



Concordance of Ethyl Glucuronide, Blood Alcohol Content, and Self-Reported Alcohol Use in Russian Women with HIV and Hepatitis C Virus Co-Infection

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Abstract

Problematic alcohol use is prevalent in Russia and is deleterious for individuals with HIV and Hepatitis C Virus (HCV). Ethyl glucuronide (EtG) and blood alcohol content (BAC) provide objective biomarkers of drinking that can be compared to self-reported alcohol use. This paper describes patterns of alcohol use measured by biomarkers and self-report along with concordance across measures. Participants were Russian women with HIV and HCV co-infection ($N=200$; Mean age=34.9) from two Saint Petersburg comprehensive HIV care centers enrolled in an alcohol reduction intervention clinical trial. Measures were: (a) urine specimen analyzed for EtG; (b) breathalyzer reading of BAC; and (c) self-reported frequency of drinking, typical number of drinks consumed, and number of standard drinks consumed in the past month. At baseline, 64.0% ($n=128$) had a positive EtG (>500 ng/mL) and 76.5% ($n=153$) had a positive breathalyzer reading (non-zero reading). There was agreement between EtG and BAC ($\kappa=0.66$, $p<.001$; Phi coefficient=0.69, $p<.001$); self-reported alcohol measures were positively correlated with positive EtG and BAC ($p's<0.001$). There was concordance between EtG and BAC measures, which have differing alcohol detection windows. Most participants endorsed frequent drinking at high quantities, with very few reporting no alcohol consumption in the past month. Concordance between biomarkers and self-reported alcohol use suggests that underreporting of alcohol use was minimal. Results highlight the need for alcohol screening within HIV care. Implications for alcohol assessment within research and clinical contexts are discussed.

Keywords Alcohol · Ethyl glucuronide · Blood Alcohol Content · HIV and HCV co-infection

The Russian Federation (Russia) previously had the highest level of per capita alcohol consumed globally [1]. The institution of national alcohol control measures in the early 2000s resulted in a decrease in all-cause mortality linked to alcohol and an overall decline in alcohol consumption

within Russia [2]. Despite these public health improvements, problematic alcohol use and alcohol use disorder continue to be prevalent among Russian individuals [3], particularly among Russian women living with Human Immunodeficiency Virus (HIV) [4, 5]. A meta-analysis estimated

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that 55% of Russians endorsed heavy episodic drinking in the past month and 58% met diagnostic criteria for alcohol use disorder [6]. Among Russian women, the World Health Organization estimates that 43.7% of female drinkers engage in heavy episodic alcohol use [4]. Problematic alcohol use and alcohol use disorder is also prevalent among people living with HIV (PLWH); a meta-analysis estimated the prevalence of alcohol use disorder among PLWH to be 29.8% [7].

Problematic alcohol use may lead to a variety of deleterious health consequences for PLWH, particularly for individuals with Hepatitis C Virus (HCV) co-infection. Long-term elevated alcohol use may result in neurocognitive impairment, diminished cerebral cortex functioning, and increased prevalence of HIV-associated dementia [8, 9]. In addition to health complications posed by alcohol directly, interactions between alcohol and antiretroviral (ARV) medications heighten the health risks posed to HIV-infected individuals who engage in problematic alcohol use, including hepatotoxicity and liver disease [10–12], which may be accelerated among those with co-morbid HCV [13]. Further, problematic alcohol use may negatively impact ARV adherence [14–16], in turn contributing to decreased viral suppression [17] and lower CD4+ cell counts [18, 19]. For example, in Russian samples, consumption of higher alcohol content drinks was associated with significantly lower CD4+ cell counts [19], higher HIV symptom burden [19], and higher HIV viral loads [20]. In addition to poor ARV adherence, drinking is also associated with poor medical treatment utilization [21–23], which may also accelerate disease progression. Given the potential adverse health consequences posed by alcohol to individuals with HIV and HCV co-infection, the accurate assessment of alcohol use within both clinical and research contexts is critical.

