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Alcohol use and abuse among patients with multidrug-resistant tuberculosis in Botswana

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SUMMARY

BACKGROUND—Data on alcohol abuse as a risk factor for the development of multidrug-resistant tuberculosis (MDR-TB) are scarce.

OBJECTIVE—To describe the patterns of alcohol use in MDR-TB patients and to determine whether alcohol use is associated with the development of MDR-TB in Botswana.

METHODS—We compared the level of alcohol use among MDR-TB patients against three control groups: 1) non-MDR-TB patients, 2) human immunodeficiency virus (HIV) infected patients without a history of TB, and 3) the general population. Alcohol use and abuse was measured with the Alcohol Use Disorders Identification Test 10 (AUDIT) questionnaire.

RESULTS—Of a total national population of 164 MDR-TB cases, 114 (70%) were interviewed. MDR-TB cases had a lifetime prevalence of alcohol use of 35.1%, which was lower than that of all control groups ($P < 0.001$). MDR-TB cases had higher 1-month prevalence of alcohol dependence symptoms and a lower 1-year period prevalence of alcohol dependence symptoms ($P < 0.01$ and $P = 0.01$ respectively). Among patients with TB, alcohol abuse was found to be a risk factor for the development of MDR-TB.

CONCLUSION—MDR-TB patients in Botswana have high rates of alcohol use and abuse. Among TB patients, alcohol abuse is associated with the diagnosis of MDR-TB, and could be an important modifiable factor.

Keywords

tuberculosis; multidrug resistance; alcohol; case control

Multidrug-Resistant tuberculosis (MDR-TB) rates had been historically low in Botswana. However, national surveys have revealed a progressive rise in the prevalence of MDR-TB,

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which, as of 2002, accounted for over 10% of the TB cases requiring retreatment.[1] While data suggest that patients with TB have excellent response to treatment in Africa, the data with regard to MDR-TB in Africa are less encouraging. Studies from South Africa have shown that patients with MDR-TB in general have extremely poor outcomes.[2] Understanding the factors leading to the development of MDR-TB is therefore critical.

Although the clearest risk factors for the development of MDR-TB are a history of previous antituberculosis treatment and human immunodeficiency virus (HIV) infection, other, potentially modifiable factors have not received enough attention.[3,4] Alcohol abuse is widespread in sub-Saharan Africa, the epicenter of the TB, MDR-TB and HIV pandemics, and has been associated with medical non-adherence, poor health status and overall worse clinical outcomes.[5–8] It has been reported that patients diagnosed with TB have higher alcohol intake than persons without TB.[9–12] Moreover, HIV-infected patients have higher alcohol consumption than non-HIV-infected patients, and patients co-infected with TB and HIV have higher alcohol consumption than either TB or HIV-infected patients.[6,8,13] Although these mechanisms strongly support the role of alcohol use as an important modifiable risk factor for the development of TB, data regarding its relative role in the development of MDR-TB are lacking.[3]

The objective of this study was to describe the patterns of alcohol use among MDR-TB patients and to determine whether alcohol use is associated with the development of MDR-TB in Botswana.

RESEARCH DESIGN AND METHODS

Design

Case-control study—Cases were patients with a microbiological diagnosis of pulmonary MDR-TB. To better control for potential, not measurable, confounders, three different control groups were selected: 1) control group A, patients with microbiologically confirmed non-MDR pulmonary TB; 2) control group B, HIV-infected patients without a history of current or prior pulmonary TB; and 3) control group C, participants from the general population without prior history of TB. To control for the confounding effect of HIV infection, only HIV-infected cases were compared with HIV-infected controls without a history of TB.

Identification of the cases—We used registries of the five referral MDR-TB clinics in Botswana to identify all MDR-TB cases who were actively in care during the study period. All cases aged >21 years were invited to participate in the study.

Selection of controls—Non-MDR-TB and HIV-infected controls were selected on a 1:1 ratio. Controls from the general population were selected on a 1:2 ratio. All controls were recruited from the same population-base as the MDR-TB cases and matched by geographic area. Non-MDR-TB controls were enrolled from the TB clinic closest to the clinic where the MDR-TB case was receiving care. HIV-infected patients without a diagnosis of TB were identified at the nearest HIV clinic. Participants from the general population were selected from the areas surrounding the area of residence of the MDR-TB case. All controls lived in the same geographic area (sub-district) as the MDR-TB case.

