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Phosphatidylethanol confirmed alcohol use among ART-naïve HIV-infected persons who denied consumption in rural Uganda

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ABSTRACT

Under-reporting of alcohol use by HIV-infected patients could adversely impact clinical care. This study examined factors associated with under-reporting of alcohol consumption by patients who denied alcohol use in clinical and research settings using an alcohol biomarker. We enrolled ART-naïve, HIV-infected adults at Mbarara Hospital HIV clinic in Uganda. We conducted baseline interviews on alcohol use, demographics, Spirituality and Religiosity Index (SRI), health and functional status; and tested for breath alcohol content and collected blood for phosphatidylethanol (PEth), a sensitive and specific biomarker of alcohol use. We determined PEth status among participants who denied alcohol consumption to clinic counselors (Group 1, $n = 104$), and those who denied alcohol use on their research interview (Group 2, $n = 198$). A positive PEth was defined as ≥8 ng/ml. Multiple logistic regression models were used to examine whether testing PEth-positive varied by demographics, literacy, spirituality, socially desirable reporting and physical health status. Results showed that, among the 104 participants in Group 1, 28.8% were PEth-positive. The odds of being PEth-positive were higher for those reporting prior unhealthy drinking (adjusted odds ratio (AOR): 4.7, 95% confidence interval (CI): 1.8, 12.5). No other factors were statistically significant. Among the 198 participants in Group 2, 13.1% were PEth-positive. The odds of being PEth-positive were higher for those reporting past unhealthy drinking (AOR: 4.6, 95% CI: 1.8, 12.2), the Catholics (AOR: 3.8, 95% CI: 1.3, 11.0) compared to Protestants and lower for the literate participants (AOR: 0.3, 95% CI: 0.1, 0.8). We concluded that under-reporting of alcohol use to HIV clinic staff was substantial, but it was lower in a research setting that conducted testing for breath alcohol and PEth. A report of past unhealthy drinking may highlight current alcohol use among deniers. Strategies to improve alcohol self-report are needed within HIV care settings in Uganda.

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Introduction

Sub-Saharan Africa (SSA) has high HIV prevalence (Heil, Townsend, Shipp, Clarke, & Johnson, 2010) and levels of harmful alcohol use (Global Status Report on Alcohol and Health, 2014), especially among persons with HIV (Pithey & Parry, 2009). Alcohol use is associated with HIV transmission and co-morbidities, and complicates HIV care (Williams et al., 2016). Thus, alcohol use is a major factor in the HIV epidemic in SSA.

In Uganda, the per capita yearly pure alcohol consumption is high, reported as 25.6 and 19.6 liters among male and female drinkers respectively compared to 18.1 and 7.8 liters respectively in the USA (Global Status Report on Alcohol and Health, 2014). Supporting HIV-infected clients to reduce alcohol use may be feasible for those interacting with health workers (Morojele, Nkosi, Kekwaletswe, Saban, & Parry, 2013). However, while studies have noted under-reporting of alcohol use by research participants (Bajunirwe et al., 2014; Hahn et al., 2012), under-reporting in HIV clinical settings has not yet been examined.

Hence, we examined the occurrence and correlates of under-reporting among ART-naïve HIV-infected patients who denied alcohol consumption in the settings of clinical care and research assessments. We

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examined these settings separately, due to differences in procedures of evaluating alcohol use and differing consequences of under-report. Under-reporting was determined using phosphatidylethanol (PEth), a sensitive and specific biomarker for alcohol use in the previous 2–3 weeks (Hahn, Anton, & Javors, 2016).

Methods

Study site, participants and study design

This was an analysis of the baseline cross-sectional data collected for a prospective Ugandan cohort of the Uganda Russia Boston Alcohol Network for Alcohol Research Collaboration on HIV/AIDS (URBAN ARCH). The study enrolled ART-naïve HIV-infected adults above 18 years attending the HIV clinic in Mbarara Regional Referral Hospital in southwestern Uganda from September 2011 through August 2014. The primary aim of the cohort was to examine the impact of unhealthy alcohol consumption on HIV disease progression prior to ART. The study enrolled participants whose recent CD4 cell count was above 350 or 500 cells/mm^3, the latter cutoff was used after February 2014, when the clinic adopted the addendum to the National ART guidelines, Uganda (Uganda Ministry of Health: Addendum to the National Antiretroviral Treatment Guidelines, 2013).