Research that informs alcohol prevention strategies and treatment outcomes involves a number of methodological challenges, including the need for accurate assessment of alcohol use [24]. The accuracy of self-reported alcohol use may be impacted by a variety of factors including the cognitive demands of recalling past behaviors and motivational biases that may result in underreporting of alcohol consumption [25–27]. For example, among a sample of Ugandan individuals with HIV, greater levels of social desirability (a form of motivational bias) were associated with lower self-reported levels of recent alcohol use [28]. Within the context of HIV care, there is also evidence to suggest that some PLWH may underreport alcohol or other substance use due to concerns about receipt of HIV treatment [29]. Despite limitations associated with self-reported alcohol use, its use is widespread within clinical and research contexts due to its convenience and low cost to administer.

Biomarkers of alcohol use including phosphatidylethanol (PEth), ethyl glucuronide (EtG), and blood alcohol content (BAC) via a breathalyzer provide objective markers of alcohol consumption over discrete time periods. Such biomarkers can also be used to assess the accuracy of self-reported alcohol use. PEth is a direct metabolite of alcohol measured by either whole blood or bloodspots with a detection window of up to four weeks among individuals consuming heavy amounts of alcohol that has increasingly been employed within alcohol research [30]. While PEth offers a longer alcohol detection window than EtG, collection of blood may not be feasible in some contexts and the laboratory processing expenses may be cost prohibitive. EtG is a urinary metabolite with an alcohol detection window between 24 and 72 h [31, 32]. The alcohol detection window in urine for EtG may be longer (e.g., up to 80 h; [33]) based on individual differences in alcohol metabolism, recency/quantity of use, and the detection threshold employed [34, 35]. Point-of-care (POC) EtG testing with urine specimens is available and requires fewer resources and is less costly to administer within clinical and research contexts [34]. As such, this study investigated POC EtG and BAC as objective markers of alcohol use.

There are only a handful of studies that have examined the concordance between EtG and self-reported alcohol use. For example, in a large population study of Dutch individuals, there was a positive agreement rate of 78.5% for those self-reporting alcohol use and EtG detection; EtG concentration levels were also linearly associated with higher self-reported alcohol consumption [31]. Among PLWH with Hepatitis B Virus co-infection in Zambia, a positive POC EtG result was highly concordant with self-reported alcohol use with a detection threshold of 500 ng/mL [36]. Similarly, Alcover and colleagues (2022) found that POC EtG with a detection threshold of 300 ng/mL was concordant with self-reported alcohol use among a sample of Ugandan PLWH, particularly for alcohol consumption that occurred in the past 24 h [34]. In contrast to studies demonstrating concordance between EtG and self-report, in a small pilot study of PLWH in South Africa, there was low concordance between EtG and alcohol use as assessed by the Alcohol Use Disorders Identification Test (AUDIT); such discrepancies may reflect differences in the timeframe measured by the AUDIT (i.e., past 12 months) relative to the detection window of EtG (i.e., ~72 h; [37]). While EtG has increasingly been used in research contexts, the use of breathalyzers to measure blood alcohol content (BAC) via expelled breath has been more commonly used in clinical settings [38]. However, there are a paucity of studies comparing BAC to EtG and self-reported alcohol use. Wetterling and colleagues (2014) compared BAC to self-reported alcohol relapse and EtG among an inpatient sample of German individuals with

alcohol use disorder. Results indicated significant discordance between BAC and EtG, with the greatest number of alcohol relapse events detected via EtG and not BAC or self-report [38].

Given the need for accurate assessment of alcohol use within both clinical and research contexts for individuals with HIV and HCV co-infection, we examined EtG and BAC as biomarkers of alcohol use along with self-reported alcohol use among a sample of Russian women with HIV and HCV co-infection engaged in HIV treatment. We report on the concordance of self-reported alcohol use relative to EtG and BAC and examined the level of agreement between EtG and BAC. Exploratory analyses were also conducted to examine whether demographic or health status variables were associated with differences in EtG and BAC results.

Methods

Participants

Participants were 200 Russian women living with HIV and HCV recruited from two comprehensive HIV care centers in Saint Petersburg, Russia to participate in a pilot clinical trial of a multi-component alcohol reduction intervention.

