Sex matters: A Bayesian Approach to Analyzing Sex Differences in an African Pediatric Cohort

P-02

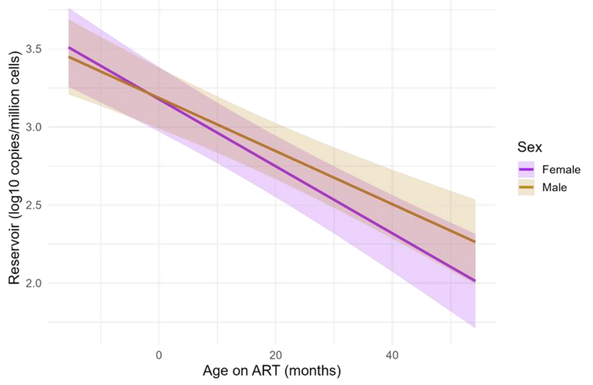
Irati Gastesi[1], Álvaro Ballesteros[1], Shaun Barnabas[2], Osee Behuhuma[3], Maria Grazia Lain[4], Tacilta Nhampossa[5], Kennedy Otwombe[6], Paolo Rossi[7], Carlo Giaquinto[8], Louise Kuhn[9], Kavidha Reddy[3], Nicola Cotugno[7], Pablo Rojo[1,10], Alfredo Tagarro[1,11], Sara Domínguez-Rodríguez[1,11] on behalf of the EPIICAL Consortium.

BACKGROUND

- Sex differences in HIV outcomes are well described in adults but remain poorly understood in infants.
- Early HIV infection is characterized by rapid reservoir establishment and immune immaturity.
- Evidence on sex-related differences in infants living with HIV is limited and inconsistent
- **Objective:** To evaluate sex-related differences in viral reservoir dynamics, severe immunosuppression, and baseline proteomic profiles in early treated infants living with HIV.

METHODS

- **Study design & population:**
  - African pediatric EARTH–EPIICAL cohort
  - Infants living with HIV initiating ART ≤3 months of age
  - N=59/215 with longitudinal HIV-1 DNA measurements
- **Data collected**
  - Longitudinal total HIV-1 DNA in PBMCs (viral reservoir)
  - CD4 percentage over follow-up
  - Baseline plasma for targeted proteomics
- **Statistical analysis (Bayesian framework)**
  - Reservoir dynamics: Multivariable Bayesian Gaussian model, adjusted with cd4% and baseline log viral load
  - Severe immunosuppression:
    - Outcome: CD4% <25%
    - Multivariable Bayesian Weibull survival model (HR), adjusted with region, baseline log viral load and suboptimal adherence.
  - Proteomics:
    - Bayesian two-sample t tests
    - Reported as $\log_2$ fold change and Bayes factor (BF_{10})



Sex-related differences were observed in pediatric HIV, with females showing trends toward greater reservoir decline, lower immunological progression risk, and distinct inflammatory signaling profiles, suggesting potential biological dimorphism relevant for HIV pathogenesis and future therapeutic strategies.

RESULTS

Reservoir dynamics

Females exhibited a greater longitudinal decline in HIV reservoir size compared with males. The estimated yearly difference was −0.005 log10 units (95% CrI: −0.012 to 0.003), corresponding to an 87.1% posterior probability of a stronger decline in females.

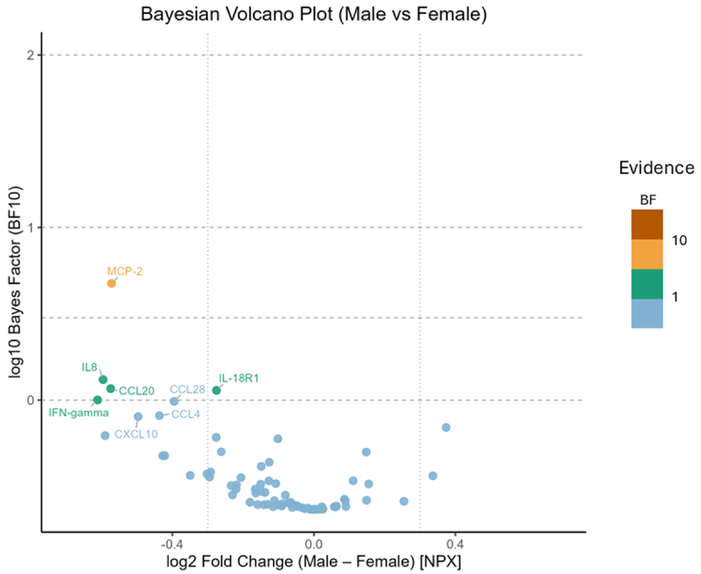
Immunological progression

Progression analyses suggested lower immunological vulnerability among females. The estimated hazard ratio for progression was 0.62 (95% CrI: 0.29–1.24), with a 91.1% posterior probability indicating reduced risk in females.

Proteomic profiling

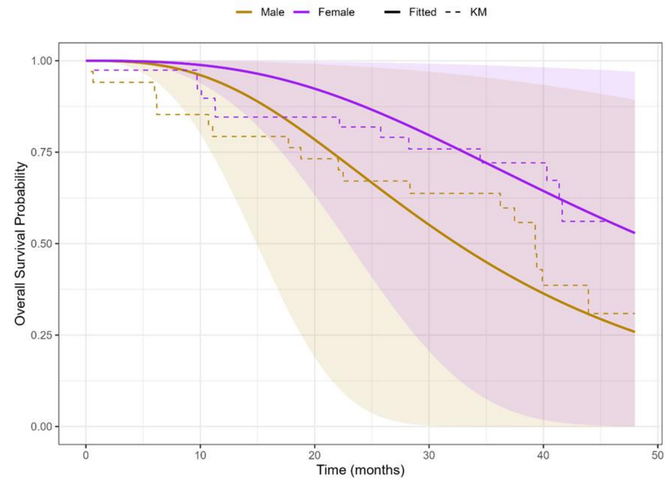
Overall, proteomic analyses showed limited sex differences, with most Bayes factors indicating weak or no evidence of differential expression ($BF_{10} < 1$).

- MCP-2 levels were higher in females with substantial evidence ($BF_{10} = 4.8$; $P(\Delta>0)=0.991$).
- IL-8, CCL20, and IFN-γ showed anecdotal evidence of higher levels in females ($BF_{10} \approx 1–2$; posterior probabilities ≈95–97%).



CONCLUSIONS

- Females showed a trend toward greater HIV reservoir decline and lower risk of severe immunosuppression.
- Proteomic data suggested higher innate inflammatory signaling in females, with MCP-2 emerging as a potential sex-specific marker.
- Additional cytokines (IL-8, IL-18R1, CCL20, IFN-γ) indicated subtle but consistent inflammatory differences.
- These findings support sex-related biological differences in pediatric HIV and highlight the importance of considering sex in future research and clinical strategies.



ADDITIONAL KEY INFORMATION

Irati Gastesi Orbegozo
Instituto de Investigación Sanitaria Hospital 12 de Octubre (imas12)
Fundación Biomédica Hospital Universitario 12 de Octubre (FIB-H12O), Madrid, Spain
Email: epico.iratigastesi@gmail.com
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PLAIN LANGUAGE SUMMARY

Female children living with HIV showed signs of slower disease progression and different inflammatory responses than males. These findings suggest biological sex may influence how HIV affects children and could help guide more personalized care.