Measures

Domains of inquiry for our surveys were based on previously validated instruments,[14] and included demographic characteristics, use of alcohol, HIV risk behaviors and history of HIV testing. To measure alcohol consumption, we used the Alcohol Use Disorders Identification

Test (AUDIT) 10 questionnaire.[15–18] The AUDIT's 10 items cover the three conceptual domains of consumption, dependence symptoms and alcohol-related consequences that are intended to parallel the World Health Organization concepts of hazardous drinking, alcohol dependence and alcoholrelated harm. We used a cut-off score of ≥8 to define heavy drinking.[15–18] Hazardous drinking was defined as a quantity or pattern of alcohol consumption that places patients at risk for adverse health events, while harmful drinking is defined as alcohol consumption that results in adverse events (e.g., physical or psychological harm). As the AUDIT 10 is a measure of the prevalence of alcohol use, we aimed to determine the point and period prevalence of alcohol use in an attempt to identify potential changes in alcohol consumption over time. Participants were asked to identify their alcohol consumption over two time periods: 1) current/recent history of alcohol consumption, defined as alcohol consumption over the month prior to the interview; and 2) chronic history of alcohol consumption, defined as alcohol use over the year prior to the time of interview. In addition, we used different definitions for frequency, to provide a more precise description of the drinking patterns. 'Any alcohol use' was defined as any quantity of alcohol use over a given period, and 'regular alcohol use' was defined as any quantity of alcohol consumed ≥3 days per week.

Statistical analysis

Pearson's χ^2 tests were used to compare dichotomous exposure variables and rank sum tests for continuous exposure variables between cases and controls. To determine correlates of MDR-TB, we used conditional multivariate logistic regression with MDR-TB case status. Independent models were built to compare the cases against each of the control groups. Specific variables controlled for in our analyses were selected based on prior literature and theory, which included 1) age (continuous by year), 2) sex (male or female), 3) income (<1000 or ≥1000 pula/month, minimum wage*), 4) education (≤ primary vs. ≥ high school education), 5) marital status (single, married, living with stable partner, or other), and 6) food security (possibility of having ≥3 meals per day vs. <3 meals per day), and 7) frequency of visits to a medical provider (<1, 2 or ≥3 visits/year).

This study was approved by the Institutional Review Boards of the Government of Botswana and the University of Pennsylvania.

RESULTS

Demographics and characteristics of MDR-TB cases and controls

Of a total of 164 MDR-TB cases, 114 (70%) were interviewed between 1 May 2010 and 30 April 2011. Of the remaining 50 MDR-TB patients actively enrolled in care in Botswana, 16 (9.8%) refused to participate in the study and 34 (20.2%) were not located. The demographics of the MDR-TB patients who were not included in the study were obtained from their records. We found no differences in terms of age distribution, sex or HIV status between patients who participated in the study and those who did not (data not shown).

MDR-TB cases were primarily male Setswanaspeaking, with high-school level education or higher and employed (69.3%), with a monthly income above the minimum wage (69.3%). HIV status was available from all cases, and was positive in 50% (Table 1). Of 114 MDR-TB cases, 40 (35.1%) reported any alcohol use in the past and 27 (67.5%) reported regular alcohol use at some point in the past (23.7% of the total MDR-TB cases). Nevertheless, the majority of cases reported that their alcohol use was in the distant past, most reporting their last drink >1 year prior to the interview (Tables 2 and 3). Chronic (1 year prior) and recent

*7 pula = US$1.

(1 month prior) period prevalence of a lcohol consumption was similar within cases (AUDIT score 7.8 ± standard deviation [SD] 5.9 vs. 8.7 ± SD 6.7, $P = 0.52$, Table 4). The mean time on MDR-TB treatment was similar among patients with a history of chronic alcohol use (8.3 months ± SD 4.2) and among those with a history of recent alcohol use (7.4 months ± SD 5.6) compared to patients without such history (7.8 months ± SD 3.9, $P > 0.5$ and 8.5 months ± SD 3.3, $P > 0.05$, respectively). The mean time on MDR-TB treatment was similar among patients with a history of alcohol use who did not stop drinking after initiation of treatment (9.0 months ± SD 5.1) vs. those who stopped drinking during treatment (8.1 months ± SD 4.8, $P > 0.05$).

