Substance Use and HIV among Subjects Attending Integrated Counseling and Testing Centre in South India: A Case Control Study

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ABSTRACT

Introduction: There is limited understanding of the association between various forms of substance use (non-injectable forms namely chewable tobacco, smoking and alcohol) and HIV. This study was conducted to assess the association between tobacco chewing, smoking, alcohol, other non-injectable substances and HIV status.

Methods: This was a case control study done among attendees in the Integrated Counseling and Testing Centre (ICTC) of a medical college hospital situated in Bengaluru. Eligible subjects were interviewed using pre-tested, semi-structured proforma prior to testing for HIV status. Information on substance use was collected using Modified Fagerstrom questionnaire for smokeless tobacco, CAGE questionnaire for alcohol, CAGE questionnaire for nicotine dependence and WHO - ASSIST V3.0 for other non-injectable substances.

Result: Age group of 26-35 years (AOR = 3.70, 95% CI : 1.02 - 13.34), those who were married (AOR = 4.01, 95% CI : 1.31 - 12.28), separated (AOR = 17.45, 95% CI : 3.07 – 98.96), those referred by a doctor (AOR = 5.15, 95% CI : 2.03 – 13.10), chewable tobacco users (AOR = 11.28, 95% CI : 1.25 - 101.64) and alcohol dependents (AOR = 7.41, 95% CI : 2.02 – 27.25) were found to be at risk for acquiring HIV.

Conclusion: Smokeless tobacco use and alcohol dependence was associated with HIV positivity.

Key words: HIV, Substance use, Case control study, ICTC

INTRODUCTION

India reported the first case of HIV in 1986. Both HIV 1 and 2 exist in India with HIV-1C being the commonest subtype reported. India has a population of more than 1.25 billion people with half of its population in the sexually active age group of 15-49 years. With heterosexual transmission as the commonest mode of HIV transmission, India has an estimated adult HIV prevalence of 0.26%.[1-4]

It is well known that substance-use affects transmission of HIV.[5] The HIV epidemic in North-Eastern states of India is driven by injectable drug use. Heterosexual transmission is the commonest mode of HIV transmission in southern India. Most studies have primarily focused on injectable drug use and a few on alcohol use leading to high risk sexual behavior. There is limited understanding on the role of tobacco, alcohol and other non-injectable substances in transmission of HIV.[1, 6-10]

In India, voluntary counseling and testing services for HIV were started in 1997 under National AIDS Control Programme Phase (NACP) I. Under NACP III, Voluntary Counselling and Testing Centres

(VCTC) and facilities providing Prevention of Parent to Child Transmission of HIV/AIDS (PPTCT) services were remodeled as 'Integrated Counseling and Testing Centre' (ICTC) to provide services to all clients under one roof. At the ICTC, clients are counselled and tested for HIV either voluntarily or as advised by a medical care provider. The main functions of ICTCs being conducting HIV diagnostic tests, providing basic information on the modes of HIV transmission, promoting behavioral changes to reduce vulnerability and link people with other HIV prevention, care and treatment services.[11] ICTC is the key to care ensuring availability of professional, client centered counseling and testing services in an easily accessible, non-discriminating environment where clients are treated with dignity and respect. Data collected in ICTC may provide important clues to understand the epidemiology of disease in a particular region.[12]

Assessing the role of non-injectable substances on acquiring HIV using prospective studies are not feasible due to indefinite incubation period for acquiring the infection. Field based studies require considerable resources in addition to associated social stigma and issues associated with acceptability to undergo HIV testing among general population. Hence an incident case control study, conducted in the ICTC is an ideal study design to measure the association between substance use and HIV. Besides, prevalent cases were not included as they might have changed their habits (or 'exposures') after being counseled for the same at the time of diagnosis in ICTC.

Even after three decades into the HIV epidemic, there is little information about the association between non-injectable substance use and HIV. Hence the present study was conducted to measure association between chewable tobacco, smoking, alcohol & other non-injectable substances and HIV infection.

METHODOLOGY

This was a hospital-based case control study among subjects who attended the Integrated Counseling and Testing Centre for retroviral testing at a medical college hospital and research centre in Bengaluru, India. Adults aged 18 years and above attending the ICTC during the study period of one year were included. Sample size was calculated based on the formula n= 2[Z α/2 + Z β]² pq/d2,where n= Number of Cases/Controls, Zα= Two-sided significance level: 0.05, Zβ= Power (chance of detecting): 0.80,p= Prevalence of substance use among cases: 0.58,q= 1-p= 0.42,d= Precision = 0.05, n = 132.64 ≈ 133 and finally Cases=133 and controls=133.

