IMMUNE MARKERS IN PREGNANT HIV+ WOMEN ON ANTIRETROVIRAL THERAPY BY MATERNAL BMI STATUS

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BACKGROUND

- Obesity impairs immune functioning & elevated body mass index (BMI) in HIV+ pregnant women could lead to immune dysregulation.
- Disruption of pregnancy associated immune processes could increase the risk of pregnancy complications.
- We investigated temporal trends of inflammatory biomarkers & the impact of maternal BMI status.

METHODS

- Cohort of ART-eligible HIV+ pregnant women (n=527) recruited at 1st antenatal care (ANC) visit at a primary care facility in Cape Town, South Africa (April 2015-October 2016).
- HIV+ women, predominately on TDF+3TC+EFV regimen, initiated either preconception or at 1st ANC visit.
- Phlebotomy & weight measured throughout pregnancy
  - At three ANC visits (< 24 weeks, ~ 28 weeks & ~34 weeks).
  - Additional visit 2 weeks post-initiation (ART initiators in pregnancy).
- Inflammatory biomarker levels measured
  - C-reactive protein (CRP) & Serum amyloid A (SAA): acute phase response (APR) proteins & early markers of systemic infection or inflammation.
  - Interferon-gamma induced protein 10 (IP-10): chemokine which may be implicated in pre-eclampsia & is associated with HIV infection.
- We assessed the median serum concentrations of biomarkers by BMI (normal weight (<24.9 kg/m^2), overweight (25-29.9 kg/m^2), obese (≥ 30 kg/m^2)).

Table 1. Baseline Characteristics of HIV+ pregnant women overall and by ART status

Characteristic	Overall, N = 527	Timing of ART initiation: In pregnancy, N = 278	Timing of ART initiation: Preconception, N = 249
Age (years), Median (IQR)	30.00 (26.00-34.00)	28.00 (25.00-32.00)	32.00 (28.00-35.00)*
Gravidity, n (%)		274	246*
<=1	87 (17%)	59 (22%)	28 (11%)
2	178 (34%)	102 (37%)	76 (31%)
>=3	255 (49%)	113 (41%)	142 (58%)
ART regimen, n (%)		278	249*
TDF-3TC-EFV	476 (90%)	268 (96%)	208 (84%)
PI-based regimen	25 (4.7%)	2 (0.7%)	23 (9.2%)
Other NNRTI-based	26 (5%)	8 (2.9%)	18 (7.2%)
BMI category (kg/m^2), n (%)	527	278	249
Normal	113 (21%)	63 (23%)	50 (20%)
Overweight	146 (28%)	71 (26%)	75 (30%)
Obese	268 (51%)	144 (52%)	124 (50%)

*P<0.05 =significant comparing ART initiated in pregnancy to ART initiated preconception.

HIV+ women on **ART preconception** or **initiating** ART in **pregnancy** show differences in **immune marker** levels throughout pregnancy

RESULTS

Most women were classified as obese (51%) or overweight (28%) at first ANC visit.

- Women who initiated ART in pregnancy had higher IP-10 & SAA levels than women who initiated ART preconception (Table 2).
- Overall, CRP levels were highest in obese women than women with a normal or overweight BMI & CRP levels were higher in early (1st & 2nd trimester, visit 1) than late pregnancy (3rd trimester, visit 3 & 4) (Figure 1A).
- IP-10 levels were higher in early pregnancy (visit 1) (Figure1B) than late pregnancy in women initiating ART in pregnancy.
- SAA levels were higher in later pregnancy (visit 3 & 4) in women with a normal & overweight BMI compared to obese women (Figure 1C).

