GEOEPIDEMIOLOGY
OF PRIMARY BILIARY CIRRHOSIS
IN CENTRAL GREECE

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Introduction

Primary biliary cholangitis

is an autoimmune hepatic disease arising from an interplay between genetic and environmental factors

Prevalence

is characterized by important geographical differences possibly attributed to the influence of infectious factors (viruses, bacteria) and xenobiotics

Van de Water J. Hepatology 2001
Long SA, Autoimmun Rev 2002
Aim

Our aim was to describe

- The geographical and seasonal distribution of PBC in central Greece
- The basic characteristics of our patients at presentation
- Response to treatment
- Prognosis
Patients and Methods

482 PBC patients
followed at Department of Medicine and Research Laboratory of Internal Medicine, University of Thessaly
during a sixteen year time period
2000-2015
Results I

Age distribution

- ♂/♀: 6.4/1
- Same age distribution (56.3 ± 13.7 years)
Results II

Mean yearly prevalence
32 patients/year

Seasonal preference
during spring
Results III

Hashimoto thyroiditis 12.9%

Risk Factors (%)

- concurrent autoimmune diseases: 28.4%
- smoking (previous/active): 26.6%
- urinary tract infections: 11%
- malignancy: 7.7%
- family history of PBC: 3.7%
- hormone replacement: 1%

Breast cancer: 3.5%
Results IV

Symptoms at presentation

<table>
<thead>
<tr>
<th>Condition</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pruritus</td>
<td>25.9%</td>
</tr>
<tr>
<td>Xerostomia / dry eyes</td>
<td>14.9%</td>
</tr>
<tr>
<td>Fatigue</td>
<td>11.8%</td>
</tr>
<tr>
<td>Arthralgia / Myalgia</td>
<td>11.2%</td>
</tr>
<tr>
<td>Abdominal Pain</td>
<td>8.7%</td>
</tr>
<tr>
<td>Rash</td>
<td>1.5%</td>
</tr>
<tr>
<td>End stage liver disease symptoms:</td>
<td></td>
</tr>
<tr>
<td>Ascites</td>
<td></td>
</tr>
<tr>
<td>Variceal bleeding</td>
<td></td>
</tr>
<tr>
<td>Hepatic encephalopathy</td>
<td></td>
</tr>
<tr>
<td>Jaundice</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2.5%</td>
</tr>
</tbody>
</table>
Results V

Symptoms at presentation

Symptoms (%)

- Females:
  - Yes: 58.8%
  - No: 41.2%

- Males:
  - Yes: 41.5%
  - No: 58.5%

End-stage symptoms (%)

- Females:
  - Yes: 1.9%
  - No: 98.1%

- Males:
  - Yes: 6.2%
  - No: 93.8%

p = 0.014

p = 0.06
Presence of cirrhosis at presentation

Factors associated with the presence of cirrhosis at baseline (multivariate analysis)

<table>
<thead>
<tr>
<th>Factors</th>
<th>Adjusted OR</th>
<th>95% CI</th>
<th>Adjusted P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (male)</td>
<td>2.437</td>
<td>1.135-5.232</td>
<td>0.02</td>
</tr>
<tr>
<td>Age</td>
<td>1.106</td>
<td>1.076-1.136</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Co-incidence of other liver disease</td>
<td>5.108</td>
<td>2.098-12.434</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Alcohol consumption</td>
<td>4.851</td>
<td>1.697-13.867</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

232/281 (82.6%) patients – Stage 0-I-II
49/281 (17.4%) patients – Stage III-IV
Results VII

Autoantibodies prevalence (%)

- **anti-gp210**: 5.4% → positive association with AST, ALT, ALP, γGT, IgM, Mayo Risk Score
- **anti-sp100**: 10% → positive association with AST, γGT, IgM
- **AMA**: 96.5%
Results VIII

GLOBE SCORE

Responders (≤0.30)  Non Responders (>0.30)

Parameters
• Age at UDCA treatment initiation
• 1st year UCDA treatment (bilirubin, ALP, Albumin, Platelets)

Lammers, Gastroenterology 2015
The 5-, 10-, and 15-year survival or transplant-free rates for non-responders were 84%, 50%, and 42%, respectively.

**Negative predictive factors for response to treatment:**
- Cirrhosis (OR=22.312, 95% CI: 5.988-83.137, P<0.001)
- Lower educational level (OR=2.993, 95% CI: 1.441-6.217, P<0.01)
Results X

Patient Outcome (mean follow up 5.1 years - 15.7 years range)

Non-liver related death (n=22) 4.6%
Liver related death / OLT (n=40) 8.3%

Alive (n=420) 87.1%

Negative prognostic factors for liver related events

<table>
<thead>
<tr>
<th>Variables</th>
<th>Adjusted OR</th>
<th>95% CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>1.065</td>
<td>0.999-1.135</td>
<td>0.050</td>
</tr>
<tr>
<td>Alcohol consumption</td>
<td>9.363</td>
<td>1.218-71.986</td>
<td>0.030</td>
</tr>
<tr>
<td>Bilirubin</td>
<td>2.564</td>
<td>1.039-6.331</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Presence of cirrhosis</td>
<td>21.902</td>
<td>4.583-104.664</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
PBC prevalence in Thessaly 582 patients/ 1 million residents
19 regions with a prevalence >800 patients/ million residents

*439/482 (91%) patients were residents in Thessaly at the time of presentation
Conclusions

• PBC has a high prevalence in Thessaly

• Geographical and seasonal distribution implies relation with environmental factors (atmosphere pollution, water pollution with toxic waste, lignite rich soil etc.)
Conclusions

- A large portion of patients is asymptomatic, with an early histological stage at the time of diagnosis

- Male patients are more likely to be cirrhotic at presentation

- Poor prognosis is related to the presence of cirrhosis, older age, increased bilirubin and alcohol consumption
Conclusions

- The GLOBE SCORE has an optimal application to the Greek population and it must be used to stratify patients with a worse chance of responding to UDCA treatment.
Thank you for your attention!