Procedures

Participants were women receiving ongoing medical care for HIV and HCV co-infection at the Leningrad Region ($n=42$) or Saint Petersburg ($n=158$) clinics, two comprehensive HIV care centers in Saint Petersburg, Russia. The Russian study coordinator, a medical doctor with specialization in infectious diseases, reviewed medical records to assess for potential eligibility. A clinician at each clinic invited potentially eligible patients to learn more about the study, assessed eligibility, and if interested and eligible, scheduled the baseline study visit. Eligibility criteria were: (a) laboratory confirmed HIV and HCV co-infection; (b) aged 21–45 years; (c) currently prescribed ARV medications; and (d) have recent alcohol use as indicated by either self-reported alcohol use in the past 30 days or a urine specimen positive for EtG. Women who were medically, cognitively, or psychologically incapable of study participation, as assessed by a research clinician were excluded. Data reported are from the baseline study visit, prior to randomization to study conditions; for additional information regarding the trial design, see [39]. At the baseline study visit, participants completed self-report questionnaires of demographics and alcohol use, provided a urine specimen to measure EtG, and were administered a breathalyzer to measure BAC. Patients' medical charts were also abstracted

for health status information. All study procedures were reviewed and approved by the Institutional Review Boards of New York University and Saint Petersburg University.

Measures

Demographic Characteristics

Demographic characteristics assessed included: (a) age; (b) current employment status (unemployed, employed); (c) current marital status (married, single, cohabiting with partner, divorced, widowed); and (d) partner's HIV serostatus (seronegative, seropositive, unknown or not reported).

Medical Chart Data

Participants' medical charts were abstracted for the following HIV and HCV health information: (a) primary HIV transmission route (injection drug use, sexual behavior, unknown); (b) history of HIV opportunistic infection(s) (no, yes); (c) most recent CD4+ cell count; (d) most recent HIV viral load status (undetectable, detectable); and (e) HCV viral load status (undetectable, detectable). CD4+ cell count, HIV viral load, and HCV viral load labs are obtained every three months clinically. Labs for CD4+ cell count and viral load were either: (a) drawn to coincide with the baseline research study visit; or (b) abstracted from clinical records, in which case labs were drawn no more than three months prior to the baseline research visit.

Ethyl Glucuronide (EtG)

EtG is an ethanol metabolite used to detect whether alcohol was consumed in the past 24 to 72 h [32]. In urine specimen POC testing, it is estimated to have sensitivity of 100% and a specificity of 97% [40]. Participants provided urine specimens that were analyzed for EtG via POC testing. The limit of detection was >500 ng/mL, a cut-off value associated with intentional alcohol consumption [31].

Blood Alcohol Content (BAC)

Blood alcohol content (BAC) was measured by breathalyzer. The breathalyzer is able to detect alcohol consumption that occurred up to 24 h previously. Participants blew for a sustained period of time into the plastic tube attached to the breathalyzer. The breathalyzer produced a BAC reading where a non-zero reading indicated a positive BAC result. The low detection threshold allows for an examination of recent alcohol consumption at lower levels relative to EtG.

Self-reported Alcohol Use

Participants self-reported on three alcohol measures used in clinical practice: (a) typical number of drinking days (less than 2 days per week vs. 2 or more days per week); (b) number of alcoholic drinks consumed in the past month; and (c) typical number of drinks consumed when drinking.

Data Analytic Approach

Statistical analyses were conducted using SPSS v. 28 [41]. Descriptive statistics were used to characterize participant demographic characteristics, EtG, BAC, self-reported alcohol use, and health information abstracted from participants’ medical charts. Kappa and phi coefficients were calculated to examine concordance between the dichotomous measures of EtG and BAC. A crosstab statistic was performed to examine patterns of positive/negative results for EtG and BAC. Point-biserial correlations between biomarkers (EtG, BAC) and continuous self-reported alcohol measures (number of drinks consumed in past 30 days, typical number of drinks consumed) were calculated. Phi coefficient was calculated to examine the association between the number of drinking days per week and biomarkers (EtG, BAC). To

explore whether there were any demographic or health status differences for positive EtG or BAC, t-tests and Chi-square statistics were performed.

