Incidence of non-alcoholic fatty liver disease in non-obese and non-diabetic individuals during normal aging

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1 BACKGROUND AND AIMS

Non-alcoholic fatty liver disease (NAFLD) is the most common cause of chronic liver disease worldwide. It is considered a direct consequence of the rising global epidemic of obesity and the associated increase in the prevalence of diabetes. As well, aging entails dramatic alterations in the liver capacity, which tends to accumulate lipids. In the last ten years, the prevalence of NAFLD has increased considerably and now is thought to affect 30% of the general population with even higher rates in aged people [1].

Recently, we have discovered a body mass index (BMI) dependent lipidomic signature associated to NAFLD [2,3]. Based on this study with 467 biopsied patients, we obtained a set of serum lipid biomarkers that discriminates between normal liver (no NAFLD) and NAFLD, with areas under the receiver operating characteristic curve (AUCROC) of 0.98 for the cohort with BMI under 30 kg/m² [4,5]. In addition, we also found a signature that differentiates between non-alcoholic steatohepatitis (NASH) and steatosis (AUCROC = 0.99 for BMI under 30 kg/m²).

We have used this diagnostic test (OWLLiverCare) to determine the incidence of NAFLD in non-obese and non-diabetic individuals during normal aging.

2 SAMPLES

This study enrolled 262 healthy volunteers, all of Caucasian origin. Inclusion criteria involved normal blood pressure, normal urine and serum biochemistry, moderate alcohol intake (lower than 30 g/day) and BMI under 30 kg/m². Individuals taking medications for diabetes, hypertension or hyperlipidemia were excluded. Serum samples were collected under fasting conditions. Volunteers were classified according to their age into four cohorts [6].

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<tr>
<td>[20,30)</td>
<td>44 (48.7)</td>
<td>156 ± 23</td>
<td>71 ± 31</td>
<td>82 ± 7</td>
<td>15 ± 7</td>
<td>15 ± 6</td>
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<td>[30,40)</td>
<td>76 (49.4)</td>
<td>172 ± 25</td>
<td>87 ± 28</td>
<td>80 ± 7</td>
<td>18 ± 7</td>
<td>13 ± 5</td>
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<td>[40,50)</td>
<td>78 (50.5)</td>
<td>183 ± 24</td>
<td>82 ± 9</td>
<td>90 ± 8</td>
<td>20 ± 8</td>
<td>17 ± 8</td>
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<tr>
<td>[50,60)</td>
<td>64 (61.5)</td>
<td>191 ± 23</td>
<td>90 ± 10</td>
<td>98 ± 10</td>
<td>22 ± 10</td>
<td>21 ± 10</td>
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<td>[60,80)</td>
<td>69 (73.5)</td>
<td>188 ± 27</td>
<td>95 ± 10</td>
<td>105 ± 10</td>
<td>25 ± 12</td>
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3 METHODS

Chloroform/methanol serum extracts were analyzed by reverse ultra-performance liquid chromatography coupled to mass spectrometry (UPLC-MS). Through this analysis, we have previously determined the sera metabolite profile of 467 biopsed individuals with normal liver histology (n=98) or diagnosed with NAFLD (n=377). This has allowed us to define a robust BMI-dependent lipidomic signature that reliably/accurately differentiates normal liver from NAFLD [3,4].

BMI-Dependent Serum Lipidomic Discrimination between no NAFLD and NAFLD (BMI < 30 kg/m²)

No NAFLD

NAFLD

ROC curves calculated for the estimation (black line) and validation (grey line) data sets in cohort of patients with BMI under 30 kg/m².

AUCROC = 0.984 (se = 0.016)

Sensitivity = 1.000

Specificity = 0.999

Conclusions:

Volunteers were diagnosed as no NAFLD or NAFLD using the OWLLiverCare diagnostic test, to determine the incidence of NAFLD in non-obese and non-diabetic population during normal aging.

4 RESULTS

If evaluated per decade, 21% of volunteers between 20-30 years of age were diagnosed with NAFLD. These percentages remained similar in the following decades. However, the percentage of individuals with NAFLD doubled (40%) between 40-50 years of age. This rise in NAFLD was mainly due to an increased incidence of steatosis in men. Between 50-60 years of age the total prevalence of NAFLD increased to 50% and the differences between women and men approached parity. These results agree with the described prevalence of NAFLD according to age and gender [1].

Percentage of prevalence of NAFLD according to the age (per decade) and gender.

5 CONCLUSIONS

The prevalence of NAFLD in 262 non-diabetic individuals with body mass index under 30 kg/m², normal blood pressure and biochemistry was evaluated using the OWLLiverCare diagnostic test, based on a serum lipidomic profiling. The incidence increases from 21% to 50% during aging (20-50 years of age). In men, the incidence of NAFLD starts to increase between 40-50 years of age whereas in women it starts a decade later.

Disclosure: Jos M Mato, Stock Shareholder OWL.

The following people have nothing to disclose: P Ortiz, R Mayo, M Pérez-Cornelsen, I Martinez-Arranz, M L Martinez-Chantar, S C Lu.