ASSOCIATIONS BETWEEN MATERNAL HIV AND INFANT IMMUNE ACTIVATION

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BACKGROUND

- Children who are HIV-exposed but uninfected (HEU) have more infectious morbidity and mortality than children who are HIV-unexposed, particularly in early life
- We therefore hypothesised that HEU children may have immunological abnormalities in infancy despite not living with HIV

METHODS

- T-cell and monocyte immunophenotyping of fixed buffy-coat cells was undertaken by flow cytometry in a subgroup of participants of the SHINE trial in rural Zimbabwe
- Proportions of T-cell and monocyte subsets, defined by surface and intracellular markers, were compared between HEU and HIV-unexposed children aged 1-month using fractional regression, adjusted for exact infant age in days at time of blood collection, infant sex, and randomised trial arm

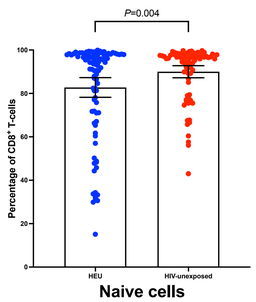
Cell markers used in flow cytometry

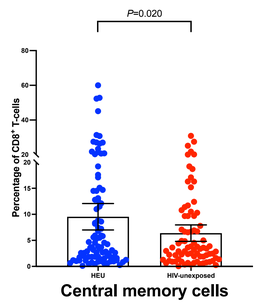
T-cell phenotypes

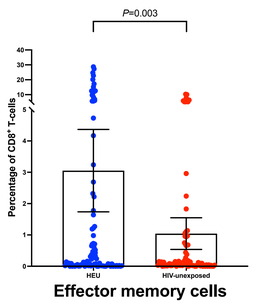
- Activated CD8$^+$ T-cells: CD3$^+$/CD8$^+$/CD38$^+$/HLADR$^+$
- Proliferating CD8$^+$ T-cells: CD3$^+$/CD8$^+$/Ki67$^+$
- Naïve CD8$^+$ T-cells: CD3$^+$/CD8$^+$/CD45RA$^+$/CD27$^+$
- Central memory CD8$^+$ T-cells: CD3$^+$/CD8$^+$/CD45RA$^-$/CD27$^+$
- Effector memory CD8$^+$ T-cells: CD3$^+$/CD8$^+$/CD45RA$^-$/CD27$^-$
- Terminally-differentiated effector memory CD8$^+$ T-cells: CD3$^+$/CD8$^+$/CD45RA$^+$/CD27$^-$
- Non-senescent CD8$^+$ T-cells: CD3$^+$/CD8$^+$/CD28$^+$/CD57$^-$
- Senescent CD8$^+$ T-cells: CD3$^+$/CD8$^+$/CD28$^-$/CD57$^+$
- Exhausted CD8$^+$ T-cells: CD3$^+$/CD8$^+$/PD-1$^+$

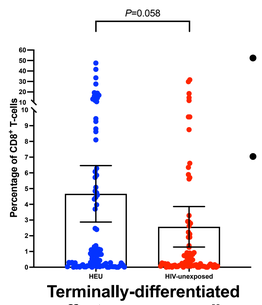
Monocyte subsets

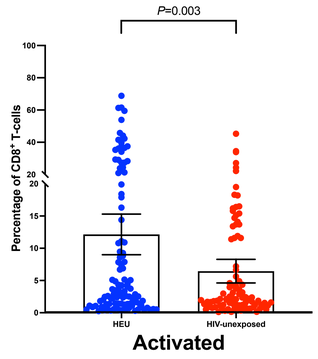
- Classical monocytes: CD3$^-$/CD19$^-$/CD20$^-$/CD56$^-$/HL-DR$^+$/CD14^{++}/CD16$^-$
- Intermediate monocytes: CD3$^-$/CD19$^-$/CD20$^-$/CD56$^-$/HLADR$^+$/CD14^{++}/CD16$^+$
- Non-classical monocytes: CD3$^-$/CD19$^-$/CD20$^-$/CD56$^-$/HLADR$^+$/CD14$^+$/CD16^{++}

