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Undisclosed Antiretroviral Drug Use in Botswana – Implication for National Estimates

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Summary

Among 3,596 HIV-positive participants enrolled in Botswana Combination Prevention Project (BCPP) who self-reported no prior ART use and were tested for viral load (n=951; 27% of all participants), 136 (14%) had HIV-1 RNA <400 copies/mL. ARV drugs were detected in 52 (39%) of 134 participants tested. Adjusting for undisclosed ARV use increased the overall estimate of virally suppressed individuals on ART by 1.4% from 70.2% to 71.6%.

Keywords

Antiretroviral therapy (ART); Antiretroviral drugs (ARVs); undisclosed ART use; Botswana; estimate of virally suppressed

Introduction

Undisclosed antiretroviral (ARV) use among virally suppressed individuals may underestimate programmatic antiretroviral therapy (ART) coverage estimates, affect interpretability of clinical trials results[1–10], and/or inflate estimates of viremic controllers[11–15]. Undisclosed ARV use has been reported in previous studies[16–18]

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including studies in Africa[8–10, 19]. While self-report is commonly used to measure ART uptake[20–23], its accuracy could be affected by undisclosed ART use.

As of 2016, Botswana was one of seven countries in the world and the only African country that was reported to have achieved targeted levels of viral suppression defined by UNAIDS[24, 25]. The goal of the study was to evaluate the extent of undisclosed ART use in Botswana and assess how lack of disclosure might alter national estimates of UNAIDS 90-90-90 targets[26, 27].

Methods

Study population

Blood specimens were collected in the BCPP study[6] in 2013–2015. The participants in this study represent a 20% random sampling of households in the 30 communities. People living with HIV (PLHIV) participating in the BCPP study verbally reported prior and current ART receipt[6]. Participants aged 18–64 years provided written informed consent (ascent for participants aged 16–17 years).

HIV-1 RNA testing

Following positive double rapid HIV testing, venous blood was collected by phlebotomy in households. The HIV-1 RNA load in plasma was quantified by Abbott m2000sp/Abbott m2000rt (Wiesbaden, Germany).

ARV drug detection

Plasma from 134 of 135 participants who reported no ART use and had undetectable HIV-1 RNA (≤400 copies/mL) was screened for ARV drugs by high-throughput liquid chromatography coupled with Q-Exactive high-resolution mass spectrometry using data-dependent fragmentation and selected reaction monitoring at resolution of 17,500[28]. To obtain qualitative results, each specimen was compared to positive and negative controls for each of 20 drugs tested. The limit of identification ranged from 5 to 10 ng/ml and is presented elsewhere[28].

Statistical analysis

Adjusted prevalence ratios (aPR) and 95% confidence intervals (CI) were estimated for factors associated with undisclosed ART use accounting for clustering, age, and gender. P-values <0.05 were considered statistically significant. Statistical analyses were performed in STATA v.14.2 (College Station, TX) and SAS v.9.4 (SAS Institute, Cary, NC).

Results

Of 12,610 adult BCPP baseline household survey participants, 3,596 (29%) were HIV-infected, and 953 (27%; 95%CI: 24–30%) self-reported no prior use of ART. Of those with an available viral load (N=951), 136 (14%) had HIV-1 RNA<400 copies/mL. Multiple ARV drugs were detected in 52 (39%, 95%CI: 30–50%) of the 134 virologically suppressed individuals tested for ARV drugs. Three ARV drugs were detected in 42 participants, two

drugs in 9 participants, and one participant had a single drug detected (efavirenz). The most commonly identified ARV combinations detected were (efavirenz/nevirapine)/emtricitabine/tenofovir which were the first-line treatment regimens most commonly prescribed in Botswana's national ART program at the time of sampling. Among 52 individuals with ARV drugs detected, 36 (69%) stated that they did not know their HIV status.

Among virologially suppressed participants with evidence of current ART use either through self-report or detection of ARV drugs (N=2,569), non-disclosure of ART use was associated with being <35 years old (aPR=4.38; 95%CI: 2.51–7.63) and sex with a younger partner (PR=1.63; 95%CI: 1.01–2.63). No significant differences were found according to sex, employment status, income, education, alcohol use, and history of concurrent sexual partnerships or transactional sex.

Discussion

We found that among HIV-infected individuals who reported not being on ART, 14% had undetectable HIV-1 RNA (≤400 copies/mL), 39% of whom had detectable plasma ARV levels. Udisclsosed ART use was also reported in Partners in Prevention study[8], HPTN 052 study[10], in Kenya[9] and South Africa[19]. After adjusting for undisclosed ARV use in BCPP study communities, the estimated proportion of PLHIV who have undetectable HIV-1 RNA on ART in Botswana increased by 1.4%, from 70.2%[6] to 71.6%. Adjusting for undisclosed ARV use provided more accurate estimates of the country progress toward the UNAIDS 90-90-90 targets[26, 27].

Testing for ARV drugs in blood is the only biomedical verification method able to either confirm or reject self-report of no ART use. While feasible in research settings, it is not practical to conduct ARV level testing in programmatic settings. However, testing may represent a viable surveillance measure in a proportion of virally suppressed persons who self-report being ART-naïve in population surveys. ART use could also be ascertained from national ARV data systems where such systems exist and ethical considerations are taken into account.

The underlying reasons of unreported ARV use could include stigma, non-adherence or desire for confirmation of HIV infection, or may represent use of non-prescribed ARVs including sharing of drugs. We found that undisclosed ARV use was associated with younger age (similar to reports from KwaZulu-Natal, South Africa[19] and Kenya[9]) and sex with a younger partner. No significant difference was found in undisclosed ARV use by gender (similar to a report by Kahle et al.[8]), employment status, income level, educational level, alcohol use, and history of concurrent sexual partnerships or transactional sex.

We tested for presence or absence of ARV drugs (at low thresholds), but did not measure ARV drug concentrations, nor could we ascertain the timing of most recent ARV dosing. ARV drug levels are affected by individual drug metabolism and timing of sample collection in relation to drug ingestion. Plasma half-life for NNRTIs is much longer than for NRTIs. We therefore cannot exclude that some ARV drugs could not be detected due to unknown time between ARV intake and sampling. Another limitation of this study is that we did not

screen for ARV drugs among individuals with detectable viral load, or individuals who said that they were receiving ART.

Conclusion

Among household survey participants in Botswana who reported no prior use of ART and had no detectable virus, undisclosed ARV use was found in 39%. Accounting for undisclosed ART increased the estimated proportion of virologically suppressed individuals among HIV-infected people in Botswana by 1.4% to 71.6%. Testing for ARV drugs in virologically suppressed individuals could supplement self-report of ART use and inform estimates of ART coverage, as well as providing valuable information to clinicians and clinical trials investigators.

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