Epidemiology of hepatitis B and D in Greece

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Epidemiological data for HBV & HDV in Greece

No data in samples representative of general population
Very few data for the prevalence of HDV

Some studies in

- **Specific low-risk groups** (blood donors, army recruits, children, pregnant women)
- **Specific high-risk groups** (IVDU, prisoners, HIV+, prostitutes, minorities)
- **Specific areas**
Changing factors affecting the current epidemiology of viral hepatitis

- Modes of transmission
- Traveling – Globalization
- Mutants
- Refugees - Immigrants

Changing profile of the population in Greece after ’90 (migration)

2001: 797,093 (7.2%) immigrants – 65% from Albania
Worldwide prevalence of chronic HBV infection

Prevalence of HBsAg
- >8 % - High
- 2-7 % - Intermediate
- < 2 % - Low

CDC
Hepatitis B: Greece. General Information

- **Estimated HBsAg prevalence in 1970-1980**: >3-5%
- **Universal HBV vaccination applied since 1998**
- **Current HBsAg prevalence**:
  - Population study: **2.1%** *(Eur J Epidemiol 2003;18:551)*.
  - Company employees: **2.6%** *(Eur J Epidemiol 2001;17:721)*.
  - Hospitalized patients (Crete): **2.7%** *(BMC Public Health 2001;1:17)*.
Estimated prevalence of HBsAg and anti-HCV in Greece (general population, blood donors & high risk groups)

<table>
<thead>
<tr>
<th></th>
<th>HBsAg+ (%)</th>
<th>anti-HCV+ (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>N=637920 (1971-2001)</td>
<td>2.12</td>
<td>2.66</td>
</tr>
<tr>
<td>N=130293 (1993-2001)</td>
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</table>
Prevalence of HBV in low-risk groups in Greece
Prevalence of HBsAg in blood donors in Athens-Piraeus greater area (1971-1996)

- Vissoulis 1972 (n=6708): 4.9%
- Kyriakis 2000 (1991-1994, n=242625): 0.84%
- Kyriakis 2000 (1995-1996, n=45504): 0.34%
Epidemiological surveillance in Greek blood donors: 2000-2001 (Σ.Κ.ΑΕ.)

<table>
<thead>
<tr>
<th>Positive units</th>
<th>N</th>
<th>%</th>
</tr>
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<tbody>
<tr>
<td>HBsAg</td>
<td>1028</td>
<td>0.35</td>
</tr>
<tr>
<td>Anti-HCV</td>
<td>204</td>
<td>0.009</td>
</tr>
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Prevalence in 41 transfusion centers (296,012 blood units)
### Epidemiology of Hepatitis B: Greece

#### Prevalence of HBsAg Carriage among Army Recruits

<table>
<thead>
<tr>
<th>Region</th>
<th>1972 (N=32,000)</th>
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<tr>
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<tr>
<td>National Average</td>
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*Vissoulis et al, 1972; Vakalopoulos et al, in press*
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<td></td>
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<td><strong>National Average</strong></td>
<td><strong>5.04%</strong></td>
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Epidemiology of Hepatitis B: Greece

Prevalence of HBsAg Carriage among Army Recruits

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<tr>
<td>Metropolitan Area</td>
<td>3.07%</td>
<td>0.86%</td>
<td>-72%</td>
</tr>
<tr>
<td>Southern Greece</td>
<td>5.57%</td>
<td>2.34%</td>
<td>-58%</td>
</tr>
<tr>
<td>Central Greece</td>
<td>5.21%</td>
<td>1.22%</td>
<td>-77%</td>
</tr>
<tr>
<td>Northern Greece</td>
<td>7.37%</td>
<td>2.38%</td>
<td>-68%</td>
</tr>
<tr>
<td>Islands (including Crete)</td>
<td>3.20%</td>
<td>0.70%</td>
<td>-78%</td>
</tr>
<tr>
<td>National Average</td>
<td>5.04%</td>
<td>1.27%</td>
<td>-75%</td>
</tr>
</tbody>
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Vissoulis et al, 1972; Vakalopoulos et al, in press
HBsAg prevalence in Greek army recruits