The subjects were assigned unique codes by the investigator to maintain confidentiality. The subjects were interviewed after the pre-test counselling, using a pre-tested, semi-structured questioner to collect details on socio-demographic profile, use of tobacco, alcohol and other non-injectable substances. In addition, information on high risk sexual behavior, intravenous drug usage, blood transfusions and HIV status of spouse was obtained.

Subjects then underwent retroviral testing and after approximately 30minutes, they received the test results. The retroviral test results were then made available to the investigator using the unique codes assigned to the subjects. Cases were defined as those detected to be HIV reactive for the first time (incident cases). Controls were defined as those detected to be HIV non-reactive on the same day as cases. The controls were selected from same population as cases. Hence, they resembled the cases with respect to their tendency to give complete and accurate information. This minimized the information bias between the cases and controls. The case to control ratio was 1:1 as the number of available cases and controls (fulfilling inclusion and exclusion criteria) was similar and the effort of obtaining information from both groups was comparable. Matching was not done for any socio demographic factors as they were also suspected risk factors. Hence this was an unmatched case control study. Required sample size was obtained over a period of 10 months.

The subjects were interviewed prior to testing for HIV status to ensure that the information gathered was unbiased (interviewer bias). In addition, the subjects were kept oblivious of the hypothesis under study to minimize response bias. After testing, every subject underwent post-test counseling as per national guidelines. Information on substance use was obtained using Modified Fagerstrom questionnaire for smokeless tobacco,[13] CAGE questionnaire for alcohol,[14] CAGE questionnaire for nicotine dependence [15] and WHO - ASSIST V3.0 [16] for other non-injectable substances. After which, association between substance use only or substance use with dependence and retroviral status was assessed among cases and controls using following operational definitions: Substance use - People who have used tobacco, alcohol, non-injectable substances like heroin, cannabis, cocaine, etc. anytime in their past. Substance dependence – was assessed based on the above mentioned scales. E.g Modified Fagerstrom - score >4, CAGE -alcohol score & nicotine score >2. Pre-operative patients attending the ICTC during the study period were excluded. As substance use history was vital, only

incident (newly diagnosed) cases were included thereby eliminating the recall bias. Besides, prevalent cases were not included as they may have changed their habits (or exposures) after being counseled for the same at the ICTCs.

Ethical Committee:

Ethical approval for the study was obtained before the start of the study from the institutional ethical committee of the medical college hospital. Permission letter from nodal officer of ICTC at the Medical college hospital and research centre to conduct the study was obtained. Permission was also given from the nodal officer, District Program Officer, District AIDS prevention and control unit. Also, the restriction of information on test results to the ICTC counselor alone ensured the confidentiality.

Statistical analysis:

Data entry was done using Epi Info 7. Data was analyzed using Stata 12.1 (Stata Corp, Texas, USA). For socio-demographic and substance use/ dependence characteristics, frequencies and proportions were calculated. Univariate logistic regression analysis was performed with HIV status as the outcome. Age, gender, education, religion, indication for HIV testing, marital status, type of family, blood transfusion, HIV status of spouse, sexual behaviour, age at marriage, type of locality and substance use (smokeless tobacco, smoking and alcohol) as apriori exposure variables. All variables with p<0.1 were included one after the other into the final model. Any variable with significant inclusion at p<0.05 and changed the OR by 10% were retained into the final model. In addition the model with added variables was tested using Liklihood ratio test.

RESULTS

A total of 266 subjects were interviewed. 133 were cases and 133 were controls, of whom 95 (71.43%) and 65 (48.87%) were males respectively. The age range of cases and controls was 18-75 years and 18-76 years respectively. Majority of both cases and controls were in the age group of 26-35 years with median ±Inter Quartile Range(IQR) age of cases and controls being 38.00±13 years &35.00±18 years respectively (table-1). Majority of the cases and controls were Hindus, educated up to High school, married, lived in nuclear families and were from urban localities (table-1). The majority of the cases 92 (69.17%) were referred by a doctor while most controls 57 (42.86%) walked in voluntarily. Premarital sexual exposure, history of having multiple sexual partners and history of having received blood transfusion was higher among cases than controls. Having a HIV positive spouse was higher among controls than cases. Substance (smokeless tobacco, smoking and alcohol) use and dependence was higher among cases than controls (table-1).

All age classes, gender, indication for testing, marital status, age at marriage, premarital sex, multiple sexual partners, blood transfusion, smokeless tobacco, cigarette smoking and alcohol were found to be associated with HIV positivity (Table 1). These variables were eligible to be included into the multivariate model.