Case-control study using non-MDR-TB patient controls

Compared to non-MDR-TB controls, cases had a lower lifetime prevalence of any alcohol use (35.1% vs. 81.6%, $P < 0.001$). However, MDR-TB cases had a higher 1-month prevalence of dependence symptoms ($P < 0.01$). When the analysis was restricted to TB patients with a history of alcohol use, MDR-TB cases had a higher lifetime prevalence of regular use of alcohol (67.5% vs. 32.3%, $P < 0.001$, Table 3). After adjustment, alcohol use was significantly associated with the diagnosis of MDR-TB when compared with non-MDR-TB (Table 5).

Case-control study using HIV-infected non-TB controls and general population controls

MDR-TB cases with HIV had a lower prevalence of any alcohol use than HIV-infected controls, and MDR-TB cases had a lower lifetime prevalence of any alcohol use than controls from the general population (35.1% vs. 97.3% and 68.9 respectively, $P < 0.001$). Among persons acknowledging a history of alcohol use, MDR-TB cases had a higher lifetime prevalence of regular use of alcohol than HIV-infected controls, but not when compared against the general population (respectively 67.5% vs. 46.0%, $P = 0.01$ and 67.5% vs. 68.2%, $P = 0.93$, Table 3). Overall AUDIT scores did not differ between HIV-infected MDR-TB cases and controls from these two groups. However, on further analysis of the different domains of alcohol consumption, MDR-TB cases were found to have significantly higher scores of harmful use of alcohol over the previous year ($P = 0.03$) than HIV-infected controls.

DISCUSSION

We found that MDR-TB subjects have an overall lower lifetime prevalence of any alcohol use than the three control groups included in our study, but only slightly lower prevalence of regular alcohol use. Most patients who reported alcohol use in the past were not currently using it and had stopped over the 6–12 months prior to the interview. MDR-TB patients currently using alcohol had higher AUDIT scores over the previous year than those who were able to stop drinking, suggesting that patients who were not able to stop drinking after appropriate counselling had a more serious alcohol abuse problem before the development of active MDR-TB. In this group, alcohol was found to be a risk factor for the development of MDR-TB when compared to other, non-MDR-TB patients.

To increase the strength of our results, we used three different control groups, each destined to control for unmeasured confounders intrinsic to each group. For example, by comparing HIV-infected MDR-TB patients with HIV-infected non-TB controls, the effect of HIV and all its associated unmeasured confounders is eliminated or significantly reduced. The sampling of three control groups thus provides a unique opportunity to understand alcohol use among MDR-TB patients, and significantly increases our confidence in the results. It is interesting that most of our positive results came from a comparison of MDR-TB cases and non-MDR-TB controls. MDR-TB can be due to a primary infection with a resistant strain or

secondary to the development of resistance of a susceptible strain during treatment. Assuming that new transmission/acquisition of susceptible and MDR-TB strains occurs at similar rates, our findings suggest that the development of MDR-TB in patients who have a significant and chronic alcohol abuse problem is primarily due to the acquisition of resistance during treatment, likely due to lack of adherence or drug interactions. While the impact of infection control measures aimed to reduce the transmission/acquisition of MDR-TB is widely accepted, our results highlight the importance of the concomitant implementation of prevention programs targeting alcohol consumption, as they may also have an impact on the MDR-TB epidemic.

Overall, we found a prevalence of heavy drinking of 20% among MDR-TB cases. This prevalence was not different from that of the control groups, and is higher than reports from other industrialized and developing countries.[7,9,11,12,17,19] As alcohol has been associated with worse health outcomes in several conditions, the high prevalence of alcohol abuse in MDR-TB cases, and in Botswana as a whole, suggests that interventions to reduce alcohol consumption could also have an important impact on other public health outcomes, in addition to TB.[5,6,13,19–21]

