HIV/HCV co-infection in children and young people in Europe: results from a cohort collaboration

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Background

- *Data are lacking on the epidemiology, clinical course and treatment of chronic HCV infection in HIV co-infected children and young adults*
- *Adult studies have shown that HIV modifies the natural history of HCV infection, including higher HCV viral loads and accelerated liver disease progression*
- *Estimates of HCV seroprevalence in paediatric HIV cohorts in EPPICC (including around 6500 children with HIV) are <1% in Northern European cohorts, 6% in Southern European and 7% in Eastern European cohorts*

Aim

To study children and young adults living in Europe who were infected with HIV and HCV vertically or in childhood in order to better understand the clinical presentation and management of this condition

Methods

- Retrospective cross-sectional cohort study within 11 European paediatric HIV cohorts participating in the European Pregnancy and Paediatric HIV Cohort Collaboration (EPPICC)
- Patients with HCV co-infection aged >18 months and <25 years and with HIV/HCV infection acquired vertically or in childhood were included
- Children were considered infected if HCV RNA was detected in ≥2 serum samples at least 3months apart and/or when testing of antibodies against HCV was positive after 18 months of age
- Data were collected according to a standard protocol from HIV cohort databases, with additional case-note review for HCV-specific variables as required

Definitions

For subjects with vertically-acquired HCV, birth date was used as the date of infection; for other subjects, date of HCV diagnosis was used as a proxy for date of infection.

The ULN cut off for AST and ALT was defined as 40 IU/L.

Spontaneous viral clearance was defined as disappearance of HCV RNA in ≥2 consecutive samples taken 6 months apart.

Results

Demographics

- Of 255 subjects, 148 (58%) were female
- Median age at last follow-up was 16.2 years (IQR 10.0, 20.3)

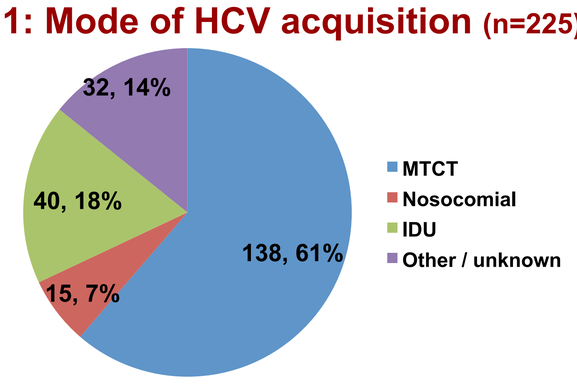
Table 1: Demographic & HIV-related characteristics

Characteristic	N (%) or median
Age at most recent visit	16.2 years (IQR 0.0-20.3)
White ethnicity	204 (91)
Area of residence	
Northern Europe	10 (4)
Southern Europe	62 (28)
Central /Eastern Europe	153 (68)
Has history of AIDS (n=198)	45 (23)
CD4 count at last visit (n=202)	655 cells/mm^3 (IQR 417-905)
On ART at last visit (n=198)	159 (80)
Undetectable HIV RNA at last visit (n=188)	114 (61)
HIV clinical staging (n=187)	
Not symptomatic	4 (2)
CDC category A / WHO stage 1 or 2	66 (35)
CDC category B / WHO stage 3	76 (41)
CDC category C / WHO stage 4	45 (23)

HCV acquisition

- Most (84%, n=188) subjects had been diagnosed with HCV in childhood
- Most subjects had vertically-acquired HCV infection (Fig 1)
- Median duration of HCV infection among those with vertical infection was 13 years (IQR 9, 18)

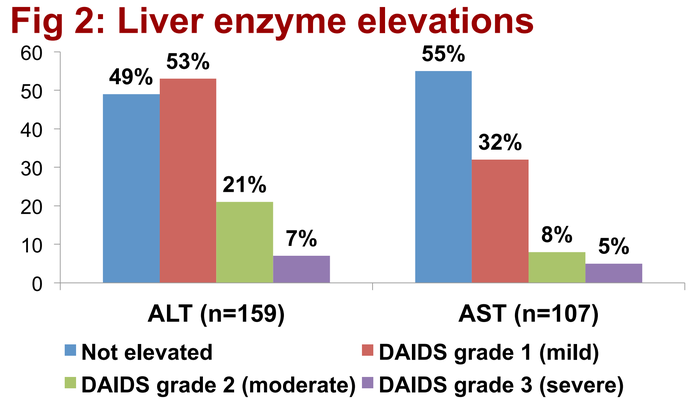
Fig 1: Mode of HCV acquisition (n=225)



