, because factors that affect HCV RNA clearance could differ from those that affect the level of viremia.

It is estimated that 20%–40% of HCV-infected persons spontaneously clear HCV RNA [2]. So far, however, studies investigating the natural course of HCV infection have considered mainly non-IDUs. Yet, in several ways, IDUs infected with HCV are not similar to other risk groups. The distribution of HCV genotypes in the former is different, with a predominance of genotypes 1a and 3. In general, IDUs are repeatedly exposed to low doses of HCV and are infected at a young age. In addition, illicit drug use and frequent coinfections also could influence the natural course of HCV infection.

Our objective was to study the relationship between HCV RNA prevalence and age among anti-HCV–positive IDUs. Indeed, repeated exposure to low doses of HCV at a young age may influence the clearance rate of HCV RNA in HCV-infected IDUs. Considering that, among IDUs, increasing age tends to be associated with longer duration of exposure, higher frequency of repeated exposure, or both, we conducted a systematic review, studying the relationship between the prevalence of HCV RNA and age among treatment-naïve IDUs who were positive for anti-HCV.

Published studies were identified by conducting a MEDLINE search and by screening the reference lists of retrieved papers. Only studies that included >50 untreated anti-HCV–positive IDUs and that reported both the prevalence of HCV RNA and the mean age of the study population were used for analysis. Homogeneity between studies was tested by use of the χ² test (Fastpro software; Academic Press). To detect associations between mean age and the prevalence of HCV RNA, linear regression analysis was performed (SPSS software; SPSS).

Eight papers were used for our analysis [3–10]. Relevant characteristics of these studies are presented in table 1. Six studies were done in Europe, one in the United States, and one in Australia. The prevalence of HCV RNA among anti-HCV–positive IDUs or former IDUs varied between 26.1% and 99.2% (P = 0.009, linear regression); however, no relationship was found between the prevalence of HCV RNA and sex or mean duration of injection drug use. When we entered (one by one) the variables sex, mean duration of drug use, and number of IDUs enrolled in the study as covariates in the linear regression model, with the prevalence of HCV RNA as a dependent variable and mean age as an independent variable, the β coefficient was not significantly altered.

We observed a statistically significant linear relation between mean age and the prevalence of HCV RNA in anti-HCV–positive IDUs. To our knowledge, this relationship has not been demonstrated previously. However, careful interpretation of our finding is indicated. First, the association we found...
Table 1. Characteristics and results of published studies selected for studying the relationship between hepatitis C virus (HCV) RNA prevalence and age among anti-HCV–positive injection drug users (IDUs).

