

The Effect of Alcohol Use on the Clinical Presentation of Tuberculosis

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Abstract

Objective: We examined whether patients with alcohol use who become ill with tuberculosis are more likely to develop cavitary disease than patients without a history of alcohol use.

Methods: Chi-square tests were used to test for differences in the distribution of alcohol users between cavitary patients and non-cavitary patients. Logistic regression was performed to obtain adjusted odds ratios (OR) and 95% confidence intervals (CI). An interaction between homelessness and alcohol use was also tested.

Results: In the crude model, alcohol use was risk factor for cavitary disease (OR 1.29, (95% CI: 1.13-1.47)). In the adjusted model, alcohol use continued to be a significant predictor of the outcome (OR 1.29, (95% CI: 1.13-1.47)).

Conclusion: Our results showed that alcohol use was a risk factor for cavitary TB. In addition, we found significant associations with age, race, HIV status, homelessness, and corrections history. Our results indicate the need for intervention in this particularly vulnerable population.

Keywords: Tuberculosis; Pulmonary disease; Clinical presentation; Cavitation; Substance abuse; Alcohol

Background

Globally, Tuberculosis (TB) remains one of the most common infectious diseases, and continues to present public health challenges. One issue which has not been addressed is whether or not alcohol use causes more advanced TB disease. Alcohol use has, in the past, been associated with the acquisition and transmission of TB infection [1]. Among patients who drink more than 40 g alcohol per day, and/or have an alcohol use disorder, the risk of active TB is significantly increased [2,3]. Suggested causes for this include specific social mixing patterns associated with alcohol and the immune-modulatory effect of alcohol on the immune system [3].

There also not been much discussion in the literature concerning what constitutes more clinically advanced TB disease. The most commonly cited factors, however, are presenting with cavitation on a chest radiograph and showing a positive sputum-smear result, which have been shown to be associated with delayed treatment, increased transmission, and increased risk of treatment failure [4].

If alcohol users are more likely to present with more clinically advanced disease, identifying and treating them more aggressively may be warranted. Therefore, the aim of this study was to describe the clinical presentation among alcohol users with TB. We hypothesized that there will be a significantly higher proportion of alcohol users among culture positive TB patients. We also hypothesized that cavitation on chest radiograph, as a surrogate for advanced disease, would be significantly associated with the proportion of alcohol use among TB patients. Lastly, we assessed the potential interaction between homelessness and alcohol use.

Methods

We conducted a retrospective analysis with de-identified clinical and demographic data obtained from contact investigations conducted by the state of Florida from January 1, 2000 to December 31, 2008. The primary goal of the investigation was to determine if patients with alcohol use history were more likely to acquire cavitary TB.

This study was reviewed and approved by Institutional Review Boards from both the University of Florida and from the Florida Department of Health (FDOH) in the Bureau of Tuberculosis and Refugee Health.

Subjects were divided into two groups: patients with cavitation on chest radiograph and those without. The alcohol variable was categorized into two levels: alcohol user or non-user.

Demographic measures included age, ethnicity and gender (male/female). Age was initially measured as a continuous variable with a normal distribution. We later decided to categorize age into four groups: age ≤ 20 , $21 < \text{age} \leq 45$, $46 \leq \text{age} \leq 65$, and age above 65. Ethnicity was categorized into White, Black, Hispanic, and Other (which included Asians, Pacific Islander, American Indian, Alaskan Native and unknown).

Health-related measures included HIV status (positive/negative/indeterminate/refused/not offered/unknown), culture status (positive/negative) and previous TB history (yes/no). Other measures included whether or not the person had been homeless in the past year (yes/no), whether or not they had been incarcerated in the past year (yes/no), and whether or not they were foreign-born (yes/no).

Statistical analysis

We used a logistic regression model with 95% confidence intervals to obtain crude and adjusted odds ratios. The multivariate

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analysis included any variables from the univariate analyses that were significant at $P < 0.20$. The final model included any variables which remained significant at $P < 0.05$ after model selection. We also assessed the potential interaction between homelessness and drug abuse.