Our results need to be interpreted in the context of their limitations. First, the case-control design makes the determination of any temporal relationship between the development of MDR-TB and the factors found to be associated with such diagnosis impossible. Although we aimed to include the entire population of MDR-TB cases enrolled in care in Botswana, 30% were either not reachable or refused to participate in the study. Although the demographic characteristics of our sample suggest that it represents the base population, we cannot rule out the presence of a selection bias. Furthermore, the MDR-TB cases enrolled in care may represent only a fraction of all MDR-TB cases in Botswana, as it is estimated that approximately 30–40% of MDR-TB patients in Botswana never receive care.[22,23] Whether our results are generalizable to that population is unknown. In addition, our results are based on the self-report provided by cases and controls, which could have introduced recall bias. It is thus possible that our results under-report the true levels of alcohol consumption in certain groups, particularly among cases with MDR-TB, as they receive frequent and intense counselling regarding the potential negative influence of alcohol use on their treatment.

Given the significant length of MDR-TB treatment, the mean and median length of treatment among these patients (around 7–9 months, depending on the subgroup) was significantly longer than that of non-MDR-TB patients, making a comparison by this factor between these two groups unfeasible (which had a mean and median length of treatment of 2–4 months). The analysis regarding the effect of the length of treatment over alcohol use was therefore restricted to the cases. It is possible that the unexpectedly low rates of alcohol used among MDR-TB cases found in our study may have been due to the increased morbidity and mortality associated with MDR-TB, which could be even higher among patients who abuse alcohol. If such bias was significant, only MDR-TB patients who survived long enough and were fit enough to engage in care were included as cases.

Time spent on anti-tuberculosis treatment may be an important determinant of alcohol use. We found no differences in terms of the mean and median times of treatment among MDR-TB cases who had never used alcohol, those who used alcohol and stopped and those who continued using alcohol during treatment. However, due to the significant differences in the treatment length for MDR-TB and susceptible TB, it was impossible to account for this variable when comparing the two groups. Finally, given the design of our study, it is impossible to determine any trends in the patterns of alcohol use. Although we attempted to minimize this limitation by asking about recent and distant alcohol use, no strong conclusions regarding trends in alcohol use could be drawn from our study. Although a

significant proportion of MDR-TB cases stopped drinking around the time of diagnosis, we cannot tell whether they went back to drinking after the disease—or symptoms from the disease —was under better control.

CONCLUSION

Alcohol abuse is prevalent among MDR-TB patients in Botswana and could be an important modifiable factor affecting health outcomes in this population. Alcohol abuse is associated with the diagnosis of MDR-TB among people with TB. Further studies of different design are needed to establish the causality and strength of this association. Longitudinal studies are also needed to determine trends in the patterns of alcohol use to improve our understanding of the role of alcohol on the development of MDR-TB.

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Table 1

Characteristics of the MDR-TB cases and three control groups in Botswana

	MDR-TB (*n* = 114) *n* (%)	TB (*n* = 114) *n* (%)	HIV (*n* = 114) *n* (%)	General population (*n* = 228) *n* (%)
Age, years				
21–29	40 (35.1)	33 (28.9)	14 (12.3)	149 (65.4)
30–39	27 (23.7)	36 (31.6)	49 (43.0)	53 (23.2)
40–49	24 (21.1)	30 (26.3)	37 (32.5)	18 (7.9)
≥50	23 (20.2)	15 (13.2)	14 (12.3)	8 (3.5)
Sex				
Male	69 (60.5)	47 (41.2)	36 (31.6)	45 (19.7)
Female	45 (39.5)	67 (58.8)	78 (68.4)	183 (80.3)
Education				
No schooling	28 (24.6)	13 (11.4)	11 (9.6)	1 (0.4)
Primary education	23 (20.2)	25 (21.9)	31 (27.2)	12 (5.3)
Secondary education	49 (43.0)	64 (56.1)	60 (52.6)	103 (45.2)
Higher education	11 (9.6)	9 (7.9)	11 (9.6)	111 (48.7)
Other	3 (2.6)	3 (2.6)	1 (0.9)	1 (0.4)
Marital status				
Single (not cohabiting)	57 (50.0)	65 (57.0)	40 (35.1)	154 (67.5)
Single (cohabiting)	37 (32.5)	30 (26.3)	43 (37.7)	37 (16.2)
Married	18 (15.8)	14 (12.3)	29 (25.4)	35 (15.4)
Divorced/widowed	2 (1.8)	5 (4.4)	2 (1.8)	2 (0.9)
Employment				
Unemployed	35 (30.7)	47 (41.2)	72 (63.2)	114 (50.0)
Employed	79 (69.3)	67 (58.8)	42 (36.8)	114 (50.0)
Monthly income				
< minimum wage	35 (30.7)	56 (49.1)	77 (67.5)	125 (54.8)
> minimum wage	79 (69.3)	58 (50.9)	37 (32.5)	103 (45.2)
Government assistance				
No	88 (77.2)	99 (86.8)	113 (99.1)	—
Yes	26 (22.8)	15 (13.2)	1 (0.9)	—
Number of meals per day				
Three	79 (69.3)	75 (65.8)	79 (69.3)	—
Two	19 (16.7)	23 (20.2)	27 (23.7)	—
One	7 (6.1)	8 (7.0)	7 (6.1)	—
Varies depending on income	9 (7.9)	8 (7.0)	1 (0.9)	—
Monthly frequency at which subject is unable to obtain food				
Every day	18 (15.8)	29 (25.4)	8 (7.0)	—
Very frequently (once a week)	12 (10.5)	11 (9.6)	30 (26.3)	—
Some times (once a month)	60 (52.6)	40 (35.1)	38 (33.3)	—
Almost never	7 (6.1)	6 (5.3)	16 (14.0)	—

