Lower Cumulative Antiretroviral Exposure in People Living with HIV and Diabetes Mellitus

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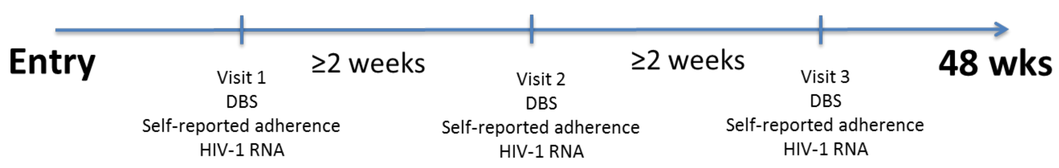
Background

- Tenofovir diphosphate(TFV-DP) in dried blood spots (DBS) is a novel pharmacologic measure of cumulative ART adherence that is predictive of viral suppression and future viremia.
- The relationship between non-AIDS comorbidities and this adherence measure is unknown.
- We aimed to evaluate the association between 3 non-AIDS comorbidities (diabetes mellitus (DM), hypertension, and hyperlipidemia) and TFV-DP in DBS in persons living with HIV (PLWH).

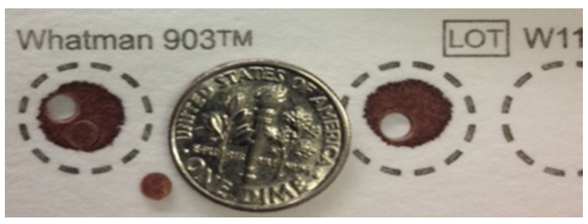
Methods

- Blood for TFV-DP in DBS and HIV viral load (VL) was collected from PLWH on tenofovir disoproxil fumarate (TDF)-based ART at University of Colorado Hospital between 2014 and 2017.[1]



Enrollment: June 2014-July 2017

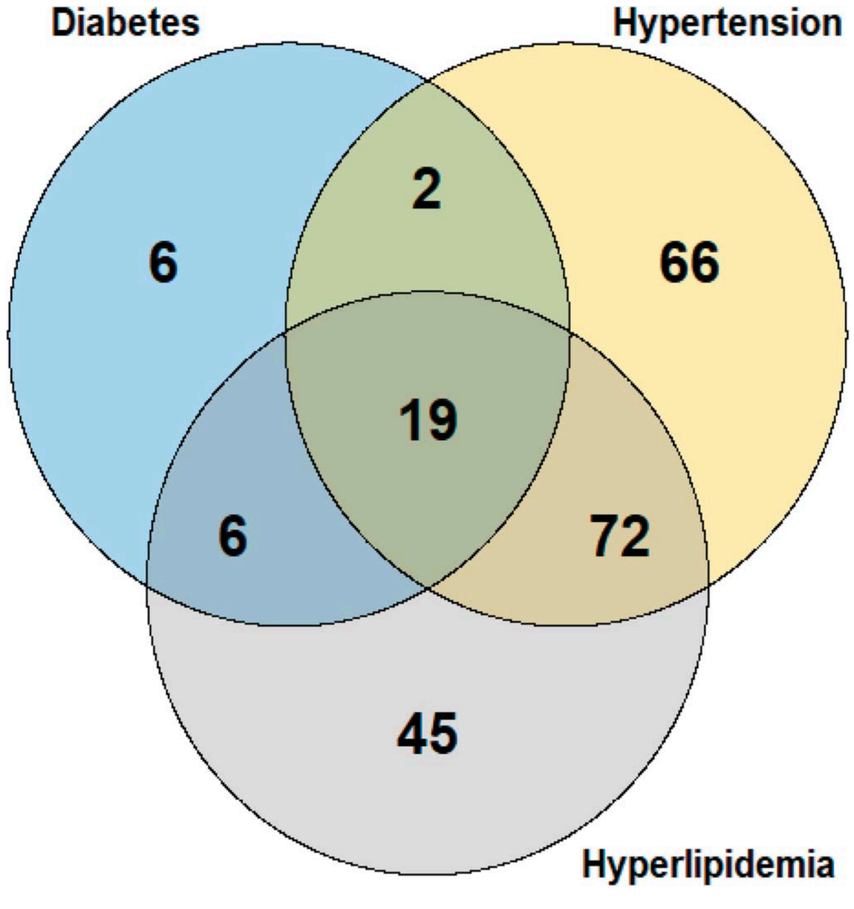
- After informed consent was signed, 4-6 mL of whole blood were obtained in EDTA from peripheral venipuncture at the time of the participant's clinical blood draw.



- For DBS, 25 mcl of whole blood (from EDTA tubes) was pipetted five times into a Whatman 903 Protein Saver card, as previously described.[2] TFV-DP was quantified from a 3-mm punch using LC-MS/MS.[2]
- Non-AIDS comorbidities were recorded in all subjects.
- Mixed effects multivariable linear regression models were used to estimate the concentration of TFV-DP in DBS according to the presence and number of comorbidities and to estimate the percent differences in TFV-DP concentrations between these groups.