Results

Participant Demographic and Health Status Characteristics

Table 1 presents demographic and HIV, HCV health characteristics for the full sample. Participants were Russian women between the ages of 22 and 45 years ($M=34.9$ years). The majority of women were currently employed (88.5%) and most were married (67.0%). Participants endorsed that their current or most recent partner’s HIV serostatus was negative (44.5%) or seropositive (22.0%), with approximately one third not reporting on partner’s serostatus (33.5%). Per participants’ medical charts, the primary HIV transmission route was via injection drug use (90.0%). Recent CD4 + cell counts ranged from 101.0 to 824.0 ($M=475.4$), with the majority with an undetectable HIV viral load (95.0%). Most women had a detectable HCV viral load (90.5%).

Table 1 Participant demographic and HIV, HCV health characteristics and exploratory analyses examining their association with EtG and BAC results* (N=200)

Characteristic	Full sample (N=200) n (%)	Negative EtG (n=72) n (%)	Positive EtG (n=128) n (%)	Test Stat.	<i>p</i>	Nega- tive BAC (n=47) n (%)	Positive BAC (n=153) n (%)	Test Stat.	<i>p</i>
Demographic Characteristic									
Age, M (SD)	34.9(3.8)	35.2(4.6)	34.7(3.3)	0.86	0.19	35.8(5.3)	34.6(3.2)	1.8	0.04
Currently employed	177(88.5)	63(87.5)	114(89.1)	0.11	0.45	41(87.2)	136(88.9)	0.09	0.76
Marital status				0.96	0.81			0.33	0.95
Married	134(67.0)	46(63.9)	88(68.8)			31(66.0)	103(67.3)		
Single	48(24.0)	18(25.0)	30(23.4)			12(25.5)	36(23.5)		
Divorced	15(7.5)	7(9.7)	8(6.3)			3(6.4)	12(7.8)		
Widowed	3(1.5)	1(1.4)	2(1.6)			1(2.1)	2(1.3)		
Partner’s serostatus				0.09	0.76			1.4	0.23
HIV seronegative	89(44.5)	30(41.7)	59(46.1)			18(38.3)	71(46.4)		
HIV seropositive	44(22.0)	16(22.2)	28(21.9)			13(27.7)	31(20.2)		
Not reported	67(33.5)	26(36.1)	41(32.0)			16(34.0)	51(33.3)		
HIV, HCV Health Characteristics									
HIV transmission route				14.7	<0.001			21.3	<0.001
Injection drug use	180(90.0)	57(79.2)	123(96.1)			34(72.3)	146(95.4)		
Sexual behavior	20(10.0)	15(20.8)	5(3.9)			13(27.7)	7(4.6)		
Past history of HIV opportunistic infection(s)	54(27.0)	24(33.3)	30(23.4)	2.3	0.13	25(53.2)	29(18.9)	21.4	<0.001
CD4 + cell count, M(SD)	475.4(118.5)	480.1(138.7)	472.8(106.1)	0.41	0.34	491.6(150.3)	470.5(107.0)	1.07	0.14
Detectable HIV viral load	10(5.0)	8(11.1)	2(1.6)	8.8	0.003	7(14.9)	3(1.9)	12.7	0.002
Detectable HCV viral load	181(90.5)	59(81.9)	122(95.3)	9.6	0.002	33(70.2)	148(96.7)	29.4	<0.001

*Note: EtG positivity corresponds to a value above the limit of detection of > 500 ng/mL. BAC positivity corresponds to a non-zero breathalyzer reading

Table 2 Crosstab for EtG and BAC positivity* (N=200)

		BAC		Total
		Negative BAC	Positive BAC	
EtG	Negative EtG	45	27	72
	Positive EtG	2	126	128
Total		47	153	200

*Note: EtG positivity corresponds to a value above the limit of detection of > 500 ng/mL. BAC positivity corresponds to a non-zero breathalyzer reading

