Hepatic steatosis and/or steatohepatitis in primary biliary cholangitis: An innocent bystander or a guilty player?


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Non-alcoholic fatty liver disease (NAFLD) is an entity with rising prevalence (25% of the adult population in the world), so coexistence of NAFLD with other liver diseases is inevitable.

Background (II)

There is an increased prevalence of PBC in Central Greece.

582 patients / 1 million residents

Gatselis, Dalekos et al (submitted)
• Previous studies in PBC patients have shown:

  – 40-50% co-incidence of steatosis

  – 6-15% co-incidence of steatohepatitis

  – association with ↑AST, ↑ALT, histologically more advanced disease
Aim

To investigate the prevalence and significance of NAFLD in patients with Primary Biliary Cholangitis (PBC) in Central Greece.
Patients and Methods

482 patients were appropriately diagnosed with PBC and followed-up between 2000-2015, in the Department of Medicine and Research Laboratory of Internal Medicine, Medical School, University of Thessaly, Larissa, Greece.

A liver biopsy was performed in 281 patients (245 females, 87.2%; median age 54 years) at the time-point of initial evaluation.
Patients and Methods

NAFLD* in PBC patients

Demographics

Presence of symptoms

Liver function tests (ALP, γGT, AST, ALT, bilirubin, PT, albumin)

AMA anti-gp210 anti-sp100 IgM

Liver biopsy staging

Response to treatment (GLOBE score)

Outcome (death/OLT)

*according to liver biopsy findings
Results (I)

Prevalence of steatosis/steatohepatitis in PBC patients

- Steatosis: 26%
- Steatohepatitis: 12%
- No: 62%

38% of PBC patients had histological findings of NAFLD
Results (II)

Association of LFTs, Mayo Risk Score & IgM with the presence of steatosis ± steatohepatitis in PBC patients
Results (III)

Association of liver biopsy stage with the presence of steatosis ± steatohepatitis in PBC patients

Ludwig’s Stage (%)

<table>
<thead>
<tr>
<th></th>
<th>no</th>
<th>steatosis ± steatohepatitis</th>
<th>steatosis</th>
<th>steatohepatitis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ludwig’s Stage</td>
<td>stage III-IV</td>
<td>23,4</td>
<td>7,5</td>
<td>92,5</td>
</tr>
<tr>
<td></td>
<td>stage I-II</td>
<td>76,6</td>
<td>92,5</td>
<td>90,6</td>
</tr>
</tbody>
</table>

p=0.001
Factors associated with the coexistence of NAFLD in PBC patients (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>ALP</td>
<td>0.997</td>
<td>0.993-1.001</td>
<td>0.131</td>
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<tr>
<td>γGT</td>
<td>1.000</td>
<td>0.998-1.003</td>
<td>0.669</td>
</tr>
<tr>
<td>bilirubin</td>
<td>0.900</td>
<td>0.484-1.672</td>
<td>0.738</td>
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<tr>
<td>IgM</td>
<td>0.966</td>
<td>0.994-0.999</td>
<td>0.002</td>
</tr>
<tr>
<td>albumin</td>
<td>1.563</td>
<td>0.859-2.846</td>
<td>0.144</td>
</tr>
<tr>
<td>advanced liver stage (III-IV)</td>
<td>0.502</td>
<td>0.208-1.213</td>
<td>0.126</td>
</tr>
</tbody>
</table>
Results (V)

Impact of the presence of steatosis ± steatohepatitis in PBC patients on response to treatment according to GLOBE score

Response to treatment (%)

- **no**: 28/72 = 38.9%
p<0.03
- **steatosis ± steatohepatitis**: 13.6/86.4 = 16%
- **steatosis**: 12.3/87.7 = 13%
- **steatohepatitis**: 16.7/83.3 = 17%

Treatment response was assessed in 199 patients (naïve at baseline) without evidence of a concurrent other liver disease treated for at least 1-year with ursodeoxycholic acid (UDCA) at 13-15 mg/kg/day.
Results (VI)

Impact of the presence of steatosis ± steatohepatitis in PBC patients on the outcome

Liver-related death / Liver transplantation (%)

<table>
<thead>
<tr>
<th></th>
<th>no</th>
<th>steatosis</th>
<th>steatosis ± steatohepatitis</th>
<th>steatohepatitis</th>
</tr>
</thead>
<tbody>
<tr>
<td>no steatosis</td>
<td>91,9</td>
<td>97,1</td>
<td>95,8</td>
<td>100</td>
</tr>
<tr>
<td>no steatosis ± steatohepatitis</td>
<td>8,1</td>
<td>2,9</td>
<td>4,2</td>
<td>0</td>
</tr>
</tbody>
</table>

P-value was estimated in 265 out of 281 patients (16 patients with non-liver related death were excluded from analysis)
Results (VII)

Outcome of PBC patients after stratification for GLOBE score and NAFLD

Treatment response was assessed in 199 patients (naïve at baseline) without evidence of a concurrent other liver disease treated for at least 1-year with ursodeoxycholic acid (UDCA) at 13-15 mg/kg/day.
Summary

1. **38%** of PBC patients had histological findings of steatosis/steatohepatitis

2. In **univariate analysis**, presence of steatosis/steatohepatitis assoc. with ↓ **ALP, γGT, bilirubin, Mayo Risk Score, IgM**, ↑ **albumin** levels and **earlier histological stages of PBC**

3. In **multivariate analysis**, presence of steatosis/steatohepatitis assoc. only with ↓ **IgM** levels

4. **Response to treatment was better** in patients with steatosis/steatohepatitis

5. **No difference was found regarding the outcome**
Conclusions

Despite the high prevalence of NAFLD in more than one-third of PBC patients, there was no evidence of acting as an aggravating factor.
Thank you for your attention!