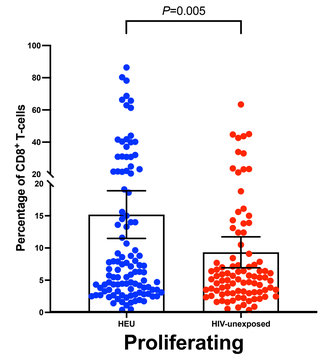


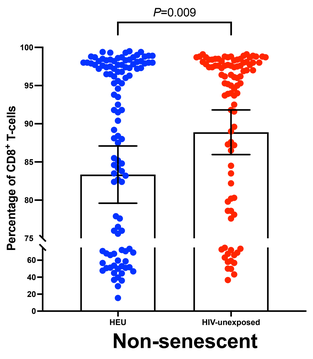


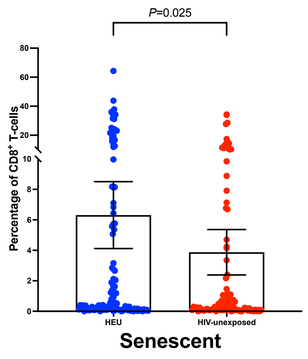


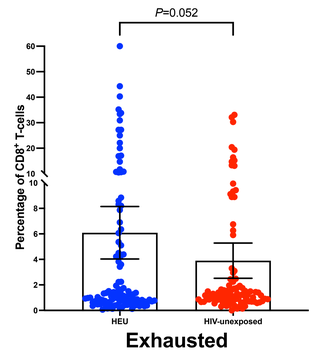


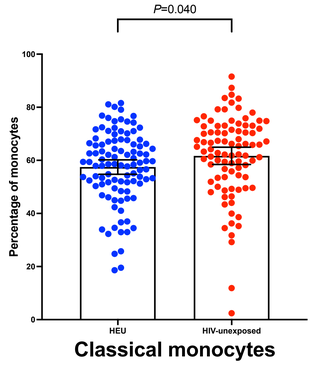


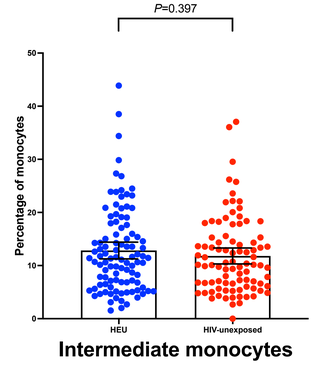


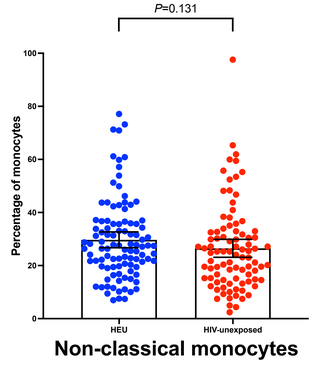












FINDINGS

- 114 HEU and 97 HIV-unexposed children were included, and ART coverage was >95%
- There were differences in CD8$^+$ T-cell maturation, activation, proliferation, senescence and exhaustion, (see Figures), but there were no differences in CD4$^+$ T-cell phenotypes
- There were subtle differences in monocyte subsets (see Figures), and compared to HIV-unexposed children, CHEU had higher concentrations of soluble CD14 (mean 1.09x10^6 pg/mL vs. 0.85x10^6 pg/mL, adjusted difference 0.25x10^6 [95%CI 0.15x10^6, 0.35x10^6]
- Monocyte population differences between CHEU and CHU were stronger in males compared to females, mostly driven by an expansion in non-classical (+6.2% [95%CI 0.0, 12.4]; *P*=0.05) rather than intermediate (-0.3% [95%CI -3.0, 0.2], *P*=0.84), monocytes
- CD8$^+$ T-cell differences for maturation, senescence and exhaustion panels were also stronger in males
- Maternal HIV/cytomegalovirus (CMV) co-infection was associated with infant CD8$^+$ cell maturation, senescence and exhaustion but not proliferation/activation

CONCLUSIONS

- Despite high maternal ART coverage, children who are HIV-exposed but uninfected have a distinct cellular immune phenotype relative to children who are HIV-unexposed
- Late gestational cytomegalovirus viraemia in pregnant women living with HIV was strongly associated with CD8+ T-cell phenotypes
- Strategies additional to antenatal ART may be required to improve outcomes amongst HIV-exposed children

Poster 00268

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