At the HIV clinic where the study occurred, alcohol use was routinely assessed by counselors via the 3-item Alcohol Use Disorders Identification Test – Consumption (AUDIT-C) (Bush, Kivlahan, McDonell, Fihn, & Bradley, 1998), or the 10-item AUDIT (Babor, Higgins-Biddle, Saunders, & Monteiro, 2001), beginning in June 2013. This information was extracted from the clinic electronic medical records for this analysis.

To examine under-reporting of alcohol use to clinic counselors, we examined patients who denied alcohol consumption in the previous year (AUDIT/AUDIT-C question 1) to clinic counselors at their initial clinic visit (Group 1). We limited this group to participants who completed their baseline research interview within 3 months of clinic entry, to ensure comparability of the data collected at clinic entry and study entry ($n = 104$). To examine under-reporting during the research interview, we examined participants who reported no current (previous 3 months) alcohol consumption at their baseline research visit (Group 2; $n = 198$).

The study protocols were approved by the National and Institutional Review Boards in Uganda, the University of California, San Francisco (UCSF), and Boston Medical Center. The participants gave written consent to participate in the study and were compensated for their transportation expenses. They were informed that their blood would be tested for a biomarker that indicates alcohol use in the previous 2–3 weeks and that their answers to survey questions would be kept confidential.

Laboratory testing

Venous blood samples were transferred to Whatman 903 cards and stored at −80°C until shipping to the United States Drug Testing Laboratory for liquid chromatography with tandem mass spectrometry testing for PEth, an abnormal phospholipid formed only in the presence of alcohol (Jones, Jones, Plate, & Lewis, 2011). We also tested for CD4+ T-cell count using a Coulter Epics XL.MCL Cytometer and HIV-1 viral load (Abbott).

Variables

The outcome variable was under-reporting, defined as PEth ≥8 ng/ml.

The independent variables examined were sex, age, literacy, religion, the Spirituality and Religiosity Index (SRI) (Ironson et al., 2002), the Marlowe-Crowne Social Desirability Scale (SDS) (Reynolds, 1982), general health status, the Physical Functioning Scale (PFS) (Wu, 1999), HIV diagnosis date and HIV symptom index adapted from Justice et al. (2001). Past unhealthy alcohol use was self-reported by the total AUDIT-C score for the period in the past during which the participants consumed most alcohol. Scores above the cutoff (≥3 for women, ≥4 for men) indicated past unhealthy drinking (Bradley et al., 2007).

Statistical analysis

We calculated frequencies and proportions for categorical variables, and medians, interquartile ranges (IQR), means, and standard deviations (SD) for continuous variables.

Initial bivariate analyses were conducted assessing the association between each factor of interest and under-reporting. Multivariable logistic regression models were then fit including those variables with $p < 0.10$ in bivariate analysis. Two-sided tests were used and p-values < 0.05 were considered statistically significant.

Results

447 participants completed baseline interviews. Two-thirds (303/447, 68.0%) were female and the participants' median age was 32 years (IQR: 27.0–40.0).

Under-reporting of alcohol consumption to clinic counselors

104 participants reported no alcohol consumption in the previous year at their initial visit to the clinic counselors (Group 1). Of these, 30 (28.8%; 95% CI: 20.0%–38.0%) were PEth positive, termed under-reporters (Table 1). The median PEth level among the under-reporters was 46.5 ng/ml (IQR: 14.2–397.0).

In unadjusted analyses, under-reporting was associated with SRI score and self-reported past unhealthy drinking; only self-reported past unhealthy drinking remained significantly associated with under-reporting in adjusted analyses (AOR: 4.7; 95% CI: 1.8–12.5).

Under-reporting of alcohol consumption on the research interview

198 participants were self-reported abstainers (previous 3 months) at the baseline research interview (Group 2); 26 (13.1%; 95% CI: 8.0%–18.0%) of these were PEth-positive and considered under-reporters (Table 2). The median PEth level among the under-reporters at research interview was 57.6 ng/ml (IQR: 13.5–625.0). In unadjusted analyses, male gender, literacy, religion, and self-reported past unhealthy drinking were associated with under-reporting; the associations between each of these variables with under-reporting remained statistically significant in adjusted analyses, except for gender.

Table 1. Baseline PEth results among participants reporting No alcohol consumption in previous year at Initial Clinic Visit[b] ($n = 104$).

