

Hepatitis B or Hepatitis C coinfection in HIV-infected pregnant women in Europe

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Introduction

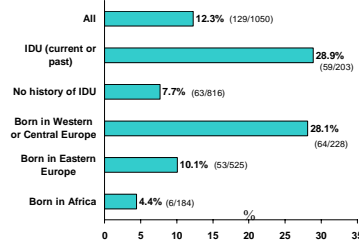
- Globally an estimated 350-400 million people are chronically infected with HBV, 190 million chronically infected with HCV and 39.5 million people living with HIV infection
- As a result of shared routes of transmission, the HIV, HBV and HCV epidemics overlap with around 10% of the HIV-infected population estimated to have chronic HBV infection and around a third, chronic HCV infection
- Clinical management of HIV-infected individuals coinfecting with HCV or HBV is challenging and HIV infection is known to have a negative impact on the outcome of HCV and HBV infections.
- Although whether or not HCV directly impacts upon HIV disease progression remains controversial, the complex interactions between HIV/HCV coinfection and HAART use and the indirect effect of these on HIV disease progression are increasingly apparent
- Few studies have addressed the issue of coinfection with HCV and/or HBV in HIV-infected pregnant women to date
- There are no data on prevalence of HIV/HCV or HIV/HBV coinfection in antenatal populations in Europe.

Methods

- The European Collaborative Study (ECS) is an ongoing cohort study in which HIV-1 infected pregnant women are enrolled and followed in pregnancy, and their children followed from birth
- Maternal information routinely collected included socio-demographic characteristics and HIV-specific information, but markers of HBV or HCV infection are not routinely recorded.
- This nested study included women from 15 ECS centres in Spain, Italy, UK, Belgium, Sweden, Germany and Ukraine who delivered Jan 1999- Oct 2005 (truncated to Jan 2003-Oct 2005 for the Ukrainian centres)
- Due to limited laboratory capacity at the time of the study, only 21% of women from the Ukraine centres had CD4 counts and none had HIV RNA levels measured
- Information on HBsAg positivity and HCV antibody reactivity was collected retrospectively from antenatal records; all centres screened all HIV-infected pregnant women for anti-HCV antibodies and HBsAg
- Analyses relating to HCV coinfection were based on HCV antibody reactivity only (i.e. may have included some women with resolved HCV infection).
- Statistical methods included logistic regression and standard linear mixed effects (LME) regression models.

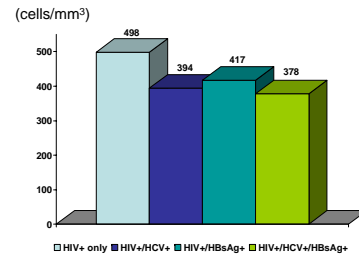
- Of the 1050 HIV-infected pregnant women, 520 were enrolled in Ukraine and 530 in W.Europe
- Most women were white, although nearly a fifth (n=184) were black Africans
- Median age was 27 years (15-43 years)
- 20% (203/1020) had an injecting drug use (IDU) history and 31% (311/1010) had a previous or current IDU partner
- Of the 129 HCV-seropositive women, 21 were concurrently HBsAg positive

Figure 1: HCV seropositivity prevalence



Immunological status

Figure 3: Median baseline CD4 counts

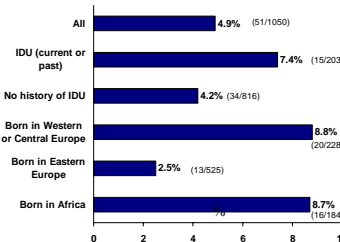


- Significantly more HCV-seropositive women had CD4 counts <200 cells/mm³ compared with HIV-monoinfected women (14% (10/73) vs 9% (46/498), p<0.001)
- The same was true for HBsAg positive women (22% (5/23) vs 9% (46/498), p<0.001)

Results (1)

- Logistic regression analysis identified the following as significantly associated with HCV seropositivity:
 - maternal age ≥ 35 y (AOR 3.45, 95%CI 1.66-7.20) vs <25y, IDU history (AOR 2.95, 1.86-4.58) vs no history and HBsAg carriage (AOR 5.80, 2.78-12.1)
- The following characteristics were significantly associated with HBsAg carriage:
 - African region of birth (AOR 2.74, 95% CI 1.20-6.26) vs European, ever having an IDU sex partner (AOR 0.38, 0.15-0.96) and HCV seropositivity (AOR 6.44, 3.08-13.5)

Figure 2: HBsAg positivity prevalence



Use of ART

Ukraine (n=520)

