HIV-related Differences in Placental Immunology: Data from the PRACHITi Cohort

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BACKGROUND

- HIV-exposed and uninfected (HEU) infants have **>70% increased risk of death** compared to HIV-unexposed and uninfected infants, mostly from infections.
- Pregnant people living with untreated HIV are **less efficient at transferring antibodies** to their infants than people without HIV.
  - Transfer of antibodies is mediated through the neonatal Fc receptor (FcRn), located in the placenta.
- **It is unclear if the decreased antibody transfer is related to HIV-associated changes in FcRn expression, placental immune dysregulation or both.**

Hypothesis:
- Maternal HIV infection, even when virally suppressed, affects placental immunology and decreases placental expression of FcRn.

METHODS

Study design: Observational longitudinal study
Study site: Antenatal clinic at BJ Government Medical College in Pune, India
Study population: Pregnant women living with and without HIV, enrolled in their 2nd trimester of pregnancy
Study procedures
- Convenience sample of 42 placenta collected at delivery
- FcRn expression analyzed by Western blot (normalized by GADPH)
- Placental CD8+ T-cell abundance assessed by immunofluorescent counting per high powered field

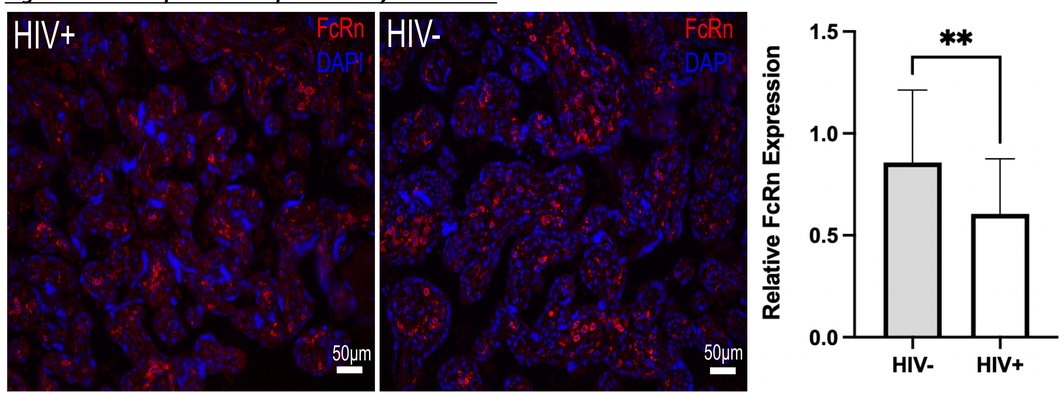
Statistical analysis:
- FcRn expression was compared using Image J.
- Continuous data (e.g. FcRn expression) were tested for normality using Grubb's test
- Statistical analysis of CD8+ immunofluorescence staining was done using GraphPad Prism

There was significantly *lower FcRn expression* and *higher CD8+ T-cell abundance* in placenta from women living with HIV, regardless of viral load.

RESULTS

- 38 placenta were analyzable with a median gestational age of 38.3 weeks (IQR: 37.5-39.1) at delivery.
- 18 (47%) placenta were from women living with HIV, who were all on combined antiretroviral therapy.
  - Median CD4+ count: 455 cells/mm^3 at study entry, 429 cells/mm^3 at delivery.
  - 10 (55%) had viral suppression(<100 copies/mL)
    - Of those with a detectable viral load, the median was 151 copies/mL (IQR 118-539334).

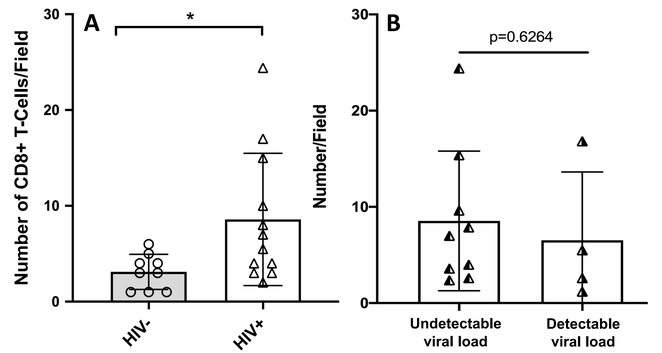
Figure1. FcRn expression in placenta by HIV status



Relative expression of FcRn was significantly lower in placenta from women living with HIV (0.54, left) compared to placenta from women living without HIV (0.84, middle) (p<0.01) and was not associated with CD4+ count or HIV viral load.

RESULTS

Figure 2. CD8+ T-cells in placenta by HIV status (A) and viral load (B)



Placental abundance of CD8+ T-cells was higher in women living with HIV compared to women without HIV (A), but was not affected by viral suppression (B).

CONCLUSIONS

1. **Pregnant women living with HIV–even when virally suppressed– have lower placental FcRn expression.**
   - This may result in lower transplacental transfer of antibodies to the fetus.
2. **Pregnant women living with HIV also had increased placental abundance of CD8+ T-cells.**
   - Increased placental CD8+ T-cells have been associated with placental inflammation and poor infant outcomes.
3. ***Our data suggest that maternal HIV causes placental immune dysregulation that is not completely reversed by combined antiretroviral therapy and may contribute to the poorer outcomes of HEU infants.***

ADDITIONAL KEY INFORMATION

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