Epidemiology of hepatitis B and hepatitis D in Turkey

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Sifting the evidence for sound studies with a take home message is laborious and the yield disappointing

BMJ, 2003

<table>
<thead>
<tr>
<th></th>
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</thead>
<tbody>
<tr>
<td>“Healthy” adults (6,800,000)</td>
<td>HBsAg</td>
<td>6.8 %</td>
<td>5.9 %</td>
<td>p&lt;0.05</td>
</tr>
<tr>
<td>Health care workers (14,000)</td>
<td>HBsAg</td>
<td>5.8 %</td>
<td>3.6 %</td>
<td>p&lt;0.05</td>
</tr>
<tr>
<td>Chronic liver disease (5,000)</td>
<td>HBsAg</td>
<td>60 %</td>
<td>56 %</td>
<td>p&lt;0.05</td>
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<tr>
<td>HBsAg positives (14,000)</td>
<td>Anti HDV</td>
<td>5.3 %</td>
<td>6 %</td>
<td>p&gt;0.05</td>
</tr>
<tr>
<td>HBV related chronic liver disease (3,000)</td>
<td>Anti HDV</td>
<td>38 %</td>
<td>27 %</td>
<td>p&lt;0.05</td>
</tr>
</tbody>
</table>

Değertekin H. Hepatit B, 2003  
Mıstık R, Balık İ. Viral Hepatit, 2001
Regional differences (1980-2000)

Eastern and Southeastern Anatolia:

- HBsAg prevalence: 8.8%
- HBsAg positivity among chronic liver disease: 68%
- AntiHDV prevalence among HBsAg carriers: 7.2%

Lower socioeconomic and educational status

Debeertekin H. Hepatit B, 2003
Mistik R, Balik İ. Viral Hepatit, 2001
HBsAg prevalence (0 - 18 years) 1990-2000

Mostly based on retrospective studies, evaluating out-patient children admitted to the local hospitals.


Mustik R, Balk I. Viral Hepatit, 2001

N: 2 683, 8 provinces. 5.4% HBsAg (+), 17% antiHBs
HBsAg prevalence - Age relation

**Graph**

- 0-5 years: İzmir
- 6-10 years: İstanbul
- 11-15 years: İzmir
- 16-20 years: İstanbul

**References**

- Pasha A et al. *Gulhane Tıp Derg* 1999;41:325-30 → n: 267 children (İstanbul)
HBsAg prevalence (0 -18 years)
2001-2008

Mardin → Cross-sectional study (n: 802) based on systematic sampling method, representing 6 – 17 years old school children (n:147 200) of the area.


İstanbul (n: 302, 9 mn – 8 yr)
AntiHBs:
9 months – 3 years: 90.4%
3 – 5 years: 89.5%
5-8 years: 73% (1% HBsAg+)

Nalbantoğlu B, 2008
<table>
<thead>
<tr>
<th>Region</th>
<th>City</th>
<th>Investigator (1990s)</th>
<th>N</th>
<th>sAg (eAg)</th>
<th>Investigator (2000s)</th>
<th>N</th>
<th>sAg (eAg)</th>
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<tbody>
<tr>
<td>Marmara</td>
<td>İstanbul</td>
<td>Çepni, 1996</td>
<td>4078</td>
<td>4.4</td>
<td>Karaca, 2003</td>
<td>460</td>
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<td></td>
<td>Bursa</td>
<td>Adatepe, 1997</td>
<td>2564</td>
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<td>602</td>
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<td>Api, 2008</td>
<td>236</td>
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<td>Aegean</td>
<td>İzmir</td>
<td>Erensoy, 1996</td>
<td>760</td>
<td>4.2 (15.2)</td>
<td>Yegane, 2003</td>
<td>760</td>
<td>4.2 (9.3)</td>
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<tr>
<td>Mediterr.</td>
<td>Mersin</td>
<td></td>
<td></td>
<td></td>
<td>Börekçi, 2004</td>
<td>114</td>
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<td>Central</td>
<td>Ankara</td>
<td>Mete, 1993</td>
<td>2831</td>
<td>5.6</td>
<td>Kölgeliler, 2001</td>
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<td>Kayseri</td>
<td>Özsoyulu, 1993</td>
<td>2667</td>
<td>3.8</td>
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<td></td>
<td></td>
<td>Abacı, 1995</td>
<td>400</td>
<td></td>
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<td>Black sea</td>
<td>Rize</td>
<td></td>
<td></td>
<td></td>
<td>Atılğan, 2009</td>
<td>1130</td>
<td>2.56</td>
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<td>Eastern</td>
<td>Erzurum</td>
<td>Kadanalı, 1997</td>
<td>282</td>
<td>6.3</td>
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<td>SouthE.</td>
<td>Urfa</td>
<td></td>
<td></td>
<td></td>
<td>Harma, 2003</td>
<td>136</td>
<td>7.3 (0)</td>
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<td>Adıyaman</td>
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<td></td>
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<td>Aslan, 2001</td>
<td>450</td>
<td>4.6 (9.5)</td>
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<td></td>
<td></td>
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<td>Kölgeliler, 2009</td>
<td>677</td>
<td>4.7</td>
</tr>
</tbody>
</table>