Among the 266 ICTC attendees, marital status (married or separated), indication for testing (referred by a doctor), alcohol dependence and having received blood transfusion were significantly associated with higher odds of having HIV. Odds of being HIV positive among married was 4.01 times (AOR = 4.01; 95% CI : 1.31 - 12.28) and among separated was 17.45 times (AOR = 17.45; 3.07 - 98.96) that of unmarried. Odds of being HIV positive among those referred by a doctor was 5.15 times (AOR = 5.15; 95% CI: 2.03 - 13.1) that of those referred by DOTS. Odds of being HIV positive among subjects with alcohol dependence was 7.41 times (AOR = 7.41; 95% CI: 2.02 - 27.25) that of alcohol non-users and Odds of being HIV positive among those who had received blood transfusion was 10.23 times (AOR = 10.23; 95% CI : 2.16 - 48.41 that of those who had not (table 2).

DISCUSSION

Among cases, majority belonged to economically productive age group similar to another study. [17] This study also adds evidence on marriage being no longer considered a protective factor against HIV as observed in another study. [18, 19] Age at marriage and age in years are known to correlate with each other and hence age was considered an intrinsic confounder. Premarital sexual exposure and history of having multiple sexual partners was higher among cases than controls, comparable to a study which showed that women with longer duration of premarital sex had higher odds of STIs, moreover women with longer duration of premarital sex were more likely to report multiple sexual partners. [20] Having a HIV positive spouse was higher among controls (consists 51% females) than cases(consists 28% females).

While studies have shown that 87% of HIV transmission is through heterosexual route, multiple studies conducted in sub-Saharan Africa showed that substance use, mental health problems and sexual risk behaviors conjoin in what is known as a syndemic to increase HIV transmission risk. [21, 22]

Table 1: Distribution of cases and controls according to sociodemographic variables and association between each variable and HIV positivity by univariate logistic regression

Variables	Cases	Controls	Crude Odds Ratio [95% CI]	P
Age (in years)	38±13*	35±18*	-	-
18-25	05(03.76)	27(20.3)	Reference	-
26-35	46(34.59)	43(32.33)	5.78 [2.04, 16.36]	0.001
36-45	43(32.33)	30(22.56)	7.74 [2.68, 22.39]	<0.001
>45	39(29.32)	33(24.81)	6.38 [2.21, 18.44]	0.001
Gender				
Female	38(28.57)	68(51.13)	Reference	-
Male	95(71.43)	65(48.87)	2.615 [1.58, 4.34]	<0.001
Education				
Secondary and above	71(53.38)	87(65.42)	Reference	-
Primary	35(26.32)	26(19.55)	1.65 [0.91, 2.10]	0.1
Illiterate	27(20.30)	20(15.03)	1.65[0.86, 3.19]	0.134
Religion				
Others	11(8.27)	12(9.02)	Reference	-
Hindu	122(91.73)	121(90.98)	1.10 [0.47, 2.59]	0.827
Referred by				
DOTS	16(12.03)	29(21.80)	Reference	-
Voluntary	25(18.80)	57(42.86)	0.79 [0.37, 1.72]	0.559
Doctor	92(69.17)	47(35.34)	3.55 [1.75,7.18]	<0.001
Marital status				
Unmarried	12(9.02)	33(24.81)	Reference	-
Married	106(79.7)	96(72.18)	03.04 [1.48, 6.21]	0.002
Separated	15(11.28)	4(03.01)	10.31 [2.85, 37.3]	<0.001
Type of Family				
Joint	13(9.77)	14(10.52)	Reference	-
Nuclear	102(76.69)	90(67.67)	1.22 [0.55, 2.73]	0.628
Three Generation	12(9.03)	21(15.79)	0.62 [0.22, 1.73]	0.358
Alone	6(4.51)	8(6.02)	0.81 [0.22, 2.96]	0.747
Type of locality				
Urban	110(82.71)	115(86.46)	Reference	-
Rural	23(17.29)	18(13.54)	1.34 [0.68, 2.61]	0.397
Age at Marriage (in years)	24±9#	20±7#		
11-20	37(30.58)	54(54.0)	Reference	-
21-30	69(57.02)	43(43.0)	2.34 [1.33, 4.12]	0.003
31-40	15(12.4)	3(3.0)	7.30 [1.97, 27.0]	0.003
Premarital sex				
No	106(79.70)27(20.30)	121(90.98)	Reference	-
Yes		12(9.02)	2.57 [1.24, 5.32]	0.011
Multiple sexual partners				
No	97(72.93)	116(87.22)	Reference	-
Yes	36(27.07)	17(12.78)	2.53 [1.33, 4.78]	0.004
HIV positive spouse				
No	91(75.21) 30(24.79)	66(66.00)	Reference	-
Yes		34(34.00)	0.85 [0.48, 1.49]	0.57
Blood transfusion				
No	115(86.47)18(13.53)	131(98.5)	Reference	-
Yes		2(01.50)	10.25 [2.33, 45.14]	0.002
Smokeless tobacco$				
No use	121(90.98)	132(99.25)	Reference	-
Use	12(9.02)	1(0.75)	13.09 [1.68, 102.18]	0.031
Cigarette smoking				
No use	94(7.68)	108(81.2)	Reference	-
Use but no dependence	21(15.79)	10(7.52)	2.41 [1.08, 5.38]	0.031
Dependence	18(13.53)	15(11.28)	1.38 [0.66, 2.87]	0.394
Alcohol				
No use	72(54.14)	103(77.44)	Reference	-
Use but no dependence	21(15.79)	19(14.29)	1.58 [0.79, 3.15]	0.148
Dependence	40(30.08)	11(8.27)	5.2 [2.50, 10.82]	<0.001

