Early-Treated Children with Perinatal HIV show Elevated Monocyte Activation into Late Childhood

1075

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BACKGROUND

- Early ART within 3 months of birth has improved long-term outcomes in children living with perinatal HIV, however these children may face decades of immune dysregulation and accumulated antiretroviral exposure.
- The long-term inflammatory profile and risk of non-communicable diseases are poorly understood.
- **Aim:** We compared biomarkers associated with inflammation, metabolic and cardiovascular damage and response markers in early ART-treated children and controls unexposed to HIV.

METHODS

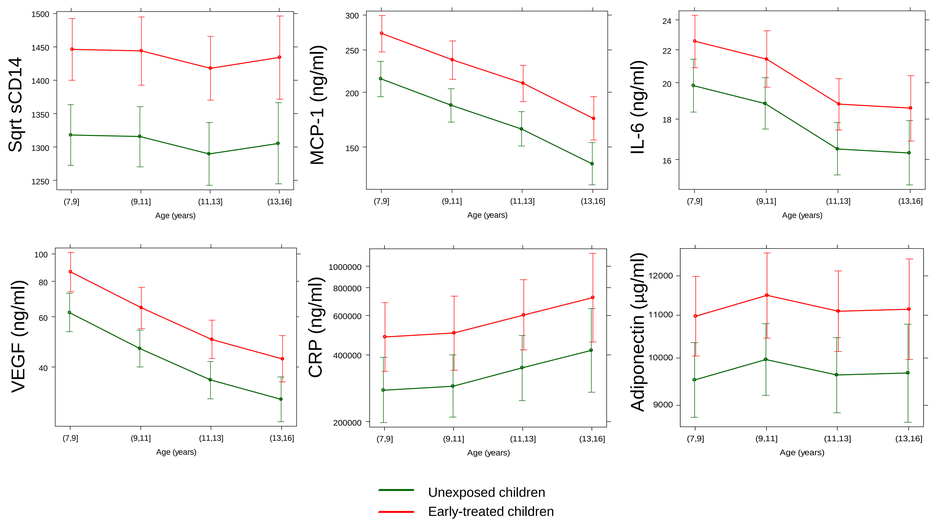
- Longitudinal study of 185 children (67 with HIV, 118 unexposed) aged 7-16 years (87 female, 98 male) previously part of CHER and P1060 trials at Tygerberg Children's Hospital, South Africa.
- Children with HIV initiated ART within 3 months of birth, were virologically suppressed (>90%), asymptomatic, with preserved CD4+ cell count and clinically well at the time of blood tests.
- Unexposed children arose from the same communities and socio-economic background.
- Children had multiple measurements (median 2, four years apart), yielding 321 total observations.
- We measured 26 inflammatory proteins in blood serum using ELISA and Luminex™ multiplex immunoassays:
  - Monocyte-derived biomarkers (IL-18, IL-6, TNF-α, MCP1, IL-1a, S100A9, IL1-ra, S100A8)
  - Lymphocyte-derived markers (IL-17, IFNγ, IL-12p70, IP-10, IL-10)
  - Response markers (CRP, sCD14, ESelectin)
  - Metabolic (leptin, adiponectin, Resistin, LBP, IL-18, FABP4), and
  - Cardiovascular markers (VEGF, ESelectin, IP-10, MCP1, PSelectin, sCD163, VCAM1, ICAM1)

Statistical analysis: Mixed effects models with child specific random effects to compare the effect of HIV group on each biomarker, adjusting for age, sex, ethnicity, smoke exposure and batch, and considered an interaction between age and HIV group. Results are adjusted for multiple comparisons.

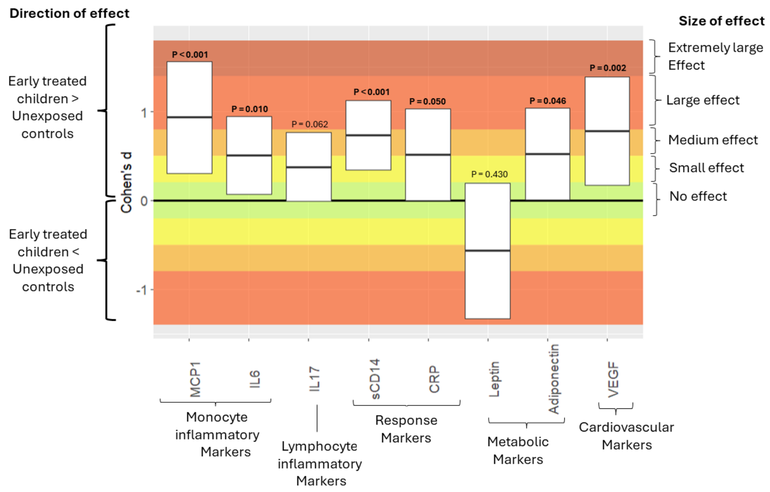
sCD14, MCP-1, IL-6, VEGF and CRP are elevated in early-treated children despite sustained viral suppression and excellent care

RESULTS

- Early treated children had significantly higher sCD14, MCP1, IL-6, CRP, Adiponectin and VEGF than unexposed. IL-17 was borderline (p=0.06) significantly higher in early treated children, after adjusting for multiple comparisons.
- Age-specific effects were observed with significantly higher PSelectin and S100A9 in children with HIV aged 7-9 years, and significantly higher S100A8 and TNF-α in ages 13-16



Results comparing early-treated children and unexposed controls. Values above zero indicate greater levels in early-treated children vs unexposed, and vice-versa. Only certain biomarkers are shown – others show no significant difference. Cohen's d and related confidence intervals, together with p-values (Holm-adjusted) are shown.



CONCLUSIONS

- Despite early-ART and sustained viral suppression, early treated children displayed extensive immune marker elevations, clustered around monocyte activation and markers associated with cardio-metabolic disease. These children remain at risk of premature vascular disease.

ADDITIONAL KEY INFORMATION

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Acknowledgements: We wish to express our gratitude to each of the study participants and their parents for their contribution to this study.

Funding: CD was supported by the nonprofit Specialists in Global Health (SiGH), www.sigh.global.