			PEth result			
Variable	Response	Overall N (%)	Positive (>=8)[c] N (%)	Negative (<8) N (%)	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
Overall		104 (100%)	30 (28.8%)	74 (71.2%)		
Prior unhealthy drinking ($N = 103$)	Hazardous drinking	38 (36.9%)	19 (63.3%)	19 (26.0%)	4.91 (1.98, 12.17)*	4.72 (1.79, 12.46)*
	Non-hazardous drinking	65 (63.1%)	11 (36.7%)	54 (74.0%)	- Ref -	- Ref -
Age	Highest tertile	20 (19.2%)	7 (23.3%)	13 (17.6%)	1.57 (0.51, 4.86)	
	Middle tertile	37 (35.6%)	11 (36.7%)	26 (35.1%)	1.23 (0.47, 3.23)	
	Lowest tertile	47 (45.2%)	12 (40.0%)	35 (47.3%)	- Ref -	
Sex	Male	21 (20.2%)	9 (30.0%)	12 (16.2%)	2.22 (0.82, 6.00)	
	Female	83 (79.8%)	21 (70.0%)	62 (83.8%)	- Ref -	
Literacy	Literate	70 (67.3%)	19 (63.3%)	51 (68.9%)	0.78 (0.32, 1.90)	
	Not literate	34 (32.7%)	11 (36.7%)	23 (31.1%)	- Ref -	
Religion	Catholic	34 (32.7%)	15 (50.0%)	19 (25.7%)	2.50 (0.98, 6.39)**	2.23 (0.79, 6.32)
	Moslem	10 (9.6%)	2 (6.7%)	8 (10.8%)	0.79 (0.15, 4.25)	1.07 (0.18, 6.30)
	Saved/Other	10 (9.6%)	1 (3.3%)	9 (12.2%)	0.35 (0.04, 3.07)	0.42 (0.04, 4.25)
	Protestant/Anglican	50 (48.1%)	12 (40.0%)	38 (51.4%)	- Ref -	- Ref -
Spirituality religiosity index (SRI)	N	103	29	74	0.95 (0.91, 1.00)*	0.96 (0.91, 1.01)
	Mean (Std Dev)	99.3 (9.5)	96.1 (10.3)	100.6 (8.9)		
	Median (25th, 75th)	102.0 (88.0, 108.0)	93.0 (88.0, 107.0)	103.5 (91.0, 108.0)		
Social desirability scale (SDS)	N	102	30	72	1.01 (0.79, 1.30)	
	Mean (Std Dev)	8.9 (1.7)	8.9 (1.9)	8.9 (1.7)		
	Median (25th, 75th)	9.0 (8.0, 10.0)	9.0 (8.0, 10.0)	9.0 (8.0, 10.0)		
Number of HIV symptoms	N	104	30	74	1.30 (0.90, 1.87)	
	Mean (Std Dev)	1.2 (1.1)	1.4 (1.4)	1.1 (1.0)		
	Median (25th, 75th)	1.0 (0.0, 2.0)	1.0 (0.0, 2.0)	1.0 (0.0, 2.0)		
MOS-HIV physical functioning scale (PFS)	N	98	28	70	0.99 (0.97, 1.01)	
	Mean (Std Dev)	90.3 (18.1)	87.5 (22.3)	91.4 (16.2)		
	Median (25th, 75th)	100.0 (83.3, 100.0)	100.0 (83.3, 100.0)	100.0 (83.3, 100.0)		
Health Status	Fair/Poor	26 (25.0%)	10 (33.3%)	16 (21.6%)	1.81 (0.71, 4.64)	
	Good/Very Good/ Excellent	78 (75.0%)	20 (66.7%)	58 (78.4%)	- Ref -	
Days since first HIV diagnosis	N	104	30	74	1.00 (1.00, 1.00)	
	Mean (Std Dev)	260.8 (528.4)	165.4 (395.5)	299.5 (571.4)		
	Median (25th, 75th)	61.0 (28.0, 213.0)	30.0 (26.0, 98.0)	74.5 (31.0, 353.0)		
CD4 cell count	N	104	30	74	1.00 (1.00, 1.00)	
	Mean (Std Dev)	557.7 (223.2)	552.0 (183.3)	560.0 (238.5)		
	Median (25th, 75th)	508.0 (383.0, 724.0)	514.0 (411.0, 685.0)	498.0 (379.0, 737.0)		
Log10 viral load[a]	N	104	30	74	0.95 (0.62, 1.48)	
	Mean (Std Dev)	3.9 (1.0)	3.8 (1.1)	3.9 (0.9)		
	Median (25th, 75th)	4.1 (3.3, 4.5)	3.7 (3.1, 4.9)	4.1 (3.4, 4.5)		

Note: (SDS) (alpha in our data = 0.49), (SRI) (alpha in our data = 0.95).