Table 3 Correlations between EtG, BAC, and Self-Reported Alcohol Measures

	1.	2.	3.	4.	5.
1. EtG	1.00				
2. BAC	0.69**	1.00			
3. Number of drinking days per week	0.47**	0.65**	1.00		
4. Number of drinks in past 30 days	0.58**	0.70**	0.53**	1.00	
5. Typical number of drinks per day	0.25**	0.35**	0.31**	0.34**	1.00

Notes. **: $p < .001$. The following variables are dichotomous: (a) EtG (negative: <500 ng/mL, positive: >500ng/mL); (b) BAC (negative: zero reading, positive: non-zero reading); (c) Number of drinking days per week (less than 2 days per week, 2 or more days a week). The following variables are continuous: (a) Number of drinks in past 30 days; and (b) Typical number of drinks per day. Point-biserial correlations calculated for the association between dichotomous variable and continuous variable. Phi coefficient calculated for the association between two dichotomous variables

Concordance Between Biomarkers and Self-Reported Alcohol Use

The majority had positive EtG ($n = 128$; 64.0%) and BAC ($n = 153$; 76.5%) results. There was a high level of agreement between EtG and BAC ($\kappa = 0.66$, $p < .001$; Phi coefficient = 0.69, $p < .001$). Table 2 presents the crosstab statistic between EtG and BAC positivity. Among those with a positive EtG, 98.4% also had a positive BAC. Among those with a negative EtG, 37.5% had a positive BAC.

The majority of participants ($n = 163$, 81.5%) reported drinking at least two days a week. The median number of total alcoholic drinks consumed in the past 30 days was 200.00; a small minority reported consuming no alcoholic drinks in the past month ($n = 4$, 2.0%). The mean number of drinks consumed per day when drinking alcohol was 5.42 ($SD = 3.11$). Table 3 presents correlations between EtG, BAC, and self-reported alcohol measures. Self-reported alcohol use across all three measures was positively associated with both positive EtG and positive BAC (p 's < 0.001).

Each of the three self-reported alcohol measures was also positively correlated across measures (p 's < 0.001).

Exploratory Analyses: Demographic and Health Status Variables in Relation to EtG and BAC Results

Table 1 presents t-test and Chi-square statistics examining potential differences for demographic and HIV, HCV health characteristics on EtG and BAC results. EtG and BAC results did not differ by employment status, marital status, or partner's serostatus. There was no difference for EtG result by age. However, participants with a positive BAC were younger ($M = 34.6$ years) relative to those with a negative BAC result ($M = 35.8$ years). There were differences in EtG and BAC results by primary HIV transmission route, HIV viral load, and HCV viral load. Additionally, there were differences in BAC results by history of HIV associated opportunistic infections; however, EtG did not differ between those with/without a history of opportunistic infections. There were also no differences in either EtG or BAC results by CD4+ cell count.

Discussion

The accurate assessment of alcohol and integration of screening practices within HIV research and treatment contexts is the critical first step to identify individuals who may benefit from further assessment and/or alcohol reduction interventions [34, 42]. Among this sample of Russian women with HIV and HCV co-infection enrolling in an alcohol reduction trial, participants self-reported drinking frequently (typically at least two days a week) and at high quantities. The elevated frequency and quantity of drinking found in this sample aligns with other studies examining patterns of alcohol use found among PLWH in Russia [5, 43–45].

The majority of participants had a positive result for both EtG and BAC. Interestingly, there was a greater proportion with a positive BAC result relative to EtG. EtG is able to detect alcohol consumed over a longer time frame (i.e., 48 to 72 h) than BAC (approximately the last 24 h). The greater proportion of BAC positive results may be the result of drinking that occurred more proximally to the assessment, potentially at lower amounts that may not have been above the POC EtG detection threshold of 500 ng/mL but were detectable with a much lower detection threshold via breathalyzer (i.e., a non-zero breathalyzer reading). Differences in positivity for the biomarkers may also have been influenced by unmeasured factors. For example, the rate of ethanol elimination may vary across individuals and thus the length of detection of EtG may also vary [35]. Despite

differences in the positivity rates between EtG and BAC, there was still a high level of agreement between the two biomarkers. This result contrasts the findings of Wetterling and colleagues (2014) where there was significant discordance between EtG and BAC among an inpatient sample with alcohol use disorder [38].

