HEPATITIS D VIRUS-RELATED ACTIVITIES AT CDC: CURRENT AND UNDER CONSIDERATION

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The findings and conclusions in this report are those of the author and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

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Viral hepatitis surveillance in the United States

- Infections under surveillance by the CDC include hepatitis A, hepatitis B (acute, chronic, and perinatal), and hepatitis C (acute, chronic, and perinatal).

- Each state and territory mandates the conditions and diseases that should be reported to HDs when identified by laboratories, health care providers, and health care facilities.

- Health departments then notify CDC of cases of conditions that are included on the Nationally Notifiable Condition (NNC) List.

- The NNC List is established through a collaboration between CSTE and CDC and is based on:
  - Conditions for which there is mandatory reporting to health departments,
  - Laboratory tests approved by the US Food and Drug Administration, and
  - Established CDC/CSTE case definitions.

- Hepatitis D is not a nationally notifiable condition.
**Anti-HDV Positivity in the US General Population, NHANES, 1999-2018**

<table>
<thead>
<tr>
<th>NHANES year</th>
<th>Anti-HBc tested</th>
<th>Anti-HBc positive</th>
<th>HBsAg positive</th>
<th>Anti-HDV positive***</th>
<th>Assay type</th>
</tr>
</thead>
<tbody>
<tr>
<td>1999–2000</td>
<td>7121</td>
<td>339</td>
<td>17</td>
<td>3 (18)</td>
<td>*</td>
</tr>
<tr>
<td>2001–2002</td>
<td>7950</td>
<td>355</td>
<td>13</td>
<td>1 (8)</td>
<td>*</td>
</tr>
<tr>
<td>2003–2004</td>
<td>7385</td>
<td>359</td>
<td>28</td>
<td>1 (4)</td>
<td>*</td>
</tr>
<tr>
<td>2005–2006</td>
<td>7393</td>
<td>327</td>
<td>22</td>
<td>0</td>
<td>*</td>
</tr>
<tr>
<td>2007–2008</td>
<td>7410</td>
<td>352</td>
<td>15</td>
<td>0</td>
<td>**</td>
</tr>
<tr>
<td>2009–2010</td>
<td>7885</td>
<td>366</td>
<td>30</td>
<td>0</td>
<td>**</td>
</tr>
<tr>
<td>2011–2012</td>
<td>7066</td>
<td>468</td>
<td>43</td>
<td>5 (12)</td>
<td>**</td>
</tr>
<tr>
<td>2013–2014</td>
<td>7656</td>
<td>437</td>
<td>38</td>
<td>19 (50)</td>
<td>**</td>
</tr>
<tr>
<td>2015–2016</td>
<td>7124</td>
<td>448</td>
<td>33</td>
<td>19 (58)</td>
<td>**</td>
</tr>
<tr>
<td>2017–2018</td>
<td>7001</td>
<td>414</td>
<td>29</td>
<td>6 (21)</td>
<td>**</td>
</tr>
</tbody>
</table>

*Explanation for high positivity rate*
- NHANES oversamples certain populations at higher risk for HBV infection
  - Populations at risk for HDV infection, e.g., immigrants
- NHANES sites change every cycle
- Impact of small number of samples tested for anti-HDV
  - Unweighted number of HBsAg positive fluctuated
  - Unweighted number of HDV positive returned to very low
- Assay was used in previous studies

*International Immunodiagnostics HDV Ab assay, a competitive enzyme immunoassay*

**DiaSorin ETI-AB-DELTAK-2 enzyme immunoassay**

***Among HBsAg + participants***

#unweighted
# Patients with Chronic Hepatitis B Tested for HDV Infection, the CHeCS Cohort, 2006-2018