**14 763 → 4.2%**  **4 611 → 3.6%**  **p=0.07**
Blood donors – Turkish Red Crescent

• 1989 to 2004 -16 years
• 22 centers
• 6 240 130 blood donors

HBsAg (+)
5.23% (1991) → 2.10% (2004)
p=0.001


<table>
<thead>
<tr>
<th>Year</th>
<th>İzmir n:61409</th>
<th>İstanbul n:19499</th>
<th>Kocaeli n:28027</th>
<th>Isparta n:51361</th>
<th>Konya n:52454</th>
<th>Adıyaman n:12384</th>
<th>Van 17200</th>
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<tbody>
<tr>
<td>2000</td>
<td>2,96</td>
<td>0,68</td>
<td>1,79</td>
<td>1,6</td>
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<td>3,67</td>
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<td>2001</td>
<td>2,62</td>
<td>2,60</td>
<td>1,74</td>
<td>1,7</td>
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<td>2,57</td>
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<td>2002</td>
<td>2,13</td>
<td>2,16</td>
<td>2,41</td>
<td>1,54</td>
<td>2,1</td>
<td>3,1</td>
<td>1,3</td>
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<tr>
<td>2003</td>
<td>2,17</td>
<td>1,88</td>
<td>1,55</td>
<td>0,90</td>
<td>2,3</td>
<td></td>
<td>2,1</td>
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<tr>
<td>2004</td>
<td>1,95</td>
<td></td>
<td></td>
<td></td>
<td>N: 242 334</td>
<td>1.8%</td>
<td></td>
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<tr>
<td>2005</td>
<td>1,76</td>
<td>1,98</td>
<td>0,84</td>
<td></td>
<td>3,0</td>
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<tr>
<td>2006</td>
<td>1,94</td>
<td>1,25</td>
<td>0,91</td>
<td></td>
<td>3,7</td>
<td></td>
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<tr>
<td>2007</td>
<td></td>
<td></td>
<td>0,92</td>
<td></td>
<td>3,5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2008</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>3,1</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>2,0</td>
<td>2,06</td>
<td>1,9</td>
<td>1,1</td>
<td>1,8</td>
<td>3,3</td>
<td>2,4</td>
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</table>
General population-1

Isparta province, 2006-07
Population (≥18 years): 134,983 → Study population: 2,852 (71.5% of target)
  Random sampling from 3 rural villages.
Markers were determined by card test, positives were confirmed by EIA
Mean age: 42.5±14.4
HBsAg: 2.5%
AHBs: 16.2%
Significant correlation between HBsAg (+)
  • Low educational status (p=0.001)
  • Male gender (p=0.009)
  • Increasing age (p=0.017)


Bolu province, 2003
Population: 74,235 → Study population: 2,204 (rural and urban regions)
HBsAg: 2.7%

Tokat province
Population (≥18 years): 530 000
Study population: 1095
  Random sampling from 70 regions selected by a cluster sampling method.
Mean age: 41.4 ± 17 (18-95)

HBsAg: 5.5%
AHBs: 22.8%

No significant difference between
• Men vs women
• Living in rural vs urban area

Yıldırım B et al. Turk J Gastroenterol 2009
General population -3

**Erzurum province**
Study population: 384, Mean age: 41.7
- HBsAg: 9.1%
- Seropositivity: 36.7%
  (vaccination: 7.3%)
  

**4 provinces: Diyarbakır, Urfa, Mardin, Batman**
Study population: 2,888 (96.3% of the target)
30-cluster sampling method
- HBsAg: 7%
- Seropositivity: 47.4% (exposure to HBV)
Risk factors: Living in rural area, male sex, higher age, family history of jaundice

Health care workers

- Population: 1158
  - HBsAg: 2.9% (vs 4.7% <2000) (p=0.005)
  - AntiHBs: 71.8%
    - Vaccinated: 56.5%
  - Seronegative: 25.2%