	MDR-TB (*n* = 114) *n* (%)	TB (*n* = 114) *n* (%)	HIV (*n* = 114) *n* (%)	General population (*n* = 228) *n* (%)
Never	17 (14.9)	28 (24.6)	22 (19.3)	—
HIV-positive	57 (50.0)	55 (48.2)	—	—

MDR-TB = multidrug-resistant TB; TB = tuberculosis; HIV = human immunodeficiency virus.

Table 2

Self-report of lifetime prevalence of alcohol use and regular alcohol use among MDR-TB cases and three control groups in Botswana

	MDR-TB (*n* = 114) *n* (%)	TB (*n* = 114) *n* (%)	HIV (*n* = 114) *n* (%)	General population (*n* = 228) *n* (%)
Any alcohol use (lifetime use)	40 (35.1)	93 (81.6)	111 (97.4)	157 (68.9)
Current any use (previous month)	3 (2.6)	14 (12.3)	44 (38.6)	130 (57.0)
Any regular alcohol use (lifetime use)	27 (23.7)	30 (26.3)	51 (44.7)	107 (46.9)
Current regular use (previous month)	3 (2.6)	6 (5.3)	21 (18.4)	91 (39.9)

MDR-TB = multidrug-resistant TB; TB = tuberculosis; HIV = human immunodeficiency virus.

Table 3

Self-report of lifetime prevalence of alcohol use and regular alcohol use among MDR-TB cases and participants from three control groups who acknowledge any prior alcohol use in Botswana

	MDR-TB *n* (%)	TB *n* (%)	*P* value	HIV *n* (%)	*P* value	General population *n* (%)	*P* value
Have you ever used alcohol?	114	114		114		228	
Yes	40 (35.1)	93 (81.6)	<0.001	111 (97.3)	<0.001	157 (68.9)	<0.001
No	74 (64.9)	21 (18.4)		3 (2.7)		71 (31.1)	
If you drank alcohol in the past, when was the last time you drank alcohol?	40	93		111		157	
Within the last week	1 (2.5)	2 (2.2)	0.45	23 (20.7)	<0.01	45 (28.6)	<0.001
Within the last month	2 (5)	12 (13.0)		21 (18.9)		85 (54.1)	
Within the last 3 months	3 (7.5)	8 (8.6)		11 (9.9)		17 (10.8)	
Within the last 6 months	6 (15.0)	15 (16.1)		7 (6.3)		7 (4.5)	
Within the last year	12 (30.0)	34 (36.6)		20 (18.0)		2 (1.3)	
Within the last 2 years	16 (40.0)	22 (23.7)		29 (26.1)		1 (0.6)	
Have you ever used alcohol regularly?	40	93		111		157	
Yes	27 (67.5)	30 (32.3)	<0.001	51 (46.0)	0.01	107 (68.2)	0.93
No	13 (32.5)	63 (67.7)		60 (54.0)		50 (31.8)	
If you drank alcohol regularly in the past, when was the last time you drank alcohol regularly?	27	30		51		107	
Within the last week	1 (4.0)	2 (6.7)	0.11	11 (21.6)	0.12	31 (29.0)	<0.001
Within the last month	2 (8.0)	4 (13.4)		10 (19.6)		50 (46.7)	
Within the last 3 months	0	1 (3.3)		2 (3.9)		19 (17.8)	
Within the last 6 months	1 (4.0)	7 (23.3)		2 (3.9)		5 (4.7)	
Within the last year	10 (37.0)	10 (33.3)		11 (21.6)		1 (1.0)	
Within the last 2 years	13 (52.0)	6 (20.0)		15 (29.4)		1 (1.0)	

