Concentrations of TFV-DP During Pregnancy Among Women Using PrEP

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Background

- Women are at increased risk for HIV during pregnancy yet pregnancy may alter PrEP pharmacokinetics.

Methods

- Samples came from women in serodiscordant couples in an open-label demonstration project in Uganda and Kenya.
- Tenofovir-diphosphate (TFV-DP), a measure of long-term PrEP use, was tested from dried blood spots (DBS) including:
  - 31 pregnant and 32 non-pregnant women.
  - A subset of 12 women before & during pregnancy.
- Tenofovir (TFV), a measure of recent PrEP use, was tested from plasma samples including:
  - 33 pregnant and 83 non-pregnant women.
  - A subset of 9 women before & during pregnancy.
- Daily adherence was assessed by MEMS.
- Concentrations between pregnant and non-pregnant women were compared by generalized estimating equations and concentrations before and during pregnancy by mixed effects models, controlling for adherence by MEMS.
- Sensitivity analysis of women with 100% adherence by MEMS.

Results

- Average age was 29 years; women had an average 2.4 children
- Pregnant and non-pregnant women had similar doses taken by MEMS over the month prior to sample collection (Table 1).
- TFV-DP was lower in pregnant compared to non-pregnant women, but only significant during 2nd trimester; TFV-DP was lower in pregnancy compared to pre-pregnancy (Table 2).
- TFV was lower in pregnancy compared to non-pregnant women and lower during pregnancy compared to pre-pregnancy (Table 3).

Concentrations Between Pregnant & Non-Pregnant Women with 100% MEMS Adherence

Figure 1. TFV-DP (DBS)

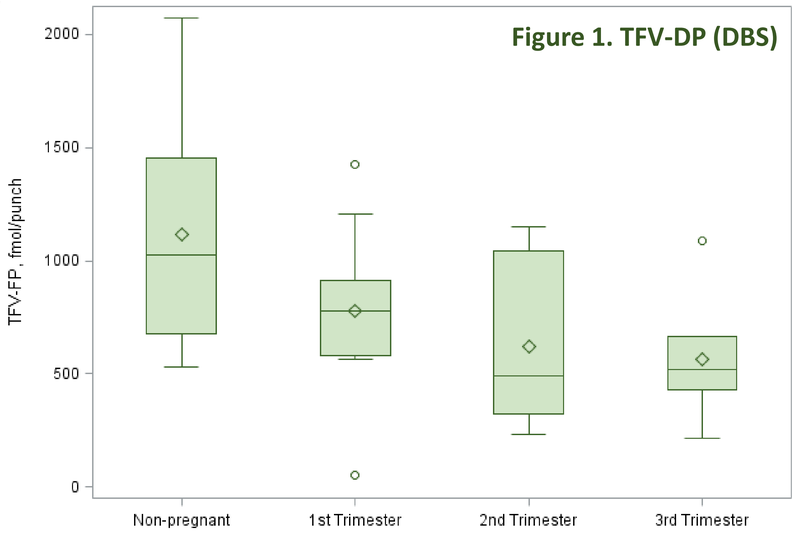

Figure 2. TFV (Plasma)