[a]Variable was not included in final multivariable model because at time of research, VL testing was not a routinely conducted test so not likely to be a feasible way to detect under-report of alcohol consumption.

[b]Participants who completed Baseline within 3 months of clinic visit.

[c]For the Participants who tested PEth-positive: $N = 30$, median PEth 46.48 (IQR 14.16–397.00), Mean PEth 247.16 (SD = 379.04).

*$P < 0.05$.

**$P < 0.10$.

Table 2. Peth status among those reporting No alcohol consumption (Abstainers) in previous 3 months at Research baseline ($n = 198$).

Variable	Response	Overall N (%)	PETH result		Unadjusted OR (95% CI)	Adjusted OR (95% CI)
			Positive (>=8)[b] N (%)	Negative (<8) N (%)		
Overall		198 (100%)	26 (13.1%)	172 (86.9%)		
Prior unhealthy drinking ($N = 196$)	Hazardous drinking	57 (29.1%)	16 (61.5%)	41 (24.1%)	5.03 (2.12, 11.95)*	4.62 (1.75, 12.18)*
	Non-hazardous drinking	139 (70.9%)	10 (38.5%)	129 (75.9%)	- Ref -	- Ref -
Age	Highest tertile	77 (38.9%)	12 (46.2%)	65 (37.8%)	1.63 (0.57, 4.64)	
	Middle tertile	62 (31.3%)	8 (30.8%)	54 (31.4%)	1.31 (0.43, 4.03)	
	Lowest tertile	59 (29.8%)	6 (23.1%)	53 (30.8%)	- Ref -	
Sex	Male	49 (24.7%)	12 (46.2%)	37 (21.5%)	3.13 (1.33, 7.34)*	2.28 (0.85, 6.08)**
	Female	149 (75.3%)	14 (53.8%)	135 (78.5%)	- Ref -	- Ref -
Literacy ($N = 197$)	Literate	130 (66.0%)	13 (50.0%)	117 (68.4%)	0.46 (0.20, 1.06)**	0.29 (0.11, 0.76)*
	Not literate	67 (34.0%)	13 (50.0%)	54 (31.6%)	- Ref -	- Ref -
Religion	Catholic	52 (26.3%)	14 (53.8%)	38 (22.1%)	4.26 (1.59, 11.42)*	3.75 (1.28, 10.97)*
	Moslem	35 (17.7%)	4 (15.4%)	31 (18.0%)	1.49 (0.41, 5.46)	1.51 (0.37, 6.23)
	Saved/Other	23 (11.6%)	1 (3.8%)	22 (12.8%)	0.53 (0.06, 4.51)	0.48 (0.05, 4.31)
	Protestant/Anglican	88 (44.4%)	7 (26.9%)	81 (47.1%)	- Ref -	- Ref -
Spirituality religiosity index (SRI)	N	196	25	171	0.99 (0.96, 1.02)	
	Mean (Std Dev)	100.0 (11.0)	98.8 (17.7)	100.1 (9.7)		
	Median (25th, 75th)	103.5 (91.0, 108.0)	105.0 (93.0, 108.0)	103.0 (91.0, 108.0)		
Social desirability scale (SDS)	N	195	26	169	1.01 (0.79, 1.28)	
	Mean (Std Dev)	9.1 (1.7)	9.1 (1.8)	9.1 (1.7)		
	Median (25th, 75th)	9.0 (8.0, 10.0)	9.0 (8.0, 11.0)	9.0 (8.0, 10.0)		
Number of HIV symptoms	N	198	26	172	0.89 (0.61, 1.30)	
	Mean (Std Dev)	1.1 (1.2)	1.0 (1.1)	1.1 (1.2)		
	Median (25th, 75th)	1.0 (0.0, 2.0)	1.0 (0.0, 1.0)	1.0 (0.0, 2.0)		
MOS-HIV physical functioning scale (PFS)	N	189	25	164	0.99 (0.97, 1.01)	
	Mean (Std Dev)	89.9 (18.3)	86.7 (24.7)	90.4 (17.2)		
	Median (25th, 75th)	100.0 (83.3, 100.0)	100.0 (91.7, 100.0)	100.0 (83.3, 100.0)		
Health status	Fair/Poor	50 (25.3%)	6 (23.1%)	44 (25.6%)	0.87 (0.33, 2.31)	
	Good/Very Good/ Excellent	148 (74.7%)	20 (76.9%)	128 (74.4%)	- Ref -	
Days since first HIV diagnosis	N	198	26	172	1.00 (1.00, 1.00)	
	Mean (Std Dev)	1269.1 (1495.8)	1199.0 (1617.7)	1279.7 (1481.3)		
	Median (25th, 75th)	623.5 (83.0, 2322.0)	259.0 (41.0, 2530.0)	695.5 (92.5, 2317.0)		
CD4 cell count	N	198	26	172	1.00 (1.00, 1.00)	
	Mean (Std Dev)	591.3 (224.0)	556.1 (158.4)	596.6 (232.2)		
	Median (25th, 75th)	566.0 (420.0, 720.0)	587.5 (368.0, 685.0)	555.5 (420.5, 725.5)		
Log10 viral load[a]	N	197	26	171	1.80 (1.16, 2.79)*	
	Mean (Std Dev)	3.6 (1.1)	4.2 (1.2)	3.6 (1.1)		
	Median (25th, 75th)	3.8 (3.0, 4.3)	4.3 (3.1, 5.1)	3.7 (3.0, 4.3)		