Table 2. Median (IQR) serum concentration of biomarkers by ART initiation status across all visits†

Immune marker	Total (N)	Initiated ART in pregnancy	Initiated ART preconception	p-value
CRP (ng/mL)	12 358.75 (7 845.04 -15 158.60)	12 252.19 (7 731.98 -15 158.60)	12 705.61 (8 102.12- 15 158.60)	0.356
IP-10 (pg/mL)	161.81 (115.37- 243.77)	188.94 (134.05 - 279.92)	134.95 (97.53 - 183.96)	<0.001
SAA (ng/mL)	9.53 (5.15 - 16.40)	9.76 (5.51 -16.96)	9.06 (4.86 -15.71)	0.017

†Women initiating ART in pregnancy had an extra visit 2 weeks post-initiation. P<0.05=significant comparing ART initiated in pregnancy to ART initiated preconception.

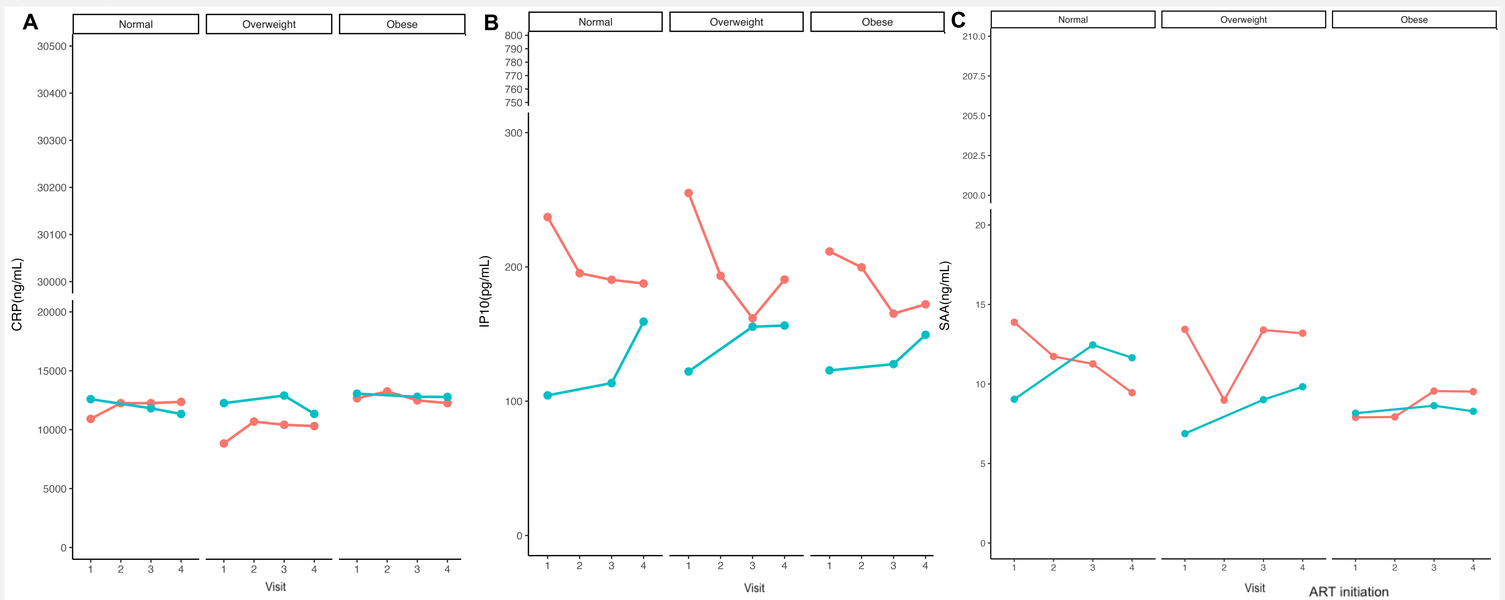

Figure 1. Median serum concentration of biomarkers at each visit A) CRP, B) IP-10, C) SAA level for women initiating ART in pregnancy (pink) and who initiated preconception (blue) stratified by BMI at baseline (1), 2 weeks post-ART (women who initiated ART in the current pregnancy) (2), ~28 weeks' gestation (3) and ~34 weeks' gestation (4).

CONCLUSION

Immune markers of systemic inflammation may help to understand the impact of maternal BMI on immunity, placental development & subsequently, on pregnancy outcomes.

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