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Tested for anti-HDV (N=416)</th>
<th>Anti-HDV result</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N (%)</td>
<td>Positive (n=20) n (%)</td>
<td>Negative (n=396) n (%)</td>
</tr>
<tr>
<td>Age category</td>
<td>N (%)</td>
<td>Positive (n=20) n (%)</td>
<td>Negative (n=396) n (%)</td>
</tr>
<tr>
<td>18-29</td>
<td>11 (2.6)</td>
<td>5 (25.0)</td>
<td>11 (2.8)</td>
</tr>
<tr>
<td>30-44</td>
<td>93 (22.4)</td>
<td>6 (30.0)</td>
<td>88 (22.2)</td>
</tr>
<tr>
<td>45-59</td>
<td>151 (36.3)</td>
<td>6 (30.0)</td>
<td>145 (36.6)</td>
</tr>
<tr>
<td>60-74</td>
<td>136 (32.7)</td>
<td>7 (35.0)</td>
<td>129 (32.6)</td>
</tr>
<tr>
<td>75+</td>
<td>25 (6.0)</td>
<td>2 (10.0)</td>
<td>23 (5.8)</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>139 (33.4)</td>
<td>7 (35.0)</td>
<td>132 (33.3)</td>
</tr>
<tr>
<td>Male</td>
<td>277 (66.6)</td>
<td>13 (65.0)</td>
<td>264 (66.7)</td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>115 (27.8)</td>
<td>9 (45.0)</td>
<td>106 (27.0)</td>
</tr>
<tr>
<td>Black</td>
<td>133 (32.2)</td>
<td>8 (40.0)</td>
<td>125 (31.8)</td>
</tr>
<tr>
<td>Hispanic</td>
<td>4 (1.0)</td>
<td>4 (1.0)</td>
<td></td>
</tr>
<tr>
<td>Asian</td>
<td>90 (21.8)</td>
<td>1 (5.0)</td>
<td>89 (22.6)</td>
</tr>
<tr>
<td>Hawaiian/PI</td>
<td>5 (1.2)</td>
<td>5 (1.3)</td>
<td></td>
</tr>
<tr>
<td>Non-Hispanic-Unknown</td>
<td>66 (16.0)</td>
<td>2 (10.0)</td>
<td>64 (16.3)</td>
</tr>
</tbody>
</table>

- Total number of persons with chronic hepatitis B = 6313
- Total number tested for HDV = 416 (6.6%)
- Total number positive for anti-HDV = 20 (4.8%)
- No risk factor information available

Preliminary analysis—CHeCS investigation team
### HDV Positivity of HBsAg Positive Samples Tested in a Commercial Laboratory, 2014-2017

<table>
<thead>
<tr>
<th>YEAR</th>
<th>HDV Ab+</th>
<th>Total HDV tested*</th>
<th>% HDV +</th>
</tr>
</thead>
<tbody>
<tr>
<td>2014</td>
<td>35</td>
<td>2302</td>
<td>1.5</td>
</tr>
<tr>
<td>2015</td>
<td>46</td>
<td>3451</td>
<td>1.3</td>
</tr>
<tr>
<td>2016</td>
<td>81</td>
<td>3886</td>
<td>2.1</td>
</tr>
<tr>
<td>2017</td>
<td>69</td>
<td>3995</td>
<td>1.7</td>
</tr>
<tr>
<td>TOTAL</td>
<td>231</td>
<td>13634</td>
<td>1.7</td>
</tr>
</tbody>
</table>

- Median age 53 years
- 37% were female and 63% were male
- Collectively, ten states accounted for 80% of the patients.
- Twenty-six states and DC were represented at least once.
- 45% of requests from hospitals and nearly 10% from other clinical laboratories.
- Overall, gastroenterologists represented 16% and internal medicine approximately 8%
- Limitations:
  - Missing clinical info/indication for HDV testing
  - Reason for testing unknown

*Unique (de-identified) HBsAg positive

Dr. Kaufman, Quest diagnostics
**ANTI-HDV AND GENOTYPE OF SAMPLES REFERRED TO CDC VIRAL HEPATITIS REFERENCE LAB (2012-2018)**

All samples in this study were sent to CDC for HDV RNA testing as potentially HDV infected
- Severe symptoms
- Some tested for anti-HDV prior to sending to us
- Samples from: Pennsylvania, California, New York, Texas, Utah, and Iowa

Testing at CDC:
- HBsAg (Vitros)
- Anti-HDV (ETI-AB-DELTAK-2) used until discontinued (In-house anti-HDV IgG test was developed and validated)
- Quantitative HDV RNA (in-house)

Genotype distribution:(N=26)
- 17 (65%) genotype 1
- 1 (4%) genotype 3
- 8 (31%) genotype 5

Unpublished data, viral hepatitis reference lab
SUMMARY

• Prevalence of infection and burden of disease is unknown
  • Studies are mainly based on small population and serologic tests
• Limited data indicate low prevalence of HDV infection
  • Not generalizable to the overall HBV infected population
• HDV testing is under-employed in the United States
  • There is no FDA-approved HDV test
  • Limited awareness and risk-based screening guidance for HDV testing
Strategies for the Elimination of HDV Infection in the United States

- Increase vaccination coverage among persons at risk
  - Universal adult hepatitis B vaccination recommendations are under consideration
- Increase linkage to care or engagement in care
  - Identification of HBV infected persons in the United States
    - Only one third of HBV infected persons are aware of their infection status
- CDC recommended HDV testing at initial evaluation of patients with HBV infection
  [https://www.cdc.gov/mmwr/preview/mmwrhtml/rr5708a1.htm](https://www.cdc.gov/mmwr/preview/mmwrhtml/rr5708a1.htm)
- Update screening recommendations for detection of HBV infection
  - New CDC Hepatitis B screening recommendations in 2022
  - Universal HBsAg screening of adults in the US general population for CHB is cost-effective and likely cost-saving compared to current CHB screening recommendations

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