HCV genotype and clinical characteristics

- HCV genotype (GT) was known for 180 (80%) of subjects, with 100 (56%) infected with GT1, 5 (3%) with GT2, 55 (30%) with GT3 and 20 (11%) with GT4
- HCV **viremic status** at last visit was available for 157 subjects who had not received HCV treatment
  - 131 (83%) were viremic and 26 (17%) non-viremic
  - The 26 did not fulfil criteria for spontaneous clearance
- 42% (85/200) had **hepatomegaly** in previous 12 months and 19% (38/200) had **splenomegaly**
- 60% (95/159) had **elevated ALT** above ULN and 63% had **elevated AST** at their most recent visit (Figure 2)
  - A greater proportion of subjects with IDU, other or unknown modes of HCV acquisition had grade 2 or 3 ALT elevations than those with MTCT or nosocomial acquisition (p=0.009)
- 95 subjects had **transient elastography** (TE) results
  - 9/12 subjects with TE >9.5 kPa were vertically infected
  - Median duration of HCV infection was 10 years (IQR 3.3, 18.0) among those with TE <9.6 kPa and 18 years (IQR 13.9, 19.2) with greater liver stiffness (p=0.033)
- 17 (8%) subjects had **liver biopsies** at a median of 13 yrs
  - 6 had bridging fibrosis and 1 had cirrhosis (at age 19 yrs)

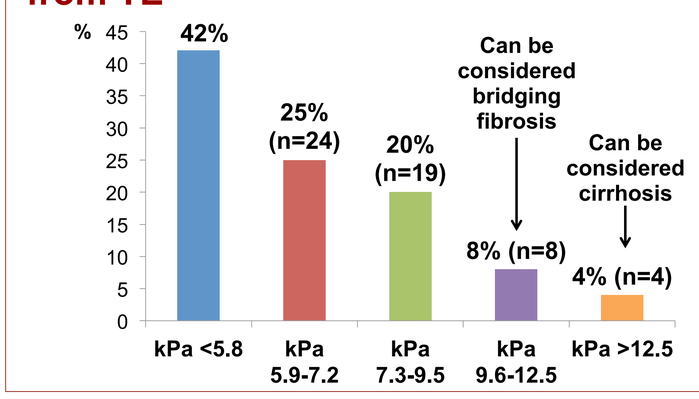
Fig 2: Liver enzyme elevations



HCV treatment

- 55 (24%) patients received HCV treatment (peginterferon alfa + ribavirin) subjects, with 13 patients having ongoing treatment
  - 28 were GT1, 1 GT2, 21 GT3, 3 GT4 and 2 GT unknown
  - Sustained virological response at 24 weeks after end of treatment (SVR24) was 33% (6/18) for GT1 and 70% (7/10) for GT3; the 1 GT2 patient had an SVR24 and 1 of the 2 patients with unknown GT

Fig 3: Liver stiffness (kPa) measured from TE



Conclusions

- Our findings with respect to clinical manifestations, liver enzymes, TE and liver biopsy data suggest that HCV-related liver disease may be worse in HIV/HCV co-infected children and young people than in those with HCV mono-infection
- With respect to HIV disease, only 5% had severe immunodeficiency, reflecting high treatment rates (80%)
- The high proportion of patients with progressive liver disease underscores the need both for close monitoring and earlier HCV treatment
- With respect to HCV treatment data, as a quarter of our treated patients do not have SVR24 data yet, our results should be considered preliminary
- However, findings to date suggest that HCV treatment success with pegIFN/RBV is substantially lower in the context of HIV co-infection than seen for children with HCV alone, particularly for GT1 and 4
- With new antivirals promising better outcomes in HCV mono- and HIV/HCV co-infected adults, there is a pressing need to initiate clinical trials in this population

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We dedicate this poster to the memory of our friend and colleague Dan Duiculescu