Results

A total of 6900 cases were assessed in this study, ranging from January 1, 2000 to December 31, 2008 (45.1 ± 17.1 years (range: 1-103 years); 2197 with cavitary disease: 31.84%; 4698 males: 68.09%; 2202 females: 31.91%. All cases were sputum and culture confirmed. The remaining socio-demographic and clinical risk factors for cases are listed in table 1.

In the univariate analysis, several covariates increased the risk of developing cavitation on chest radiograph including alcohol use (Odds Ratio (OR) 1.46, (95% Confidence Interval (95% CI): 1.30-1.63)), being sputum culture positive (OR, 4.12 (95% CI: 3.52-4.81)) and age (Age 21-45 OR 1.33, (95% CI: 1.07-1.66)); (Age 46-65 OR 1.29, (95% CI: 1.03-1.62)). Several factors also decreased this risk, including being HIV positive (OR 0.23, (95% CI: 0.20-0.28)), refusing an HIV test (OR 0.58, (95% CI: 0.48-0.70)), not being offered an HIV test (OR 0.46, (95% CI: 0.32-0.64)), being foreign born (OR 0.87, (95% CI: 0.79-0.97)), recent corrections history (OR 0.67, (95% CI: 0.53-0.86)), being African American (OR 0.76, (95% CI: 0.67-0.86)), and being a member of the "other" race category (OR 0.59, (95% CI: 0.47-0.74)).

After employing several model selection procedures we developed a final multivariate model (significant at $p < 0.0001$) (Table 1). As part of this model, we tested an interaction between recent history of homelessness and alcohol use and found it to be not significant ($p = 0.2462$). Therefore, it was not included in the final model. Although gender was not significant in the univariate model it was retained in the final model for reasons of epidemiological and biological significance.

In this adjusted model, several covariates continued to increase the risk of developing cavitary TB including age (Age 21-45 OR 1.31, (95% CI: 1.04-1.66)), being an alcohol user (OR 1.29, (95% CI: 1.13-1.47)) and being sputum culture positive (OR 4.12, (95% CI: 3.51-4.83)). Being a member of the "other" race category (OR 0.64, (95% CI: 0.51-0.81)), having a previous case of TB (OR 0.77, (95% CI: 0.61-0.98)), having a recent corrections history (OR 0.53, (95% CI: 0.41-0.68)), being HIV positive (OR 0.20, (95% CI: 0.17-0.24)), refusing an HIV test (OR 0.71, (95% CI: 0.58-0.87)), and not being offered an HIV test (OR 0.52, (95% CI: 0.37-0.75)) continued to decrease the risk of cavitation on chest radiograph, after adjusting for all other factors in the model. Homelessness was borderline significant in this model as well (OR 0.82, (95% CI: 0.68-1)).

Discussion

In this study, we found that alcohol use was a good predictor for developing cavitation on chest radiograph for those with active