There was concordance between self-reported alcohol and EtG, a finding aligned with past studies among global populations of PLWH [34, 36] and in one large national study [31]. While there is a limited number of studies comparing self-report to both EtG and BAC (e.g., [38]), results also suggest concordance across three different self-report alcohol assessments, EtG, and BAC. Concordance between EtG, BAC, and self-report suggests that there may be minimal underreporting of alcohol use in this sample. This may be due in part to sample characteristics as participants were individuals enrolled in an alcohol reduction trial. As such, there may have been decreased perceived need to respond in a socially desirable fashion. Additionally, any discrepancies observed may be due in part to differences in the timeframes used for self-report assessments and the detection windows for the two biomarkers. For example, the self-report alcohol measures employed in this study were those commonly used in clinical practice and assessed the past 30 days of alcohol use along with relative quantity and frequency measures.

While analyses examining differences in alcohol biomarker positivity were exploratory in nature, there were differences in EtG and BAC positivity based on age along with HIV and HCV health markers. For example, there was a greater proportion of those with a primary HIV transmission risk factor of injection drug use who were positive for both EtG and BAC. Findings have been mixed across past studies regarding whether there is greater discordance between self-report and alcohol biomarkers based on either demographic characteristics or other health status variables [34, 45]. Given the exploratory nature of these analyses coupled with mixed findings in the literature, additional research is needed to further examine the extent to which participant characteristics or biological factors may affect biomarkers of alcohol use, the validity of self-reported alcohol use, and the concordance across measurement types.

Strengths and Limitations

A strength of this study was inclusion of multiple biomarkers of alcohol use (EtG, BAC) that can be more feasibly administered in both clinical and research contexts. Additionally, our study is the first to report on a sample all of whom had HIV and HCV co-infection, where the metabolism of alcohol may be affected by factors such as liver damage/disease or interactions with antiretroviral medications [10–12]. A limitation of our study was the lack of concordance across

time periods between the detection windows for EtG, BAC, and self-reported alcohol use. Additionally, the detection thresholds for EtG and BAC differed, with EtG having a much higher detection threshold (i.e., > 500 ng/mL) relative to BAC (i.e., non-zero breathalyzer reading). Further, self-reported alcohol use was collected via measures commonly used within the Russian HIV clinical context and thus may not generalize to other self-reported measures of alcohol use. We also did not collect data that may point to individual variations in EtG or BAC. For example, we did not assess alcoholic drink type and corresponding ethanol content level or factors linked to alcohol metabolism (e.g., weight). Since participants were Russian women with HCV co-infection enrolling in an alcohol reduction trial within an HIV clinical treatment setting, results may not generalize to the broader HIV clinical population served at the clinic.

Conclusions

Clinicians and researchers may need to consider strengths and limitations of alcohol assessment modalities when measuring alcohol use. For example, the detection windows for alcohol biomarkers combined with feasibility of their administration (e.g., cost, laboratory resources required, etc.) may be important considerations. Further, the sensitivity and specificity of the biomarker test would be important. Indeed, EtG and BAC are markers of *recent* alcohol consumption and may be a less desirable assessment approach if one's primary interest is in chronic alcohol use and/or identifying individuals engaging in problematic alcohol use or those who may meet criteria for alcohol use disorder. Additionally, when considering use of self-report, strategies to bolster the accuracy of self-reported assessments should be considered. For example, self-report assessment modalities that afford greater confidentiality such as computerized assessments and reduce motivational biases to present in a socially desirable way should be considered [46]. Further, strategies that decrease the likelihood of recall errors such as alcohol timeline followback assessments should be considered. As feasible, multimodal alcohol assessment may be advisable, particularly for individuals with HIV and HCV co-infection where the impact of alcohol use may be more deleterious.

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Declarations

Conflict of Interest None of the authors has any conflict of interest regarding this manuscript.

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