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HBV AND HCV CO-INFECTIONS IN HIV1-INFECTED PREGNANT WOMEN: OBSTETRICAL OUTCOMES

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ABSTRACT

Background. Data on the impact of chronic HBV or HCV co-infections on the immunovirological response to antiretroviral therapy (ART) and obstetric outcome in HIV-infected pregnant women are scarce and conflicting.

Methods. We analyzed data from all HIV-1 infected women included in the national ANRS-CO1 French Perinatal Cohort between 2005 and 2013. Prenatal testing for HBV and HCV infections was performed in most cases (95%). HBV/HIV and HCV/HIV co-infected mothers were compared with those infected only with HIV; the rare mothers with all three infections were excluded. Bivariate and multivariate analyses were performed..

Results. Among 6548 pregnancies, the overall prevalences of HCV (RNA+) and HBV (HBsAg+) infections were 1.6% [95%CI: 1.3-1.9] and 6.9% [6.2-7.5], respectively. As expected, HCV infection was strongly associated with a history of drug use, whereas HBV infection was six times more frequent in women originating from sub-Saharan Africa compared with those from mainland France. HIV viral load, CD4 cell count at pregnancy initiation and HIV care were similar in co- and mono-infected HIV mothers except, for ART, with 90% of HBV/HIV co-infected women receiving tenofovir and /or 3TC or FTC, with potential to decrease efficiently HBV viral load. No efficient treatment against HCV was prescribed in the HCV/HIV group. HCV coinfection was significantly associated with poorer HIV immunovirological status during the third trimester, and higher risks of gestational diabetes (OR=1.9 [1.0-3.7], p=0.05), cholestasis (OR=8.9 [4.9 – 16.3], p<0.001) and preterm delivery (OR=3.3 [1.9-5.5], and OR=4.2 [2.3-7.9], p<0.001) for moderate and very preterm delivery, respectively: p<0.001). The association with prematurity remained significant after adjustment for known risk factors, HIV viral load and antenatal complications (aOR=2.3 [1.1-5.0], p=0.03). In HBV/HIV women no association was found with any of these outcomes.

Conclusions. In HIV-infected pregnant women, chronic HBV infection, efficiently treated, had no major impact on mother health during pregnancy. In contrast, HCV co-infected mothers, without any efficient treatment against HCV, showed a poorer HIV immunovirological response to ART and higher risk of antenatal complications and prematurity. This suggests that efficient control of HCV activity, before conception, as likely to be obtained in HBV infection, may limit the deleterious impact of co-infection.

OBJECTIVE

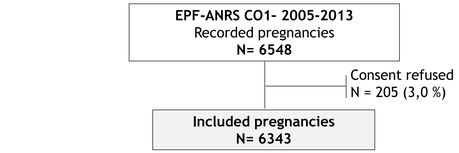
- Systematic hepatitis B and C screening recommended by French guidelines in pregnant HIV-infected women.
- Scarce and conflicting data on the impact of these coinfections on the immunovirological response to antiretroviral therapy (cART) and obstetric outcomes in this population.

→ To estimate the prevalence of HBV and HCV coinfections in pregnant HIV-infected women in France.
→ To investigate the relations between chronic hepatitis co-infections and maternal CD4 count, HIV-viral load during pregnancy and pregnancy outcomes.

PATIENTS AND METHODS

- **The French Perinatal Cohort EPF (ANRS CO1/CO11):** HIV infected women and their children included since 1985 in 90 French centres.
- **Eligible for the study :** HIV-1 infected pregnancies included in EPF with deliveries between 2005 and 2013 (N=6548), HBV/HCV co-infected women excluded (n=2).
- **Main outcomes during pregnancy:**
  - maternal CD4 cell count and plasma HIV RNA
  - Preeclampsia, gestational diabetes, cholestasis, preterm delivery (<37 gestational weeks)
- **Statistical analysis**:
  - Prevalence of of HBV and HCV hepatitis estimated with exact 95% confidence interval
  - Trends in CD4 counts and HIV viral load over the pregnancy: lowess curves
  - Associations between HBV and HCV hepatitis and obstetrical outcomes: bivariate and multivariate logistic regressions, with each outcome as dependent variable.
  - Analysis of preterm birth restricted to single pregnancies consulting to the obstetrical center before 28 weeks gestation