MDR-TB = multidrug-resistant TB; TB = tuberculosis; HIV = human immunodeficiency virus.

Table 4

AUDIT 10 scores of MDR-TB cases and three control groups and their breakout by the three conceptual domains of consumption, dependence symptoms and alcohol-related consequences over two different time periods in Botswana

	MDR-TB mean ± SD	TB mean ± SD	*P* value	HIV mean ± SD	*P* value	General population mean ± SD	*P* value
Hazardous alcohol use	3.0 ± 2.3	3.5 ± 2.1	0.22	3.8 ± 2.1	0.04	3.7 ± 2.0	0.06
Dependence symptoms							
Over last year	1.4 ± 2.4	0.5 ± 1.3	<0.01	1.0 ± 1.9	0.29	0.8 ± 1.7	0.07
Over last month	0.8 ± 1.7	1.9 ± 2.5	0.01	0.9 ± 1.9	0.77	1.4 ± 2.2	0.11
Harmful alcohol use							
Over last year	3.6 ± 3.9	3.5 ± 3.2	0.88	2.4 ± 2.6	0.03	2.9 ± 3.3	0.11
Over last month	2.9 ± 3.4	2.6 ± 2.9	0.61	2.1 ± 2.3	0.10	2.7 ± 3.0	0.72
Overall AUDIT score over last year	7.8 ± 5.9	10.4 ± 6.0	0.02	8.4 ± 5.0	0.54	9.8 ± 6.4	0.07
Overall AUDIT score over last month	8.7 ± 6.7	8.6 ± 5.6	0.50	8.5 ± 5.8	0.52	9.5 ± 6.0	0.13

AUDIT = Alcohol Use Disorders Identification Test; MDR-TB = multidrug-resistant TB; TB = tuberculosis; HIV = human immunodeficiency virus; SD = standard deviation.

Table 5

Multivariate analyses of factors associated with the diagnosis of multidrug-resistant tuberculosis in Botswana

	vs. TB			vs. HIV			vs. General population		
	aOR	**95%CI**	***P* value**	**aOR**	**95%CI**	***P* value**	**aOR**	**95%CI**	***P* value**
AUDIT risk category									
0	1.00			1.00			1.00		
1–7	3.66	1.11–12.07	0.03	0.80	0.26–2.45	0.69	1.01	0.38–2.72	0.97
8–14	1.19	0.20–7.07	0.84	0.70	0.18–2.61	0.58	0.57	0.23–1.46	0.24
≥15	4.27	1.09–21.48	0.05	0.57	0.12–3.65	0.62	0.86	0.03–20.54	0.92
Age	0.95	0.90–1.00	0.06	0.91	0.92–0.97	<0.01	1.00	0.99–1.01	0.14
Male sex	1.26	0.41–3.89	0.69	5.48	1.96–15.26	<0.001	2.13	1.2–3.78	<0.01
Education: ≥ high school	0.43	0.14–1.30	0.13	0.55	0.19–1.59	0.27	0.10	0.05–0.21	<0.001
Marital status: living with a partner	5.08	1.55–16.60	<0.01	0.65	0.24–1.74	0.27	1.32	0.75–2.35	0.33
Meals/day: ≥2	0.36	0.13–0.97	0.04	0.91	0.38–2.17	0.83	1.22	0.67–2.21	0.51
HIV-positive	3.48	1.11–10.92	0.03	NA	—	—	NA	—	—

TB = tuberculosis; HIV = human immunodeficiency virus; aOR = adjusted odds ratio; CI = confidence interval; AUDIT = Alcohol Use Disorders Identification Test; NA = not applicable.