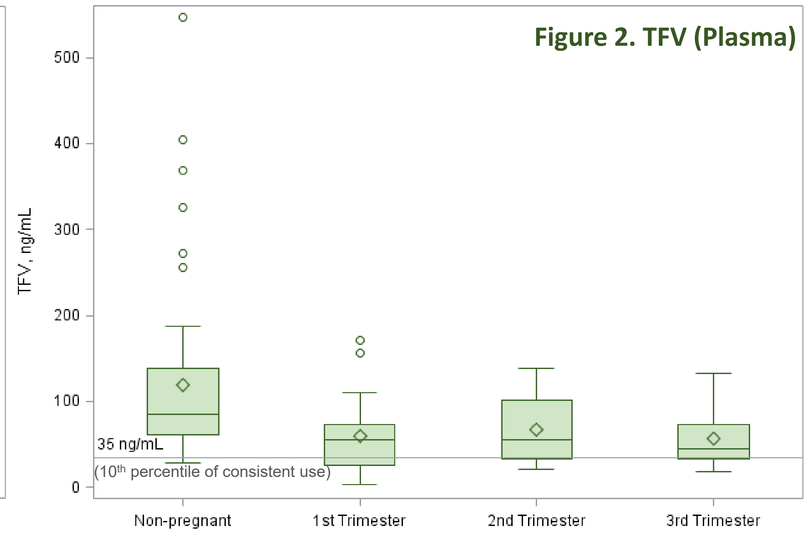

Table 2. Differences in TFV-DP Concentration

Between Pregnant and Non-Pregnant Women	Pregnant	1st Trimester	2nd Trimester	3rd Trimester
Adjusted Difference in TFV-DP fmol/punch* (95%CI)	-136.6 (-318.0, 44.8)	-52.0 (-249.6, 145.7)	-187.1 (-367.9, -6.3)	-178.7 (-373.2, 15.7)
Between Pregnancy and Pre-Pregnant Periods	**Pregnant**	**1st Trimester**	**2nd Trimester**	**3rd Trimester**
Adjusted Difference in TFV-DP fmol/punch** (95%CI)	-289.2 (-439, -139.3)	-302.4 (-487.0, -117.9)	-256.0 (-451.3, -60.8)	-319.8 (-549.1, -90.5)

Adjusted for MEMS cap over prior month
*N=63 women, 102 samples. GEE models with unstructured correlation matrix and non-pregnant as reference; also adjusted for age & BMI.
**N=12 women, 39 samples. Mixed effects models with random intercept and pre-pregnant as reference.

Table 3. Differences in TFV Concentration

Between Pregnant and Non-Pregnant Women	Pregnant	1st Trimester	2nd Trimester	3rd Trimester
Adjusted Difference in TFV ng/mL* (95%CI)	-50.4 (-68.3, -32.5)	-40.0 (-66.8, -13.3)	-49.4 (-69.5, -29.2)	-59.2 (-77.7, -40.7)
Between Pregnancy and Pre-Pregnant Periods	**Pregnant**	**1st Trimester**	**2nd Trimester**	**3rd Trimester**
Adjusted Difference in TFV ng/mL** (95%CI)	-28.1 (-52.3, -4.0)	-24.5 (-53.7, 4.7)	-26.8 (-56.0, 2.4)	-35.8 (-67.7, -3.8)

Adjusted for MEMS cap over prior 2 days
*N=116 women, 389 samples. GEE models with unstructured correlation matrix and non-pregnant as reference.
**N=9 women, 66 samples. Mixed effects models with random intercept and pre-pregnant as reference.

Table 1. PrEP Use & Tenofovir Concentrations in Pregnant & Non-Pregnant Women

TFV-DP (n=63 women)	Non-Pregnant (n=32)	Pregnant (n=70)
Mean doses over prior month(SD)*	20.7 (10.6)	21.4 (10.5)
Mean TFV-DP fmol/punch (SD)	636.7 (523.0)	450.3 (388.1)
TFV (n=116 women)	**Non-Pregnant (n=226)**	**Pregnant (n=163)**
Mean doses over prior month(SD)*	23.1 (9.4)	22.2 (10.1)
Mean TFV ng/mL (SD)	86.5 (90.6)	34.7 (44.5)

*By MEMS

Conclusions

- After controlling for adherence, TFV and TFV-DP were 45-58% lower during pregnancy, with the largest differences generally in later pregnancy.
- This finding is consistent with changes in TFV found in HIV-infected women using ART during pregnancy.
- Clinical implications are unclear.
  - Most women reporting consistent use are above established 10th percentile while pregnant (Figure 2).
  - Pregnant women may require different cut-offs when evaluating adherence.
- Additional studies are needed to determine the efficacy and protective levels of PrEP during pregnancy.

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