<table>
<thead>
<tr>
<th>Author et al. [reference]</th>
<th>Country</th>
<th>Setting</th>
<th>Method of assignment</th>
<th>Study population</th>
<th>Diagnostic test</th>
<th>No. of subjects enrolled</th>
<th>Percentage HCV RNA positive (95% CI)</th>
<th>Age, mean years</th>
<th>Duration IDU, mean years</th>
<th>Percentage male</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pirisi et al. [3]</td>
<td>Italy</td>
<td>CTA</td>
<td>NDA</td>
<td>IDU in MMT</td>
<td>RT-PCR&lt;sup&gt;a&lt;/sup&gt;</td>
<td>189</td>
<td>56.1 (48.9–63.0)</td>
<td>29.8</td>
<td>NDA</td>
<td>75.1</td>
</tr>
<tr>
<td>Tonutto et al. [4]</td>
<td>Italy</td>
<td>CTA</td>
<td>Consecutive IDU</td>
<td></td>
<td>RT-PCR&lt;sup&gt;a&lt;/sup&gt;</td>
<td>86</td>
<td>61.5 (51.0–71.4)</td>
<td>30.2</td>
<td>9.9</td>
<td>80.2</td>
</tr>
<tr>
<td>Roy et al. [5]</td>
<td>Scotland</td>
<td>Hospital</td>
<td>NDA</td>
<td>IDU</td>
<td>RT-PCR&lt;sup&gt;a&lt;/sup&gt;</td>
<td>50</td>
<td>66 (52.1–78.1)</td>
<td>31</td>
<td>NDA</td>
<td>66.6</td>
</tr>
<tr>
<td>Coppola et al. [6]</td>
<td>Italy</td>
<td>CTA</td>
<td>Consecutive IDU</td>
<td></td>
<td>Simplified RT-PCR&lt;sup&gt;b&lt;/sup&gt;</td>
<td>88</td>
<td>26.1 (17.7–36.0)</td>
<td>26.1</td>
<td>6.3</td>
<td>NDA</td>
</tr>
<tr>
<td>Semprini et al. [7]</td>
<td>Italy</td>
<td>NDA</td>
<td>Ex-IDU</td>
<td>RT-PCR</td>
<td>Amplicor HCV test&lt;sup&gt;c&lt;/sup&gt;</td>
<td>63</td>
<td>52.4 (40.1–64.5)</td>
<td>32.1</td>
<td>10.7</td>
<td>100</td>
</tr>
<tr>
<td>Tong et al. [8]</td>
<td>US&lt;sup&gt;d&lt;/sup&gt;</td>
<td>Hospital</td>
<td>NDA</td>
<td>IDU</td>
<td>RT-PCR</td>
<td>125</td>
<td>99.2 (96.1–99.9)</td>
<td>43.5</td>
<td>NDA</td>
<td>70.4</td>
</tr>
<tr>
<td>Latt et al. [9]</td>
<td>Australia</td>
<td>CTA</td>
<td>Consecutive Pregnant IDU</td>
<td>RT-PCR</td>
<td></td>
<td>125</td>
<td>62.4 (53.7–70.6)</td>
<td>28.7</td>
<td>10.7</td>
<td>0</td>
</tr>
<tr>
<td>Trisler et al. [10]</td>
<td>Croatia</td>
<td>CTA</td>
<td>NDA</td>
<td>IDU</td>
<td>Amplicor HCV test&lt;sup&gt;c&lt;/sup&gt;</td>
<td>70</td>
<td>61.4 (49.7–72)</td>
<td>26.9</td>
<td>6.3</td>
<td>NDA</td>
</tr>
</tbody>
</table>

NOTE. CI, confidence interval; CTA, Centre for Treatment of Addiction; MMT, methadone maintenance treatment; NDA, no data available; RT-PCR, reverse-transcription polymerase chain reaction.

<sup>a</sup> Primers from 5′ noncoding region.
<sup>b</sup> Primers from 5′ noncoding region, without an RNA extraction step.
<sup>c</sup> Manufactured by Roche.
<sup>d</sup> California.

is based on a limited number of studies. Second, not all authors used the same diagnostic method for the detection of HCV RNA, and, even if this were the case, large inequalities in laboratory performances have been described elsewhere [11]. Furthermore, the absence of HCV RNA in an anti-HCV–positive patient can be due either to a resolved infection or to undetectable levels of virus in the serum. Also, fluctuating HCV RNA load profiles with intermittent undetectable levels of HCV RNA have been described elsewhere [12]. Last, the limited amount of data did not allow us to look for all possible confounders. For example, alcohol use has been reported to be correlated with higher serum levels of HCV RNA [13]. Other possible confounders are coinfections (HIV or hepatitis B virus), the distribution of HCV genotypes, and the amounts and types of drugs used [1].

If HCV infection in IDUs is more likely to resolve at a younger age, the higher prevalence in the older age groups could be due to continuing exposure and reinfection, which results in a chronic infection; otherwise, the natural course of HCV infection in IDUs could be characterized by frequent initial long periods of undetectable virus loads. Both scenarios could have major implications for our understanding of the dynamics of HCV transmission, the natural course of HCV infection, and the therapeutic approach to HCV infection in IDUs. To either confirm or refute this result, an individual patient-based meta-analysis of the studies seems to be warranted.

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References


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