Characteristics		Cavitary (N=2197)	Non-cavitary (N=4703)	Crude Odds Ratio 95% Confidence Interval	Adjusted Odds Ratio 95% Confidence Interval
Alcohol					
	Non-user	1514(68.91)	3590(76.33)	1.0 (referent)	1.0 (referent)
	User	683(31.09)	1113(23.67)	1.46(1.3,1.63)	1.29(1.13,1.47)
Age Group					
	Age under 20	124(5.64)	327(6.95)	1.0 (referent)	1.0 (referent)
	Age 21-45	1063(48.38)	2100(44.65)	1.33(1.07,1.66)	1.31(1.04,1.66)
	Age 46-65	789(35.91)	1610(34.23)	1.29(1.03,1.62)	1.18(0.92,1.5)
	Age 66 or older	221(10.06)	666(14.16)	0.88(0.68,1.13)	0.75(0.57,0.99)
Race					
	White	603(27.45)	1090(23.18)	1.0 (referent)	1.0 (referent)
	Black	894(40.69)	2132(45.33)	0.76(0.67,0.86)	0.99(0.86,1.14)
	Hispanic	572(26.04)	1088(23.13)	0.95(0.82,1.1)	0.97(0.83,1.13)
	Other	128(5.83)	393(8.36)	0.59(0.47,0.74)	0.64(0.5,0.81)
Gender					
	Male	1518(69.09)	3180(67.62)	1.0 (referent)	1.0 (referent)
	Female	679(30.91)	1523(32.38)	0.93(0.84,1.04)	1(0.89,1.13)
Country of Origin					
	U.S.	1242(56.53)	2500(53.16)	1.0 (referent)	--
	Foreign	955(43.47)	2203(46.84)	0.87(0.79,0.97)	
HIV Status					
	Negative	1830(83.30)	2985(63.47)	1.0 (referent)	1.0 (referent)
	Indeterminate	0(0.00)	10(0.21)	0(0..)	0(0..)
	Not offered	43(1.96)	154(3.27)	0.46(0.32,0.64)	0.52(0.37,0.75)
	Positive	160(7.28)	1112(23.64)	0.23(0.2,0.28)	0.2(0.17,0.24)
	Refused	152(6.92)	429(9.12)	0.58(0.48,0.7)	0.71(0.58,0.87)
	Unknown	12(0.55)	13(0.28)	1.51(0.69,3.31)	1.55(0.68,3.54)
Homeless					
	No	1973(89.80)	4243(90.22)	1.0 (referent)	1.0 (referent)
	Yes	224(10.20)	460(9.78)	1.05(0.89,1.24)	0.82(0.68,1)
Corrections					
	No	2109(95.99)	4428(94.15)	1.0 (referent)	1.0 (referent)
	Yes	88(4.01)	275(5.85)	0.67(0.53,0.86)	0.53(0.41,0.68)
Culture status					
	Negative	211(9.60)	1431(30.43)	1.0 (referent)	1.0 (referent)
	Positive	1986(90.40)	3272(69.57)	4.12(3.52,4.81)	4.12(3.51,4.83)
Previous TB History					
	No	2071(94.26)	4453(94.68)	1.0 (referent)	1.0 (referent)
	Yes	126(5.74)	250(5.32)	1.08(0.87,1.35)	0.77(0.61,0.98)

Table 1: Characteristics and logistic regression of culture positive tuberculosis patients.

pulmonary TB. There have been few other studies which have looked at this issue. According to a previous study, alcohol use was not found to be independently associated with increased prevalence of cavitory disease [5]. A previous study pointed out that alcohol impairs development of adaptive immunity to BCG if alcohol is being actively consumed prior to vaccination [6,7]. Another study also found that homeless patients with alcoholic issues and a previous history of TB developed cavitory disease more readily than those without previous TB history [6]. This brings up an interesting finding of our study because we found that previous TB reduced the risk of advanced cavitory disease in the multivariate model. In other studies of pulmonary TB infection, previous TB disease was one of the strongest risk factors for subsequent development of cavitation and other manifestations of advanced disease [8]. One reason for this finding could be the small number of persons with previous disease history in our population. Another reason could be the inability of a retrospective study to accurately capture previous TB history.

Another interesting finding of this investigation was that corrections history served as a protective factor for cavitory disease, which is also not consistent with previous studies. However, in the state of Florida these patients are monitored much more closely and more frequently for evidence of active TB disease. Therefore, it may be that they are less likely to develop manifestations of advanced infection, such as pulmonary cavitation.

There are no previous studies which look at the effect of age on the formation of cavitation on the lung. However, as cavitation is arguably a function of protective immunity it would make sense that the younger age group would be more likely to manifest pulmonary cavities.

Our study is consistent with a previous study that HIV-negative patients are more likely to have cavitation on the lung compared with HIV-positive patients [9]. In our study, we also found that for people not offered an HIV test, the odds of cavitory disease increased compared with those were HIV positive. It is highly possible that the patients who were not offered testing or refused testing, either were not considered suspects for HIV or did not consider themselves likely to be HIV positive.

This study has certain limitations. This data didn't include information about smoking or diabetes status. Another problem related to this study is that alcohol use is self-reported as a result we may be under-estimating the effect of alcohol use on cavitation.

Conclusion

Alcohol users remain a group with a high risk of TB infection and disease and may play an important role in the HIV-TB epidemic. The fact that they are more likely to develop advanced disease, and are therefore more likely to spread disease, is a serious public health issue. Advanced TB disease prevention targeting this group is, therefore, both necessary and warranted.

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