50-80% decrease of HBsAg prevalence from '70s to '80s
Change in risk factors
Low vaccination rate in late '90s. 1999: Anti-HBs (+) 32.6%

Papaevangelou G, Vaccine 1998
*Stamouli M et al, Eur J Epidemiol 1999
HBsAg prevalence in women at reproductive age in Greece

- Albanian (n=500): 13.4%
- Total (n=13581): 1.15%
- Greek: 0.3%
- Albanian: 5.1%
- Eastern European: 1.1%
- African: 0.4%
- Asian: 4.2%

Malamitsi A et al.  
Eur J Epidemiol 1996

Elefsiniotis IS et al.  
Origin of HBsAg(+) women at reproductive age in Greece

- Albania (71.3%)
- Eastern Europe (7.0%)
- Africa (1.3%)
- Asia (2.6%)
- Greece (17.8%)

4.5% HBeAg (+)

Prevalence of HBV in high-risk groups in Greece
HBV infection in anti-HCV (+) Greek IVDU

Elefsiniotis I et al. Eur J GE Hep 2006; 18: 1227-31
Epidemiological surveillance in Greek IVDU

IVDU, n=1094

- HBsAg (+): 4.8%
- anti-HCV (+): 67.9%

ΕΚΤΕΠΝ, 2002
HBV/HCV infection in prisoners in Greek prisons

Giotakos O et al. Epidemiol Infect 2003; 130: 497-500

- IVDU (n=544)
  - HBsAg (+): 6.5%
  - anti-HBc (+): 57.6%
  - anti-HCV (+): 58.2%

- Non-IVDU (n=194)
  - HBsAg (+): 13%
  - anti-HBc (+): 49%
  - anti-HCV (+): 6.5%
HBV infection in Greek HIV (+) patients

- 61% HBeAg (+)
- HBV DNA (10^7-10^{12} cp/mL)

HBV prevalence in immigrants in Greece

- **Albanians in NW Greece** (n=1020)
  - HBsAg (+): 22%
  - anti-HBc (+): 71%

- **Albanians in Athens** (n=130)
  - Roussos A et al. World J GE 2003
  - HBsAg (+): 15%
  - anti-HBc (+): 53%

- **Immigrants from former USSR in Thrace** (n=463)
  - Papoutselis K et al. EASL 2001
  - HBsAg (+): 4%
  - anti-HBc (+): 17%
Prevalence of HBV in specific areas of Greece
Age-specific prevalence of HBV infection in selected Greek areas

HBsAg prevalence in Thrace

Papoutselis K et al. EASL 2001
HBV infection in Greece: Modes of transmission
Risk factors associated with acute hepatitis B cases in Greek adults

- Homosexual activity: 12%
- Heterosexual activity: 22%
- IVDU: 35%
- Transfusions: 11%
- Health care workers: 5%
- Iatrogenic: 1%
- Unknown: 1986-1990 N=1387

Possible source of infection in Greek adults with chronic HBV infection

- Vertical transmission: 7.4%
- Intrafamilial spread: 16.9%
- Heterosexual contact: 3.5%
- Iatrogenic: 4.1%
- Other: 3.5%
- Unknown: 64.6%

HBV cohort – KEELPNO, N=3353
G Touloumi, personal communication
Intrafamilial spread: the most common mode of transmission in Greeks with chronic HBV infection

HBV infection:
The burden of disease in Greece
HBV: the most common cause of acute viral hepatitis in Greek adults

N=2076
1986-1990

HAV: 14%
CHB: 9%
Non-(A-C)*: 4.5%
HCV: 5.5%

*incl. 0.1% HEV

Natural history of chronic HBV infection

- Immune tolerant phase
- HBeAg sero-conversion phase
- Inactive chronic HBV carrier state
- HBeAg(-) CHB

- Serum HBV DNA, log_{10} IU/mL
- ALT
- ULN

HBeAg(+)

