4.1

Hepatitis C virus seroprevalence in the Netherlands

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ABSTRACT

A population-based anti-hepatitis C virus (HCV) prevalence is important for surveillance purposes and it provides insight into the burden of disease. In the Netherlands, a recent HCV seroprevalence estimate is not available. This national population-based cross-sectional serosurvey (PIENTER-2) resulted in a weighted national HCV seroprevalence of 0.30% (95% confidence interval 0.05 – 0.55%). About 70% of the HCV-positive individuals found were born in an HCV-endemic country.
INTRODUCTION

The estimated hepatitis C (HCV) prevalence in Europe ranges from 0.1% to 6.0%, with the highest prevalence (> 2%) in Southern and Eastern Europe [1]. Knowledge of the HCV prevalence in the general population of The Netherlands is limited. A Dutch cross-sectional serosurvey in 1995 – 1996 (the PIENTER-1 study) estimated a national HCV seroprevalence of 0.1% (95% confidence interval [CI] 0.01 – 0.2%) [2]. However, groups with higher risk profiles, such as individuals originating from HCV endemic regions, were underrepresented in this study, which resulted in a possible underestimation of the HCV prevalence. In 1997 the Dutch Health Council estimated a HCV seroprevalence for the general Dutch population of 0.1 – 0.4% (www.gezondheidsraad.nl). Furthermore, three seroprevalence studies were performed in urban areas in the Netherlands and these prevalences ranged from 0.2% to 1.1% [3-5]. Two of these studies oversampled individuals with a non-Western nationality and resulted in higher HCV seroprevalences than those estimated for the general Dutch population [3, 5]. In addition, an overall HCV prevalence of 0.4% was modelled in The Netherlands including (suboptimal) data from risk groups.

This current study (PIENTER-2) is an update of the previous national population-based survey (PIENTER-1) [6]. Individuals with non-Dutch nationalities were better represented in PIENTER-2, so that an improved and more recent estimation of the national HCV seroprevalence could be made.

METHODS

Between 2006 and 2007, cross-sectional serum samples and questionnaires from the Dutch population aged 0 – 79 years, selected from municipal registers, were collected. The questionnaire covered demographics, vaccination history, activities possibly related to infectious diseases and information related to sexually transmitted diseases (this latter was only asked of individuals aged ≥ 15 years). In total, 19 781 individuals were invited, including an oversampling of the largest migrant groups in The Netherlands. The study design is described more in detail elsewhere [6].

Laboratory methods

The presence of HCV-antibodies was determined using a micro particle enzyme immunoassay (MEIA; Abbott Laboratories, North Chicago, IL, USA) with immunoblot confirmation (INNO-LIA HCV score; Innogenetics, Belgium). The anti-HCV confirmed positive samples were tested for the presence of HCV RNA [7]. HCV genotypes 1 – 4 were detected by sequencing a 436-nt fragment of the NS5B region [7]. Viral load was determined using a published quantitative HCV PCR method [8].

Statistical analyses

For estimation of the HCV seroprevalence in PIENTER-2, we weighted by gender, age and ethnicity to account for deviations of the sample distribution from the general population in The
Netherlands in 2007 (Statistics Netherlands; http://statline.cbs.nl). We included all persons aged 15 – 79 years. Ethnicity was classified into the following groups: indigenous Dutch inhabitants, first-generation migrants born in low-endemic countries (estimated HCV prevalence < 2%), first-generation migrants born in intermediate/high-endemic countries (HCV prevalence ≥ 2%), second-generation migrants with parent(s) born in low-endemic countries and second-generation migrants with parent(s) born in intermediate/high-endemic countries. The classification of low- and intermediate/high-endemic countries was based on a recent review of Esteban et al [1] for European countries, and the Centers for Disease Control and Prevention (CDC) overview of Perz et al [9] for countries outside of Europe. Intermediate/high-endemic is referred to as high-endemic in this study. We also adjusted for the two-stage cluster sampling by taking into account regions and municipalities [6].

RESULTS

PIENTER-2 included 6386 samples from individuals aged 0 – 79 years (response 32%). Groups less likely to participate were: men, certain age groups and first-generation migrants. In the age group of 15 – 79 years a total of 4446 serum samples were tested for antibodies against HCV.

The median age of men (n = 1926) and women (n = 2520) was 48 years (inter quartile range [IQR] 31 – 63 years). For the first-generation migrants (n = 542) this was 54 years (IQR 36 – 64 years). Among these 542 first-generation migrants, the most reported countries were Surinam (19%), Indonesia (11%), Turkey (10%), Morocco (7%), Germany (6%) and the former Netherlands Antilles (5%). Ten percent (n = 465) reported having a tattoo or piercing (2% unknown). Eight persons reported having injected drugs (3% unknown), and three persons reported an HIV infection (10% unknown).

HCV seroprevalence

In PIENTER-2, 14 of the 4446 samples tested anti-HCV positive, including three samples with low antibody levels (Table 4.1.1), corresponding with a weighted seroprevalence of 0.30% (95% CI 0.05 – 0.55%). Extrapolating this to the national population (15- to 79-years old), it corresponds to approximately 38 800 HCV-positive individuals. The weighted seroprevalence for indigenous Dutch inhabitants was 0.17% (95% CI 0.00 – 0.36%) and 2.12% (95% CI 0.46 – 3.78) for first-generation high-endemic migrants. All other migrant groups were HCV negative.