Demir İ, et al. İnfeksiyon Dergisi, 2006
Yılmazlar A, et al. Türk Anest Rean Der Dergisi, 2005
Pre-op screening

- Population: 12,756
  - HBsAg (+) 3.6% (2.3 - 4.5)

Children scheduled for elective surgery
- Population: 429
- Age: 6.02±4.14 (0-16)
  - HBsAg: 1.6%
  - AntiHBs: 39.6%
  - Seronegative: 54%

Çöl C, et al. Klinik Bilimler, 2004
### Etiology of acute hepatitis

<table>
<thead>
<tr>
<th>Reference</th>
<th>Year</th>
<th>n</th>
<th>HAV %</th>
<th>HBV %</th>
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<tbody>
<tr>
<td>Kandemir, 2007</td>
<td>1990-2004</td>
<td>561</td>
<td>48.2</td>
<td>41.5</td>
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<tr>
<td></td>
<td></td>
<td>17</td>
<td>17</td>
<td>28</td>
</tr>
<tr>
<td>Yamazhan, 2001</td>
<td>1993-1997</td>
<td>246</td>
<td>43</td>
<td>45.9</td>
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<tr>
<td></td>
<td></td>
<td>15-20</td>
<td>21-30</td>
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<tr>
<td>Çolpan, 2003</td>
<td>2001-2003</td>
<td>73</td>
<td>54.8</td>
<td>39.8</td>
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<td></td>
<td></td>
<td>20.4±6.1</td>
<td>30.9±12.5</td>
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<tr>
<td>Ertuğrul, 2006</td>
<td>2004-2005</td>
<td>46</td>
<td>87</td>
<td>13</td>
</tr>
<tr>
<td></td>
<td></td>
<td>12.35</td>
<td>37.33</td>
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</tr>
</tbody>
</table>

- HAV is the major cause before the age of 20
- HBV is seen mainly in the adult population (20 to 40 years of age)
Hepatocellular Carcinoma

HCC incidence: 0.83/100 000
(similar between 2000 and 2003) - MoH,2003

1994 – 1997 → 7 hospitals
n: 207
Uzunalimoğlu, 2001

1994 – 2007 → 5 hospitals
n: 221
Alacacioğlu, 2008

18% of the HBV positives were infected with HDV

2% of the HBV positives were infected with HDV
Horizontal transmission is the major route

- HBsAg prevalence increases with age among children
  - Peaks between 5-15 years of age
- Intra-familial transmission is common (parents to child, sibling to sibling)
  - 302 children with CHB
    - Risk for intra-familial transmission - 71.9%
    - Risk for parenteral transmission – 23%
  - Risk is higher when both the parents are HBsAg(+)  
  - Risk increases proportionately with the number of children in the family

Değertekin H, Public Health, 2008
Doğancı T, et al. World J Gastroenterol, 2005
HDV-1

Anti-HDV positivity in asymptomatic HBsAg carriers

<table>
<thead>
<tr>
<th>Year</th>
<th>n</th>
<th>Anti-HDV %</th>
<th>Reference</th>
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<td>1980-1990</td>
<td>659</td>
<td>4.1</td>
<td>Değertekin, 2006 (General Turkish population)</td>
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<td>1991-2000</td>
<td>5162</td>
<td>5.4</td>
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<td>2000-2005</td>
<td>792</td>
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<tr>
<td>2002-2005</td>
<td>889</td>
<td>6</td>
<td>Celen, 2006 (Diyarbakır)</td>
</tr>
</tbody>
</table>


HDV-2
AntiHDV positivity in chronic hep B
(n: 5231)

Summary - HBV

Turkey is a country of intermediate endemicity for HBV

- Prevalence of HBV shows a regional difference (higher in southeastern and eastern parts of Turkey)
- HBsAg - peaks around 10-20 years of age
- Decrease in HBsAg prevalence (field studies = 2.5 – 9.1%)
  - Decrease among children
    - Possibly by preventing perinatal and horizontal transmission by the vaccination program
  - Decrease among blood donors (5.23% → 1.8%)
    - Quality of the pre-donation screening
    - Increase of civilian vs military donors
  - Decrease among HCW (4.7% → 2.9%)
  - No significant decrease among pregnant women

6.8% → 5.85% → 3.8% (n:28,000) (2.2% inc.BD, n:270,000)

Summary - 2

• HBV is the leading cause of chronic hepatitis and HCC.

• HDV is still an important problem although the prevalence is decreasing
  – More prevalent in the east and southeast
    • Lower socioeconomic and educational status

• Well-designed studies needed for more reliable data