Immune markers during pregnancy and birth outcomes in South African women living with HIV

1002

Thokozile R Malaba[1], Clive M Gray[2], Tariq Webber[2], Hlengiwe P Madlala[1], Berenice Alinde[2], Landon Myer[1], Marie-Louise Newell[3], for the PIMS Study Group
[1]Division of Epidemiology and Biostatistics, School of Public Health, University of Cape Town, Cape Town, South Africa, [2]Division of Molecular Biology and Human Genetics, Department of Biomedical Sciences, Stellenbosch University, Cape Town, South Africa, [3]School of Human Development and Health, University of Southampton, Southampton, United Kingdom

BACKGROUND

- Maternal immune activation and systemic inflammation are implicated in preterm delivery (PTD) and small for gestational age (SGA) infants in women living with HIV (WLH), but underlying mechanisms remain unclear.
- Limited data on immune marker trajectories during pregnancy hampers early risk identification and targeted interventions for adverse birth outcomes.
- Characterising immune profiles in WLH could provide critical insights into pathways driving PTD and SGA, informing risk stratification and clinical management.

METHODS

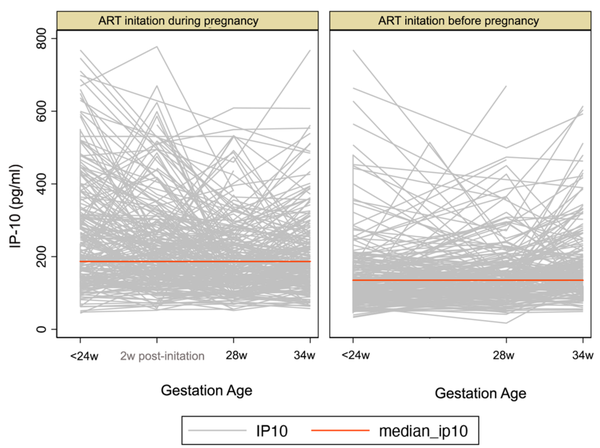
- We followed a cohort of ART-eligible pregnant WLH recruited at their 1st antenatal visit at a large primary care facility in Cape Town, South Africa (Apr 2015-Oct 2016).
- WLH were predominately on TDF+XTC+EFV regimen, initiated either pre-conception or during pregnancy.
- Phlebotomy conducted at all study visits throughout pregnancy which included:
  - Baseline < 24 weeks gestational age (GA) (Visit 1)
  - 2 weeks post ART initiation (if starting ART during pregnancy (Visit 2)
  - 28 weeks GA (Visit 3)
  - 34 weeks GA (Visit 4)
- Inflammatory biomarker levels measured at these timepoints included:
  - C-reactive protein (CRP)
  - Interferon gamma-induced protein 10 (IP-10)
  - Serum amyloid A (SAA)
- Group-based trajectory modelling (GBTM) identified distinct biomarker trajectories throughout pregnancy.
- Modified Poisson regression assessed associations between these trajectories and PTD (<37 weeks) and SGA (<10th percentile for GA) adjusted for age, BMI and ART timing (before vs during pregnancy).

Atypical increases in IP-10 throughout pregnancy, especially in ART initiators, associated with higher risk of preterm delivery in WLH.

RESULTS

- 505 women with a livebirth were included in this analysis:
  - median age 30 years; median gestation at enrolment 14 weeks; 23% nulliparous.
  - 48% (n=241) initiated ART preconception (84% TDF+XTC+EFV, 8% PI-based regimen) and 52% (n=264) initiated during pregnancy (97% TDF+XTC+EFV, 1% PI-based regimens).
- Median CRP and SAA levels over time did not differ by ART status, however IP-10 levels were higher in women initiating ART during pregnancy than preconception ART initiators (Figure 1). Given these differences, we further explored IP-10 trajectories.

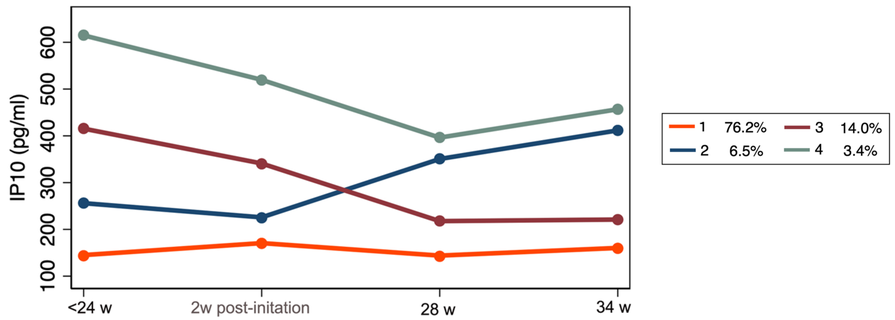
Figure 1: Median IP-10 levels by ART status



RESULTS Cont.

- We identified 4 distinct IP-10 trajectories, with one group (6.5% of women) showing a pattern that was different from other groups, with IP-10 levels steadily increasing throughout pregnancy (traj 2 [blue line]) compared to stable (traj 1, [orange line]) or decreasing (traj 3 [maroon line] and 4 [green line]) (Figure 2).

Figure 2: IP-10 group based modelling trajectory



- Those with atypical IP-10 trajectories had significantly higher PTD risk (ARR2.08, 95% CI 1.03-4.19) than other groups.
- No associations were observed between CRP and SAA with PTD, and none between either of the three biomarker trajectories and SGA.

CONCLUSIONS

- Persistent inflammation as indicated by atypical increases in IP-10, was associated with a higher risk of PTD but not SGA.
- Women initiating ART during pregnancy had higher IP-10 levels suggests potential immune activation related to timing of ART initiation.
- Lack of associations with SAA and CRP, highlight the specificity of IP-10 as a potential biomarker for pregnancy risk stratification.
- Monitoring IP-10 trajectories in pregnant WLH could aid in early identification of those at increased PTD risk, allowing for targeted interventions.

Author contact: thoko.malaba@uct.ac.za

NIH Eunice Kennedy Shriver National Institute of Child Health and Human Development
School of Public Health and Family Medicine
Isikolo Sempilo Yoluntu kunye Namayeza Osapho
Departement Openbare Gesondheid en Huisartskunde
UNIVERSITY OF CAPE TOWN
UNIVERSITY OF Southampton