- 16 (3%) received no ART, 88 (17%) single dose (sd) NVP only, 393 (71%) antenatal monotherapy +/- sdNVP and 23 (4%) HAART
- 14% (7/49) of HCV-seropositive women received HAART vs 3% (16/464) of HIV-monoinfected

Western/Central European Centres (n=530)

- 51 (10%) received no antenatal ART, 159 (30%) mono/dual therapy and 320 (60%) HAART
- 43% (10/23), 43% (28/65), 47% (7/15) and 64% (275/427) of HIV+/HBsAg+, HIV+/HCV+, HIV+/HCV+/HBsAg+ and HIV-monoinfected women respectively received HAART
- HCV-seropositive women were less likely to receive HAART than seronegative women (AOR 0.34 [95%CI 0.20-0.58] p<0.0001), after adjusting for CD4 count and timing of HIV diagnosis

Results (2)

- HCV serostatus, CD4 count and HAART use were significant predictors of detectable HIV RNA in the 3rd trimester/at delivery univariably. In adjusted analysis (n=370) including all these variables, HCV-seropositive women were nearly twice as likely to have detectable viral load vs. HIV monoinfected women (AOR 1.95 95% CI 1.00-3.78)
- In an LME model, adjusting for time of measurement, baseline CD4 count and HAART use, HCV seropositivity was associated with a higher HIV RNA level (+0.28 log₁₀ copies/ml vs. HIV-only infected women, p=0.03)
- By the 3rd trimester/delivery, HCV-seropositive women had an estimated mean level of 2.84 log₁₀ HIV RNA copies/ml vs. 2.56 log₁₀ copies/ml in other women

Conclusions

- Prevalence of HBsAg is consistent with the lower ranges reported by other HIV cohorts in developed country settings
- The reduced risk of HBsAg positivity among IDUs may be due to unmeasured HBV immunity (naturally acquired or due to vaccination).
- Pregnancy may have compounded concerns regarding the increased potential for HAART-associated hepatotoxicity with HCV coinfection
- Consensus is lacking on the best therapeutic approach for HIV/HCV coinfecting pregnant women, particularly for women with high CD4 counts, who are at increased risk of HAART-related toxicity and for whom HAART may not have been considered if they were not pregnant
- HCV-seropositive women (and those with HBsAg) were significantly more immunosuppressed than HIV-only infected women (but we could not explore whether this was due to longer durations of infection and/or less effective ART)
- HCV-seropositive women had slightly but significantly higher HIV RNA levels than other women and were nearly twice as likely to have detectable HIV RNA at the end of pregnancy, theoretically placing them at greater risk of MTCT and of development of drug resistance

Acknowledgements

The ECS is a coordination action of the European Commission (PENTA/ECS 018865); the coordinating centre received support from the UK MRC Sexual Health and HIV Strategy Committee. Claire Thorne holds a Wellcome Trust Research Career Development Fellowship.
We would like to thank the women who participated in the Study. The ECS collaborators at the participating centres were Dr P Barlow, Prof J Levy, Dr M Hainaut, Dr T Goetghebuer, Dr Y. Manigat (Brussels); Dr V Savasi, Dr S Fiore, Prof E Ferrazzi, Dr A Viganò, Dr V Giacomini, Dr M Crivelli (Milan); Prof P Martinelli, Dr A Agangi, Drssa W. Buffalano, Dr R Tiseo, Drssa M Sansone (Naples); Dr C Tibaldi, Dr S Marini, Dr G Masulli, Prof C Benedetto (Turin); Prof I Grosch Wörner, Dr C Feiteira-Sperling, Dr S Casteleyn (Berlin); Dr AB Bohlin, Dr S Lindgren, Dr K Elfgrén, Dr B Anzén and Dr K Lidman (Huddinge and Solna); Prof A Mir, Dr A Payá, Dr MA López-Vilchez, Dr R Carreras (Barcelona); Dr J Jimenez (Madrid); Dr O Coll, Dr S Hernández, Dr J Pascual (Barcelona); Dr S Alberico, Dr M Rahnson, M Bernardoni (Trieste); Dr R Maluyuta, Dr I Semchenko, Dr I. Shevchenko, T Filipenko, Dr D. Richko, Y. Khomut (Perinatal Prevention of AIDS Initiative, Odessa); Dr S Poshakova, Dr T Kuleva, Dr A. Shtyag, Dr S. Servetky (Odessa); Dr A. Stelmah, Dr G. Kiseleva, Dr O. A. Zalata (Crimean Republic).