Note: (SDS) (alpha in our data = 0.49), (SRI) (alpha in our data = 0.95).
[a]Variable was not included in final multivariable model because at time of research, VL testing was not a routinely conducted test hence not likely to be a feasible variable to affect under-report of alcohol consumption.
[b]For the Participants who tested PEth-positive: $N = 26$, median PEth 57.55 (IQR 13.51–625.00), Mean PEth 289.45 (SD = 403.76).
*$P < 0.05$.
**$P < 0.10$.

Discussion

This study describes substantial under-reporting of alcohol consumption to clinic counselors among ART-naïve HIV-infected clients, with more than a quarter (28.8%) testing PEth-positive after denying past year alcohol use. Testing PEth-positive after denying alcohol use on the baseline research interview was less common (13.1%); this may be because the participants had consented to have a breathalyzer test and blood biomarker testing to detect alcohol use, and were ensured confidentiality in the research protocol. Another study in this setting found increased self-reports after consent for alcohol biomarker testing (Hahn et al., 2012) and other research studies found PEth-confirmed under-reporting (Bajunirwe et al., 2014; Hahn, Emenyonu, et al., 2016). While under-reporting in any setting may be due to social desirability and recall bias, the increased level of under-reporting to clinic counselors suggests that patients may fear being denied ART (Papas et al., 2012) or some other consequence if they report drinking alcohol at the clinic.

We found that self-reported past unhealthy drinking was associated with higher odds of under-reporting among participants denying alcohol use in both groups. This suggests that probing about past unhealthy alcohol

consumption may help detect current alcohol consumption among deniers. The literate study participants had lower odds of under-reporting alcohol consumption to research staff, consistent with previous study findings in Uganda (Bajunirwe et al., 2014).

Valid reporting of alcohol use is needed for HIV clinical care, in order to assess and intervene on alcohol-related adherence challenges and/or alcohol-related drug toxicities. Under-reporting of alcohol consumption may limit the reach of interventions that have been efficacious in reducing alcohol consumption in SSA (Papas et al., 2011; Zule et al., 2014). Valid reporting is also essential to reaching valid conclusions in research studies.

The limitations of this study include that it was limited to ART-naive HIV-infected individuals with high CD4, and may not be generalizable to those with lower CD4 counts or on ART. PEth is not 100% sensitive for detecting any alcohol use (Hahn, Anton, et al., 2016) so we might have missed a few under-reporters. Lastly, the study had modest sample size, which may have reduced the power to detect statistically significant differences. This may explain why some associations were statistically significant in the analyses within Group 2 ($n = 198$) but not within Group 1 ($n = 104$). The study strengths included the use of PEth which is highly specific, hence a PEth-positive result when alcohol abstaining is reported, especially for 3 months or a year, is highly suggestive of under-report (Hahn, Anton, et al., 2016).

In this study, we found that a substantial fraction of ART-naïve HIV-infected patients denying alcohol use to clinic counselors are indeed consuming alcohol. Under-reporting to researchers testing alcohol biomarkers exists, but to a lesser magnitude. Probing for past unhealthy alcohol use may help identify current drinkers. Strategies to improve alcohol self-report are needed to improve clinical care in the Ugandan HIV clinic setting.

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Disclosure statement

No potential conflict of interest was reported by the authors.

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