Regional Differences across Europe in Advanced Fibrosis and Cirrhosis among HIV/HCV Co-infected Persons between 2010-2015

S Amele1, L Peters2, JD Lundgren3, J K Rockstroh4, H Sambatakou5, T Staub6, F Maltez7, C Leen8, C Pedersen9, JM Gatell10, S Moreno11, R Matulionyte12, G Kyselyova13, J Karpov14, D Jilich15, M Parczewski16, K Zilmer17, H Elinav18, J M Gattell1

1Department of Infection and Population Health, University College London, London, UK. 2Copenhagen HIV Programme, Faculty of Health Science, University of Copenhagen, Copenhagen, Denmark. 3Department of Infectious Diseases, Rigshospitalet, Copenhagen, Denmark. 4University Hospitals Klinik Bonn, Germany. 5Hospitalet General Hospital, Greece. 6Centre Hospitalier de Luxembourg, Luxembourg. 7Hospital Curry Cabral, Portugal. 8Western General Hospital, United Kingdom. 9Östere Hospitalh, Faro, Iceland. 10Hospital Clinic, Spain. 11Hospital Ramon y Cajal, Spain. 12Vilnius University Hospital Santariskiu Klinikos, Lithuania. 13Crimen Republican AIDS centre, Ukraine. 14Belarus State Medical University, Belarus. 15Faculty Hospital Bulovka, Czech Republic. 16Pomeramian Academy of Medicine (PAM), Poland. 17West-Tallinn Central Hospital, Estonia. 18Hadassah Hospital, Israel. 19Hospital Universitaria Vaudes, Switzerland. 20University Clinical Centre Ljubljana, Slovenia.

BACKGROUND
The increasing availability of directly acting antivirals (DAAs) for the treatment of hepatitis C coinfected persons has in some countries led to targeting DAAs to those most at need (fibrosis ≥F3) because of their cost. The prevalence of fibrosis ≥F3 across Europe is largely unknown, nor is the extent to which it is changing in different regions of Europe.

AIMS:
• To investigate regional differences in the prevalence of fibrosis ≥F3 or liver events in persons co-infected with HIV/HCV.
• To investigate factors associated with developing fibrosis ≥F3 and how this changes over time across different regions.

METHODS:
• Individuals co-infected with chronic HCV (defined as being HCV-AB positive and HCV-RNA positive) with a liver fibrosis biomarker (liver biopsy, APRI, hyaluronic acid or FibroScan) result whilst under follow-up in EuroSIDA on January 1st each year from 2010 to 2015 were included in this study.
• The proportion of HCV-RNA positive patients with fibrosis METAIVR ≥F3 or liver events (hepatic decompensation, hepatocellular carcinoma) was compared between regions over time. Fibrosis ≥F3 was defined by:

<table>
<thead>
<tr>
<th>Liver fibrosis biomarker</th>
<th>Result</th>
</tr>
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<tbody>
<tr>
<td>Liver biopsy</td>
<td>≥F3</td>
</tr>
<tr>
<td>APRI</td>
<td>score ≥1.75</td>
</tr>
<tr>
<td>Hyaluronic acid</td>
<td>&gt;250mg/mL</td>
</tr>
<tr>
<td>FibroScan</td>
<td>≥9kPa</td>
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</table>

• Adjusted odds ratio of an individual having fibrosis ≥F3 was assessed using logistic regression. Generalised estimating equations were used to allow the inclusion of individuals under follow-up in multiple years. This method was also used to investigate the effect of time within each region on the odds of developing fibrosis ≥F3.

RESULTS:
• There were 3712 individuals with chronic HCV and a liver fibrosis biomarker in the study, 965 of which had fibrosis ≥F3 at some point during follow-up (characteristics of patients shown in Table 1). 1411, 1367, 1317, 1382, 1371 and 2121 persons were under follow-up on 1/1/2010-2015 respectively.
• The proportion of individuals with fibrosis ≥F3 under follow-up on 1/1/2010-2015 was 20.3%, 26.5% to 34.5%.

LIMITATIONS:
• Not every individual had information on the date they were diagnosed, therefore detailed analysis of late presenters was not feasible.
• The proportion of patients with a liver-related event was also small, which precluded regional comparisons.

