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Detection of antiretrovirals in transgender women with HIV is not altered by hair treatments

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Adherence to antiretroviral therapy (ART) significantly decreases mortality among people with HIV and reduces transmission, with a positive impact on public health [1]. Since 1998, Argentina has provided free ART to all individuals. Despite the provisions made by the government of Argentina, 33% of those on ART do not achieve an undetectable viral load [2]. Self-reported ART adherence is lower among transgender women (TW) compared with other people with HIV [3, 4]. Factors influencing low adherence in this population include depression [5], concerns regarding potential antiretroviral (ARV) drug interactions with gender-affirming hormone therapy [3, 4], socioeconomic factors [5], and gender-related stigma and discrimination in healthcare [6].

The most common method of assessing ART adherence is self-report, but it is susceptible recall and social desirability biases, leading to overestimation [7]. Viral load is currently the most practical method in clinical settings to assess adherence, yet, by the time virologic failure has occurred and been identified, the optimal time to intervene may have passed. As such, other metrics to objectively assess ART adherence include ARV levels in plasma and urine [3]. However, these metrics reflect short-term adherence and cannot reveal patterns of poor adherence [8].

Longer term ARV adherence using hair sample analysis addresses the limitations associated with both self-reported ART adherence and short-term ART adherence metrics [9, 10].

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Informed consent: Written informed consent was obtained from all participants in the study before the conduct of any research activities.

Hair grows an average of 1cm per month, which can determine adherence over a month [11]. Hair sample collection is non-invasive, and the collection, storage, and shipping of hair is simpler and more cost-effective than that of blood, as hair samples can be stored at room temperature without biohazard precautions [12]. Measuring ARV in hair has been increasingly used to assess ART adherence in HIV treatment and prevention studies [9, 10]. However, when measuring ART levels in people with treated hair (e.g., dye, bleach), the possible degradation of ART or other drugs by hear treatments may affect the accuracy of this measure [13].

Work in the UCSF Hair Analytical Laboratory has shown that only hair bleach decreases ARV concentrations in hair in laboratory-based studies [14, 15]. However, there has been no real-world research utilizing this method in TW, a population in whom hair treatments are common. TW with HIV have been identified as experiencing healthcare and treatment avoidance, making the use of objective adherence markers especially critical [16]. This study assessed the feasibility of hair sample analysis for determining ART adherence among TW in Argentina. As there are a limited number of real-world studies assessing treated hair, we determined ARV concentrations in TW with a range of hair treatments.

Methods

TW in HIV care (n = 19) were enrolled. Data were collected by an Argentine research team from gender-affirming sites and community-led organizations (Fundacion Huesped, Casa Trans, and Hotel Gondolin. Inclusion criteria were 1) 18 years of age or older; 2) diagnosed with HIV for more than six months; and 3) self-identified as a TW.

Women reported sociodemographic characteristics, HIV history, and any hair treatments they had undergone. HIV RNA viral loads for patients were retrieved from medical records and are provided in number of HIV-1 RNA copies per milliliter (mL). Viral suppression was defined as less than 100 HIV-1 RNA copies per ml.

The process for obtaining hair samples, as well as development of methods for extracting, measuring, and analyzing ARVs in small samples of hair has been previously summarized [9, 17]. Previous work also details calibration standards and quality assurance [9, 17]. Samples involving 20-30 strands of hair (approximately 1-3 milligrams) were collected in Argentina between March 26, 2021, and April 15, 2021, and transported to the home study site in Miami Florida in March and May of 2021 in two separate badges, and then shipped together the UCSF hair laboratory on June 3, 2021. ART quantification in hair was performed in the UCSF Hair Analytical Laboratory using liquid chromatography coupled with tandem mass spectrometry for darunavir (used for participants taking a darunavir regimen) and tenofovir (used for participants taking a non-darunavir based regimen).

Results

All 19 invited TW agreed to have hair samples collected and provided written informed consent. Women were on average 35.84 (10.53) years of age, and 36.8% completed high school. Sample characteristics are described in Table 1. HIV viral loads (2-12 months prior to the assessment) were available for 14 women (73.7%). Most women were virologically suppressed (*n* = 11; 78.6%), and 21.4% (*n* = 3) were not. ARVs were not detected in *n* = 2 (10.5%) and detected in *n* = 17 (89.5%) participants.

Nearly all participants reported using hair dye (*n* = 17; 94.4%). About two-thirds (*n* = 8; 42.1%) of women reported having hair botox, and 42.1% (*n* = 8) reported having keratin (straightening) treatments. Only one participant reported permanent waving treatment (1; 5.3%). These types of treatments did not differ by whether ARVs were detected or not (hair dye: $X^2 = 0.13$, $p = .716$; botox: X2 = 0.06, $p = .811$; keratin: $X^2 = 1.63$; $p = .202$). Concentration levels of ARVs were broken down into tertiles for all ARVs tested; no differences emerged in these tertiles by hair treatment modality (botox: $X^2 = 1.67$, $p = .435$; keratin: $X^2 = 0.60$, $p = .741$). These tertiles could not be analyzed by hair dye or permanent wave procedures given that only two participants reported not dying her hair, and only one reported perming her hair.