Of the 14 HCV-positive individuals, 8 were male and 6 were female. Median age was 54 years. Four HCV-positive individuals were indigenous Dutch inhabitants. The other 10 individuals were born in high-endemic countries (Egypt [n = 2], Morocco [n = 2], Pakistan [n = 2], Surinam [n = 2], Indonesia [n = 1] and Ukraine [n = 1]) and lived there for at least 20 years before migrating to The Netherlands. Besides country of birth as a risk factor, one Moroccan reporting intravenous drug use, one Egyptian reported having a tattoo/piercing and an Egyptian partner, and both Egyptians reported occupational patient contact. Risk factors for persons born in The Netherlands were

<table>
<thead>
<tr>
<th>Age</th>
<th>Sex</th>
<th>Country of birth</th>
<th>HCV genotype</th>
<th>Viral load (IU/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>24</td>
<td>Female</td>
<td>The Netherlands</td>
<td>RNA negative</td>
<td></td>
</tr>
<tr>
<td>34</td>
<td>Female</td>
<td>Ukraine</td>
<td>1b</td>
<td>5.5 x 10⁴</td>
</tr>
<tr>
<td>34</td>
<td>Female</td>
<td>Pakistan</td>
<td>3a</td>
<td>7.5 x 10⁶</td>
</tr>
<tr>
<td>42</td>
<td>Male</td>
<td>The Netherlands</td>
<td>RNA negative</td>
<td></td>
</tr>
<tr>
<td>47</td>
<td>Female</td>
<td>Morocco</td>
<td>2i*</td>
<td>&lt;5.0 x 10⁷</td>
</tr>
<tr>
<td>51</td>
<td>Male</td>
<td>Egypt</td>
<td>RNA negative</td>
<td></td>
</tr>
<tr>
<td>53</td>
<td>Male</td>
<td>The Netherlands</td>
<td>RNA negative</td>
<td></td>
</tr>
<tr>
<td>55</td>
<td>Male</td>
<td>Pakistan</td>
<td>RNA negative</td>
<td></td>
</tr>
<tr>
<td>56</td>
<td>Male</td>
<td>The Netherlands</td>
<td>RNA negative</td>
<td></td>
</tr>
<tr>
<td>59</td>
<td>Female</td>
<td>Morocco</td>
<td>2i*</td>
<td>7.6 x 10⁷</td>
</tr>
<tr>
<td>59</td>
<td>Male</td>
<td>Egypt</td>
<td>4a*</td>
<td>3.9 x 10⁷</td>
</tr>
<tr>
<td>65</td>
<td>Male</td>
<td>Surinam</td>
<td>2***</td>
<td>&lt;5.0 x 10⁷</td>
</tr>
<tr>
<td>71</td>
<td>Male</td>
<td>Indonesia</td>
<td>1b</td>
<td>7.6 x 10⁶</td>
</tr>
<tr>
<td>79</td>
<td>Female</td>
<td>Surinam</td>
<td>2***</td>
<td>5.6 x 10⁴</td>
</tr>
</tbody>
</table>

*Endemic strains.

**Unclassified HCV subtypes, but phylogenetically linked to Surinam.

intravenous drug use (n = 2) and a tattoo/piercing placed before 1992 (n = 1). For the fourth indigenous Dutch person no risk profile could be obtained.

Among the 14 HCV-positive samples, 8 samples (57%) had detectable HCV RNA. Genotyping showed different HCV-genotypes (Table 4.1.1). Persons from Indonesia (n = 1) and Ukraine (n = 1) had genotype 1b, Moroccan (n = 2) and Surinamese (n = 2) persons had genotype 2, one Pakistani had genotype 3a and one Egyptian had genotype 4a, corresponding all with genotypes often found in their country of birth [10]. All four patients born in The Netherlands lacked HCV RNA.

**DISCUSSION**

The weighted anti-HCV seroprevalence among Dutch inhabitants aged 15- to 79-years old (total of 13 million inhabitants) is calculated at 0.30% (95% CI 0.05 – 0.55%) resulting in an estimated 38 800 individuals having anti-HCV. This prevalence equals the range of previous estimations for the general Dutch population, despite changes in HCV epidemiology. The chance to acquire HCV through blood transfusion has become negligible, the HCV-incidence among intravenous drug users (IDU) has sharply declined and HCV emerged as a sexually transmitted infection among HIV-positive men who have sex with men (MSM) [11]. In PIENTER-2, limited information was obtained on the HCV prevalence among high-risk groups like IDU and HIV-positive MSM. Despite the high number of total participants, the number of HIV-positive MSM and of participants reporting IDU was very small. Moreover, information on (former) IDU and HIV status were missing in 3 – 10% of the total study population. A possible underrepresentation of these groups could have resulted in an underestimation of the national HCV seroprevalence.
Most HCV-positive individuals were first-generation migrants, supporting the observation that immigration from HCV-endemic regions has significantly contributed to the changes in HCV epidemiology in European countries in the past 15 years [1]. No positive anti-HCV samples were found among other migrant groups (second-generation migrants and migrant from low-HCV-endemic regions). Based on the results, screening of individuals living in or migrating to The Netherlands from countries where HCV is highly endemic should be considered. Future research should focus on the cost-effectiveness of preventing complications of HCV by screening migrants born in high-endemic countries and prevention of HCV transmission.

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