Fig. 1– Prevalence of chronic HCV and HBV infections



HEPATITIS C	HEPATITIS B
Prenatal testing performed	
5854 (92,3 %)	5908 (93,1 %)
Prevalence	
Seropositivity (Positive anti-HCV Ab)	Chronic infection: Hepatitis C (Positive plasma HCV RNA) / Hepatitis B (Positive HBV Ag)
3.2% [2.9 - 3.8] (n=190)	**1.6 %** [1.3 - 1.9] (n=91) / **6.9 %** [6.2- 7.5] (n= 408)

Tab.1 – Medical care during pregnancy

	HBV-HIV n=366 (1) %	HCV-HIV n=85 (2) %	HIV only n=5179 (3) %	(1) vs (3) p	(2) vs (3) p
First visit to obst. center					
≤ 28 GW*	94.1	94.0	92.6	0.36	0.71
≥ 29 GW	5.9	6.0	7.5		
HIV diagnosis					
Before conception	81.8	95.2	83.7	0.88	0.03
≤ 28 GW	16.3	4.8	14.4		
≥ 29 GW	1.9	0.0	1.9		
cART initiation					
Not treated	0.6	1.2	1.3	0.13	0.35
Initiated before conception	45.5	55.9	50.5		
≤ 28 GW	45.6	39.3	41.7		
≥ 29 GW	8.3	3.6	6.6		
First line NRTI					
Tenofovir and/or 3TC	90.4	27.1	25.0	<0.0001	0.13
Other	5.5	7.1	3.9		
None	4.1	9.4	5.8		
First line PI					
boosted	75.9	63.5	71.4	0.16	<0.0001
Not boosted	6.0	18.8	6.8		
None	18.1	17.7	21.8		

GW: Gestational weeks

Fig. 2–Relation between chronic hepatitis and pregnancy outcomes compared to mono HIV infected pregnant women

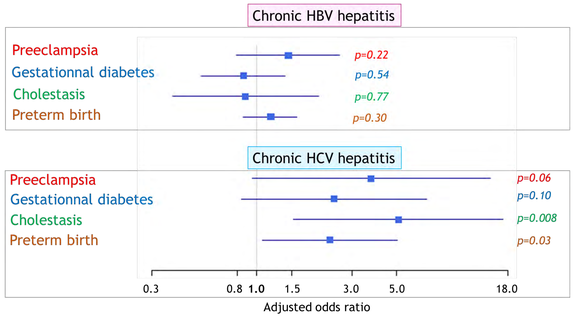


Fig. 3 – Trends in CD4 counts and HIV viral load during pregnancy

RESULTS

Chronic hepatitis B

- Prevalence : 6.9% [95%CI: 6.2-7.5]
- Six times higher in women from sub-Saharan Africa than from mainland France
- 90% of HBV/HIV co-infected women treated with tenofovir and /or 3TC or FTC
- No increase in antenatal complications or preterm birth compared to HIV monoinfected pregnant women

Chronic hepatitis C

- Prevalence : 1.6 % [95%CI: 1.3-1.9] (Positive plasma HCV RNA)
- Strongly associated with IDU, older maternal age at delivery
- No HCV treatment
- Significantly associated with
  - poorer HIV immunovirological status during the third trimester,
  - higher risks of preeclampsia (AOR= 3.7 [%IC:0.9-14.6]), cholestasis (AOR= 5.1 [1.5-17.0]) and preterm birth (AOR=2.3 [1.2-5.0]).

CONCLUSION

•Treated chronic HBV infection has no major impact on antenatal complications, preterm delivery and HIV immunovirological status.

•HCV co-infected mothers, with positive plasma HCV RNA, showed:

- a poorer HIV immunovirological response to ART,
- a higher risk of antenatal complications and prematurity.

This suggests that efficient control of HCV activity, before conception, as likely to be obtained in HBV infection and easier to achieve with the new therapeutic options for HCV infection, may limit the deleterious impact of co-infection.

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