CONCLUSIONS:
26% of individuals with HIV/HCV had fibrosis ≥F3, with significant differences between regions likely attributable to duration of HCV infection. The odds of developing fibrosis ≥F3 was increasing by a small amount each year, with the most marked increases in Southern Europe. Although recent HCV diagnoses were uncommon, there was still a considerable proportion of recently diagnosed individuals with fibrosis ≥F3. The prevalence of fibrosis ≥F3 and the relationship between CD4 and fibrosis ≥F3 highlights the need to prioritise HIV and HCV screening, linkage to care and treatment across Europe. If for any reason HCV cannot be treated, the relationship between CD4 count and fibrosis ≥F3 also highlights the importance of encouraging patients to start ART while waiting for HCV treatment, to maintain HIV suppressions and increase their CD4 cell count.

Table 1: Characteristics of HIV/HCV co-infected persons, by level of fibrosis

<table>
<thead>
<tr>
<th>Region of Europe</th>
<th>Overall (n=3712)</th>
<th>North (n=1212)</th>
<th>Central West (n=1411)</th>
<th>Central East (n=1367)</th>
<th>East (n=1382)</th>
<th>South (n=1371)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age group</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>01‐01‐2010</td>
<td>3069 (82.4)</td>
<td>775 (64.1)</td>
<td>1096 (77.7)</td>
<td>1005 (73.5)</td>
<td>988 (72.4)</td>
<td>987 (72.2)</td>
</tr>
<tr>
<td>01‐01‐2011</td>
<td>2817 (75.9)</td>
<td>687 (56.6)</td>
<td>962 (67.5)</td>
<td>915 (65.7)</td>
<td>873 (63.7)</td>
<td>956 (70.3)</td>
</tr>
<tr>
<td>01‐01‐2012</td>
<td>2573 (71.7)</td>
<td>632 (52.2)</td>
<td>878 (61.5)</td>
<td>859 (62.3)</td>
<td>795 (57.3)</td>
<td>872 (63.2)</td>
</tr>
<tr>
<td>01‐01‐2013</td>
<td>2343 (64.0)</td>
<td>554 (45.7)</td>
<td>740 (54.6)</td>
<td>732 (53.4)</td>
<td>689 (49.5)</td>
<td>754 (55.1)</td>
</tr>
<tr>
<td>01‐01‐2014</td>
<td>2143 (58.0)</td>
<td>487 (39.5)</td>
<td>583 (42.2)</td>
<td>543 (39.2)</td>
<td>495 (35.5)</td>
<td>543 (39.3)</td>
</tr>
<tr>
<td>01‐01‐2015</td>
<td>1972 (53.0)</td>
<td>416 (33.5)</td>
<td>421 (30.5)</td>
<td>413 (30.0)</td>
<td>385 (27.6)</td>
<td>414 (30.2)</td>
</tr>
</tbody>
</table>

*HIV‐RNA (cp/ml)
<500,000 1337 (36.0) 1015 (36.9) 322 (33.4)
No 189 (5.1) 153 (5.6) 36 (3.7)

**HCV‐RNA (IU/ml)
<500,000 1337 (36.0) 1015 (36.9) 322 (33.4)
No 189 (5.1) 153 (5.6) 36 (3.7)

†Men Who Have Sex With Men

Gender
Male 2650 (71.4) 1909 (69.5) 741 (76.8)
Female 1062 (28.6) 838 (30.5) 224 (23.2)

HCV Risk
Yes 3523 (94.9) 2594 (94.4) 929 (96.3)
No 2906 (78.3) 2172 (79.1) 734 (76.1)

CD4 count (cells/mm3)
>200 3046 (82.1) 2353 (85.7) 693 (71.8)
500‐10000 255 (6.9) 180 (6.6) 75 (7.8)
<500 421 (11.0) 169 (6.1) 53 (5.4)

HIV‐RNA (cp/ml)
>500,000 961 (25.9) 655 (23.8) 306 (31.7)
<500,000 1337 (36.0) 1015 (36.9) 322 (33.4)
No 189 (5.1) 153 (5.6) 36 (3.7)

Download poster at: www.chip.dk

EuroSIDA study group: http://www.chip.dk/Studies/EuroSIDA/Study-group

Sarah Amele
sarah.amele.16@ucl.ac.uk
Research Department of Infection and Population Health
University College London
Tel: +44 20 7794 0500 Ext 34611

http://www.chip.dk