Hepatitis E in Italy

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Viral hepatitis in Italy
*(60 million inhabitants)*

2,500 new cases/year of acute viral hepatitis (i.e. 4.2 per 100,000 inhabitants)

- **Hepatitis A**: 50.2%
- **Hepatitis B**: 32.3%
- **Hepatitis C**: 10.9%
- nAnC hepatitis: 6.6%

Source: SEIEVA 2003-2008
### Anti-HEV prevalence in Italy

<table>
<thead>
<tr>
<th>Region</th>
<th>North (anti-HEV)</th>
<th>Centre (anti-HEV)</th>
<th>South/Islands (anti-HEV)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Milan (0.95*)</td>
<td></td>
<td>Florence 1.4</td>
<td>Foggia 3</td>
</tr>
<tr>
<td>Genoa 1.3</td>
<td></td>
<td>S.Marino 2.3</td>
<td>Catania 3</td>
</tr>
<tr>
<td>Venice 2.6</td>
<td></td>
<td>Latina 3</td>
<td>Cagliari 5.4</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Messina 6.2</td>
</tr>
</tbody>
</table>

Higher rate among IVDUs expecially those infected with HIV, homosexuals and those with chronic hepatitis C.

* confirmed by WB
Hepatitis E in Italy

Site: Institute of Virology, University of Milan

Period: January 1994 - December 2008

Study population: 601 consecutive pts with acute nAnC hepatitis
(negativity for IgM anti-HAV, HBsAg, IgM anti-HBc, anti-HCV, HCV-RNA and exclusion of autoimmunity, alcohol or hepatotoxic drugs)

Gender: 61.5% M, 38.5% F

Age: mean 36.8 yrs, median 35 yrs, range 1-79 yrs

ALT: mean 1582 IU/ L, median 1207 IU/ L, range 101-12520 IU/ L
Acute hepatitis E: case definition

Detection of:

- HEV RNA in sera or stools by nested RT-PCR
- IgM anti-HEV
- Seroconversion to anti-HEV IgG

To identify risk factors, all patients were interviewed with a pre-coded questionnaire.
**Laboratory diagnosis of hepatitis E**

122/601 (20.3%) pts were diagnosed with acute hepatitis E
- 83% males; median age 31.5 yrs (3-68 yrs);
- ALT median peak 2106 IU/L (122-12290 IU/L)

122
- IgM and IgG anti-HEV +

81* (66.4%)
- HEV RNA + (serum samples)

37**/601 (6.2%)
- IgG anti-HEV +
- but both IgM anti-HEV and HEV RNA -

* Stools available from 36/81 patients were also HEV RNA +
** 44.8% of these patients were immigrants from or travelled to endemic areas
Risk factors associated to hepatitis E

- Unknown: 3.1%
- Contact with an infected patient: 7.1%
- Travel to:
  - India: 89.8%
  - Bangladesh, Pakistan, Marocco, Somalia, Angola, Sri Lanka, Capo Verde: 0%
Hepatitis E in Italy: Results

Phylogenetic tree (unrooted) of 28 viral strains from patients with acute hepatitis E
HEV RNA among farming swine and wild boars in Northern Italy

<table>
<thead>
<tr>
<th>Animals</th>
<th>N° samples tested</th>
<th>HEV RNA + (RT-PCR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>a Randomly selected pigs*</td>
<td>274 stools</td>
<td>115 (42%)</td>
</tr>
<tr>
<td>b Killed wild boars</td>
<td>88 bile</td>
<td>22 (25%)</td>
</tr>
</tbody>
</table>

* from six different swine farms

\( ^a \text{Di Bortolo et al, Vet Microbiol 2008} \)
\( ^b \text{Martelli et al, Vet Microbiol 2008} \)
Viral hepatitis E in Italy
Conclusions - 1

- Acute clinically overt hepatitis E is quite uncommon in Italy, accounting for approx 1.2% of cases yearly reported to the surveillance system (approx 30 cases/year).

- Most acute hepatitis E are travel-related.

- Sporadic cases of non-travel related hepatitis E have been reported in non-endemic areas, including Italy.
Non-travel related diseases are usually caused by genotype 3.

Wide-spread genotype 3 in pigs, wild boars and other mammals suggests that human infections may have zoonotic origin.
Viral hepatitis E
Conclusions - 3

- Discrepancies between anti-HEV prevalence and autochthonous hepatitis E incidence may be due to inapparent infections caused by native, attenuated HEV strains that rarely cause clinical diseases.

- Predilection of genotype 3-related disease for elderly and immunologically compromised individuals, adds weight to this hypothesis.