Discussion

This study evaluated the detection of ARVs in hair samples from TW with HIV in Argentina. Results suggest that hair collection is acceptable to TW; that adherence measured by detection of ARVs in hair was high; and that ARVs can be detected in hair even in the context of hair treatments.

TW with HIV have lower levels of adherence than cisgender people with HIV, and measuring adherence is challenging [3]. Detection of ARVs in hair can be used as a predictor of HIV virological suppression, and it is a promising method to evaluate ART adherence and HIV outcomes [9, 17]. However, no previous study to examine ARV concentrations in hair has exclusively focused on TW.

The main finding of this study is that TW had high rates of ARV detection despite hair treatments. Hair products can cause degradation of cannabinoids, which is more prominent with bleach than with perming or coloring [14]. Although there is extensive literature on the effect of hair treatment in the detection of illegal substances, data on ARV detection in treated hair is scarce. Rosen et al. evaluated the detection of ARVs in hair strands treated with dye, bleach, and relaxer, and concluded that those hair treatments had little or no effect on the detection of cobicistat, abacavir, dolutegravir, maraviroc, efavirenz, and darunavir; but the treatments removed emtricitabine in hair samples [18, 19]. The UCSF Hair Analytical examined hair treatments on hair samples in the laboratory and found that only bleaching (not dyes or permanent wave treatment) reduced ARV concentrations in hair [15].

Botox and keratin are hair treatments commonly used by women in South America and were used by most of the study participants. Because Botox and keratin-based hair treatments adhere to the hair follicle, they have the potential to degrade ARVs more than other hair treatments. Contrary to this hypothesis, our results suggest that botox or keratin treatments do not alter ARV detection among TW. Therefore, we conclude that measures of ARV in hair is a reliable method to assess ARV adherence and viral suppression in treated and untreated hair.

This study was important due to several factors. No previous study has exclusively examined ARV concentrations in hair among TW, and this study examined the effect of hair treatments on ARV detection. Since hair treatments with certain products may impair ARV detection in hair [18, 19], and TW have high rates of hair treatments, this study was also important to examine the effect of hair treatments on ARV detection [18, 19]. Other important findings include the high rates of ARV adherence as measured by ARV in hair samples which was comparable to other populations, high rates of viral suppression, and acceptability of hair sample collection in this population [3].

This study has several limitations, including the small sample from Argentina, limiting generalizability to other TW and settings. Future studies should aim to replicate these findings in other sites treating TW with HIV. Hair treatments were self-reported; there is a possibility of variability among products used. In addition, we did not have measures of viral load at the time of hair collection, which prevented us from evaluating the relationship between hair levels and virologic suppression.

Despite these limitations, results are relevant to both HIV treatment and prevention. The study provides important preliminary data to support the use of hair in TW as a reliable method of evaluating detection and evaluation of ARV adherence and potential viral suppression. Incorporating hair ARV levels and other objective measures of ARV adherence in ongoing HIV research and clinical care settings is a priority in this vulnerable population with high rates of HIV and non-adherence.

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Table 1.

Sample Characteristics (N = 19)

Variables	**M (SD)** **N (%)**
Age	35.84 (10.53)
Education	
Less than high school	9 (47.4%)
High school	7 (36.8%)
Trade, vocational school, or some college	3 (15.8%)
Unstable Housing	
No	12 (63.2%)
Yes	7 (36.8%)
HIV Viral Load (n = 14)	
Undetectable	11 (78.6%)
Detectable	3 (21.4%)
ART Regimen	
DRV/NRTI 3 drug regimen	1 (2.5%)
DTG/NRTI 3 drug regimen	2 (5.0%)
EFV/NRTI 3 drug regimen	2 (5.0%)
DLG/3TC Two-drug regimen	1 (2.5%)
Hormone Use	11 (52.4%)
Hair Treatments	
Hair Color	2.37 (1.46)
Less than 30 days ago	5 (26.3%)
Between 30 and 60 days ago	3 (15.8%)
Between 60 and 90 days ago	9 (47.4%)
More than 90 days ago	1 (5.3%)
Hair Botox	8 (42.1%)
Less than 30 days ago	1 (5.3%)
Between 30 and 60 days ago	2 (10.5%)
Between 60 and 90 days ago	1 (5.3%)
More than 90 days ago	3 (15.8%)
Keratin Treatment	8 (42.1%)
Less than 30 days ago	2 (10.5%)
Between 30 and 60 days ago	1 (5.3%))
Between 60 and 90 days ago	2 (10.5%))
More than 90 days ago	2 (10.5%)
Permanent Wave	1 (5.3%)
More than 90 days ago	1 (5.3%)

Note. DRV = darunavir; NRTI = nucleoside reverse transcriptase inhibitor; DTG = dolutegravir; EFV = Efavirenz.