MATERNAL BIOMARKERS OF ENDOTHELIAL DYSFUNCTION BY HIV STATUS, ART-EXPOSURE AND BIRTH OUTCOMES

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BACKGROUND

- Access to 3-drug antiretroviral therapy (ART) during pregnancy has dramatically reduced new pediatric HIV infections globally and has improved maternal health.
- HIV-infected women who take ART are at significantly higher risk of having an adverse pregnancy outcome (stillbirth, preterm delivery, and small for gestational age [SGA]), particularly if ART is started prior to conception[1,2].
- The underlying mechanisms for this increased risk are unknown.
- Given that more than 1.5 million HIV-infected women deliver annually[3], it is crucial that we study mechanism(s) underlying these adverse birth outcomes to design interventions to improve maternal and child outcomes.
- HIV infection and ART use have been independently associated with manifestations of endothelial dysfunction, including cardiovascular disease (CVD)[4,5].
- In pregnancy, where endothelial function is critical for placentation, maternal volume expansion, and placental perfusion, markers of endothelial dysfunction are associated with preterm delivery in HIV-uninfected women[6].

METHODS

- We measured plasma levels of biomarkers endothelial activation [soluble vascular adhesion molecule 1 (VCAM-1), intercellular adhesion molecule 1 (ICAM-1) and E-selectin] in the Tshipidi observation cohort.
- We compared log biomarkers levels by HIV status and timing of ART initiation using t-tests and Kruskal-Wallis rank test.
- We evaluated the association between these biomarkers and adverse birth outcomes (stillbirth, small for gestational age) using univariate and multivariate log-binomial regression controlling for age and timing of ART.

RESULTS

- **Specimens were available for 414 women, 372 living with HIV and 42 HIV-negative. Median age at sample collection was 30 weeks (Q1,Q3: 26,35) (Table 1).**
- **WLHIV had statistically significantly higher median VCAM1 (p=0.0002) than HIV-negative women. HIV-negative women higher median ICAM1 (p=0.04) and there was no statistically significant difference in e-Selectin levels.**
- **ICAM1 and e-Selectin were not statistically different by timing of ART (initiated pre-conception, initiated post-conception and ART-naïve).**
- **Women on ART during pregnancy had higher log10 VCAM1 levels than those on ART before conception, regardless of whether tested sample was collected before (p=0.02) or after (p=0.03) ART initiation.**
- **Univariate and adjusted analyses did not show significant associations between levels of any of these biomarkers and adverse birth outcomes (stillbirth or SGA).**

TABLE 1. Demographics and clinical characteristics of pregnant WLHIV and pregnant HIV-uninfected women(N= 414)

Variables	All women	HIV-infected	HIV-uninfected	p-value
Age (years)	**n=414**	**n=372**	**n=42**	
Median (Q1,Q3)	28 (23, 32)	23 (21, 30)	28 (24, 33)	<0.001
Highest Education level, n (%)	n=413	n=371 (90)	n=42 (10)	
Junior Secondary school or lower	278	262 (94)	16 (6)	<0.001
Senior Secondary school	99	81 (82)	18 (18)	
Tertiary	36	28 (78)	8 (22)	
Income per month (in BWP)	n=394	n=356 (90)	n=38 (10_	
<200	215 (55%)	192 (89)	23 (11)	0.045
200 - 500	30 (8%)	30 (100)	0	
501 - 1000	76 (19%)	72 (95)	4 (5)	
> 1000	73 (19%)	62 (85)	11 (15)	
Delivery type				
SVD, n (%)	376 (95)	338 (90)	38 (10)	0.154
C/section, n (%)	18 (5)	18 (100)	0	
Gestation Age at the time of blood collection (weeks), m	30 (26, 35)	30 (26, 35)	34 (26, 37)	0.044
Gestation age at delivery (weeks), median (Q1,Q3)	40 (38, 41)	39 (38, 41)	41(39, 42)	<0.001
Stillborn, n	9	8	1	0.063
Preterm delivery, n	53	51	2	0.087
Small for Gestation Age (SGA), n	11	72	1	0.466

RESULTS

FIGURE 1. Comparison of biomarkers (VCAM-1, ICAM-1 and e-Selectin) by HIV status

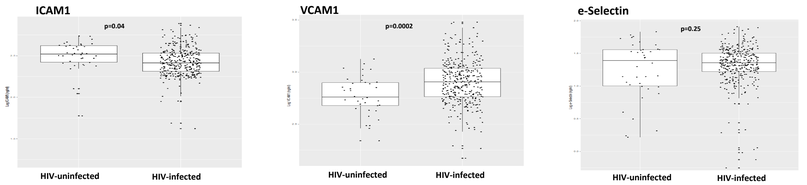
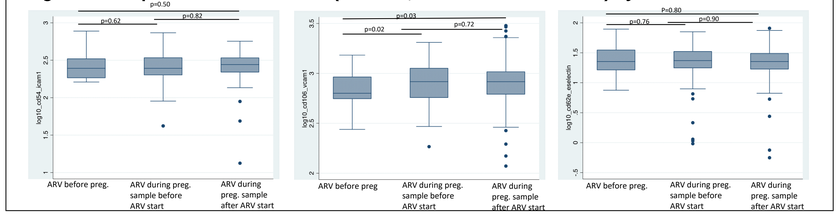


Figure 2:Comparison of biomarkers (VCAM-1, ICAM-1 and e-Selectin) by ART status



CONCLUSION

- VCAM-1 level, an indication of greater endothelial activation, was associated with positive maternal HIV status, not being on combination ART or being on ART for shorter period among pregnant women. This is consistent with findings in non-pregnant adults.
- Levels of biomarkers of endothelial activation were not associated with stillbirth or SGA. This provides some evidence against endothelial activation as a mechanism for adverse birth outcomes in this small study.

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