Profile of Greek HBsAg(+) patients in primary care

Chronic HBV patients, %

- HBeAg(+) CHB: 5.3%
- HBeAg(-) inactive carriers: 76.4%
- HBeAg(-) CHB: 18.3%

N=263

Patients with chronic HBV infection at Hippokration hospital, Athens, Greece (2002-2006)

N=632

- HBeAg(+) CHB/Ci: 6%
- HBeAg(-) inactive carriers: 46%
- HBeAg(-) CHB/Ci: 48%
Patients with chronic HBV infection at Hippokration hospital, Athens, Greece (2002-2006)

- **N=632**

<table>
<thead>
<tr>
<th>Chronic HBV patients, %</th>
<th>HBeAg(+) CHB</th>
<th>HBeAg(-) inactive carriers</th>
<th>HBeAg(-) CHB Ci*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>5.3%</td>
<td>46%</td>
<td>41%</td>
</tr>
<tr>
<td></td>
<td>0.8%</td>
<td></td>
<td>7%</td>
</tr>
</tbody>
</table>

*Decompensated Ci
Proportion of immigrants among patients with chronic HBV infection in Greek hospitals (1997-2006)

<table>
<thead>
<tr>
<th>Category</th>
<th>Number of Cases</th>
<th>Proportion (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All HBV+ cases</td>
<td>n=3234</td>
<td>19%</td>
</tr>
<tr>
<td>HBV+ adults</td>
<td>n=3112</td>
<td>17%</td>
</tr>
<tr>
<td>HBV+ children</td>
<td>n=122</td>
<td>57%</td>
</tr>
</tbody>
</table>

HBV cohort – KEELPNO
G Touloumi, personal communication
Proportion of immigrants among patients with chronic HBV infection at Hippokration hospital, Athens, Greece (2002-2006)

- All HBV+ cases: 24% (n=632)
- HBeAg(+) CHB/Ci: 41% (n=39)
- HBeAg(-) inactive carriers: 22% (n=290)
- HBeAg(-) CHB/Ci: 24% (n=303)

Significant differences are indicated by p-values:
- P=0.014
- P=0.038
HDV Epidemiology in Greece
HDV infection

HDV + HBV coinfection
HDV + HBV acute infection

HDV superinfection
HDV infection on chronic HBV infection
HDV superinfection as a cause of acute hepatitis in chronic HBV patients in Greece

Papatheodoridis et al. Hepatology 1994; 20: 297A
HDV as a cause of acute hepatitis in Greek IVDU with acute or chronic hepatitis B

Tassopoulos et al. Prog Clin Biol Res 1993; 382: 221-7
Patients with chronic HBV ± HDV infection at Hippokration hospital, Athens, Greece (2002-2006)

N=655

- **Chronic HBV±HDV patients, %**
  - **HBV:** 96.5%
  - **HDV:** 3.5%
Proportion of cirrhotics among patients with chronic HBV ± HDV infection at Hippokration hospital, Athens, Greece (2002-2006)

Patients with decomp. cirrhosis, %

- HBV excluding carriers: 15% (n=342)
- HDV: 48% (n=23)

P<0.001
Proportion of immigrants among patients with chronic HBV ± HDV infection at Hippokration hospital, Athens, Greece (2002-2006)

- HBV: 24% (n=632)
- HDV: 52% (n=23)

P=0.005
HBV/HDV Epidemiology in Greece: Summary

- Decrease of HBsAg prevalence over the past decades
  - Improvement of social-economic status
  - Improvement in health care system
  - Better awareness of high-risk groups
  - Vaccination

- Still areas of high HBsAg prevalence – Surveillance

- Increasing age of chronic HBV patients:
  increasing probability of clinical events (decompens., HCC)

- HDV: mainly in IVDU or specific areas – More severe disease

- Immigrants after 1990: 1/10-1/12 of Greek population
  - High HBsAg prevalence
  - Higher rates of HBeAg(+) – Younger age, HBV genotypes
  - Higher rates of HDV infection