Results

Figure 1. Number of study participants according to concomitant non-AIDS comorbidities



Results (continued)

Table 1. Study Participants Demographics

Characteristic	Total (N = 523)	Comorbidity (Participants May Appear Multiple Times): No Comorbidities (n = 307)	Hypertension (n = 159)	Hyperlipidemia (n = 142)	DM (n = 33)
Age, median (IQR)	45 (36–52)	40 (33–49)	51 (46–57)	52 (46–57)	51 (45–56)
Gender, n (%)					
Male	448 (86%)	261 (85%)	141 (89%)	121 (85%)	29 (88%)
Female	75 (14%)	46 (15%)	18 (11%)	21 (15%)	4 (12%)
Race/ethnicity, n (%)					
White	302 (58%)	175 (57%)	91 (57%)	85 (60%)	20 (61%)
Black	98 (19%)	55 (18%)	38 (24%)	22 (15%)	4 (12%)
Hispanic	99 (19%)	61 (20%)	24 (15%)	28 (20%)	7 (21%)
Others	24 (5%)	16 (5%)	6 (4%)	7 (5%)	2 (6%)
BMI (kg/m^2), median (IQR)	26 (23–29)	25 (22–28)	28 (25–31)	27 (24–31)	27 (25–31)
eGFR (mL/min/1.73 m^2), median (IQR)	87 (74–102)	89 (75–104)	86 (73–103)	84 (69–98)	84 (70–99)
Hematocrit (%), median (IQR)	45 (42–47)	45 (42–47)	45 (42–48)	45 (42–48)	43 (42–46)
CD4$^+$ T-cell count (cells/mm^3), median (IQR)	592 (346–826)	553 (334–792)	660 (388–888)	714 (472–919)	748 (416–960)
Concomitant NRTI, n (%)					
FTC	455 (87%)	270 (88%)	133 (84%)	123 (87%)	28 (85%)
ABC	5 (1%)	2 (1%)	3 (2%)	2 (1%)	0 (0%)
3TC	4 (1%)	1 (<1%)	2 (1%)	3 (2%)	1 (3%)
AZT	4 (1%)	1 (<1%)	2 (1%)	3 (2%)	1 (3%)
Type of ART, n (%)					
INSTI-based	189 (36%)	133 (43%)	39 (25%)	35 (25%)	11 (33%)
NNRTI-based	138 (26%)	73 (24%)	50 (31%)	39 (27%)	12 (36%)
b/PI-based	129 (25%)	74 (24%)	41 (26%)	38 (27%)	6 (18%)
Multiclass	67 (13%)	27 (9%)	29 (18%)	30 (21%)	4 (12%)
Pharmacologic booster, n (%)					
No	256 (49%)	145 (47%)	83 (52%)	68 (48%)	21 (64%)
Yes	267 (51%)	162 (53%)	76 (48%)	74 (52%)	12 (36%)
Three-month self-reported adherence (%), median (IQR)	98 (90–100)	97 (90–100)	98 (90–100)	100 (94–100)	99 (90–100)
HIV viral load (copies/mL), n (%)					
<20	362 (69%)	203 (66%)	116 (73%)	105 (74%)	23 (70%)
≥20	97 (19%)	62 (20%)	25 (16%)	23 (16%)	6 (18%)
≥200	64 (12%)	42 (14%)	18 (11%)	14 (10%)	4 (12%)
Total pMRCI score, median (IQR)	18 (10–29)	14 (8–23)	26 (15–38)	24 (15–38)	33 (19–46)
TFV-DP in DBS (fmol/punch), median (IQR)	1635 (1180–2313)	1609 (1157–2248)	1654 (1238–2316)	1816 (1369–2490)	1509 (790–1794)

3TC, lamivudine; ABC, abacavir; AZT, zidovudine; b/PI, booster protease inhibitor; BMI, body mass index; FTC, emtricitabine; INSTI, integrase strand transfer inhibitor; IQR, interquartile range; MRCI, patient-level medication regimen complexity index; NNRTI, nonnucleoside reverse transcriptase inhibitor; NRTI, nucleoside reverse transcriptase inhibitor.

- Data from a total of 1,144 person visits was derived from 523 participants (with concentrations of TFV-DP in DBS).
- There was no association between the number of non-AIDS comorbidities (0, 1, 2, or 3) and the concentrations of TFV-DP in DBS (p=0.40).
- Participants who had diabetes mellitus had 24% (95% CI: -36%, -12%; p<0.001) lower concentrations of TFV-DP in DBS compared to participants without diabetes.

Conclusions

- PLWH who have diabetes mellitus have lower concentrations of TFV-DP in DBS compared to those without diabetes.
- Additional research is needed to identify the mechanisms underlying these findings to better understand ART adherence and improve treatment options among PLWH with chronic comorbidities.

References and acknowledgements

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1. *Castillo-Mancilla JR, Morrow M, Coyle RP, et al. Tenofovir diphosphate in dried blood spots is strongly associated with viral suppression in individuals with human immunodeficiency virus infections. Clin Infect Dis. 2019;68:1335–1342*
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