* Mean ± Standard Deviation; # Median ± Interquartile range; $ Smokeless tobacco dependence was not observed in any controls.

Table 2: Association of individual variable with HIV positivity among subjects attending an ICTC

Variables	Crude Odds Ratio	Adjusted Odds ratio [95% CI]	P
Age (in years)			
18-25	Reference	Reference	-
26-35	5.78 [2.04, 16.36]	3.7 [1.02, 13..34]	0.046
36-45	7.74 [2.68, 22.39]	2.14 [0.54, 8.47]	0.277
46-55	6.38 [2.21, 18.44]	1.80 [0.44, 7.45]	0.415
Gender			
Female	Reference	Reference	-
Male	2.61 [1.58, 4.34]	1.83 [0.80, 4.18]	0.151
Marital status			
Unmarried	Reference	Reference	-
Married	3.04 [1.48, 6.21]	4.01 [1.31, 12.28]	0.015
Separated	10.31 [2.85, 37.30]	17.45 [3.07, 98.96]	0.001
Referred			
By DOTS	Reference	Reference	-
Voluntary	0.79 [0.37,1.72]	1.35 [0.49, 3.69]	0.562
By Doctor	3.55 [1.75,7.18]	5.15 [2.03, 13.1]	0.001
Smokeless tobacco			
No use	Reference	Reference	-
Use	13.09 [1.68, 102.18]	11.28 [1.25, 101.64]	0.031
Cigarette smoking			
No use	Reference	Reference	-
Use	2.41 [1.08, 5.38]	1.38 [0.42, 4.45]	0.598
Dependence	1.38 [0.66, 2.87]	0.25 [0.07, 0.85]	0.027
Alcohol			
No use	Reference	Reference	-
Use	1.58 [0.79, 3.15]	1.07 [0.37, 3.09]	0.898
Dependence	5.2 [2.50, 10.82]	7.41 [2.02, 27.25]	0.003
Blood transfusion			
No	Reference	Reference	-
Yes	10.25 [2.33, 45.14]	10.23 [2.16, 48.41]	0.003
Multiple sexual partners			
No	Reference	Reference	-
Yes	2.53 [1.33, 4.78]	1.86 [0.72, 4.81]	0.198

In this study, there was a statistically significant association between alcohol dependence and HIV positivity, similar to other studies. In contrast to other studies this study found alcohol dependence alone as a risk factor.[23-25] Unadjusted odds ratio for alcohol use in this study was higher than the pooled unadjusted odds ratio from 20 studies (which was 1.7). Similarly in other studies, the pooled estimate of HIV risk was lower for alcohol users than alcohol dependents. [23-25] Similar observation was found in this study with higher unadjusted odds for alcohol dependence (OR = 5.2; 95% CI: 2.50 - 10.82) than alcohol use (OR = 1.58; 95% CI: 0.79 - 3.15) when compared to alcohol non-users.

Higher HIV prevalence among men was associated with history of sex with men, blood transfusion, multiple lifetime women sex partners, consuming alcohol before sex, recreational drug use. Higher HIV prevalence among women was associated with illiteracy, dissolved marriage, having more than one lifetime sexual partner. [20, 26, 27] Having a dissolved marriage (being widowed/ divorced/ separated) was the strongest predictor of HIV

among women.[26] Similar observation was found in this study. The majority of the cases (69.17%) were referred by a doctor while majority of the controls (42.86%) got tested voluntarily reflecting the healthy worker effect.

Additionally, increased or frequent consumption of alcohol can affect the immunological response leading to increased susceptibility to HIV among those consuming alcohol. In this study, there was a statistically significant association between alcohol dependence and HIV positivity independent of high risk sexual behavior though there is a possibility of underreporting of high risk behavior as observed in a study among general population based-sample. [28-30, 31s-33s]

Also, smokeless tobacco use was an independent risk factor for HIV infection in this study. But, similar to other studies cigarette smoking was not associated with HIV infection. [33s,34s] There was no association observed between tobacco(chewable or smoking cigarettes) and HIV agreeing with conclusions from many studies . [34s]

All cases of HIV infection detected in the ICTC

were new or incident cases. As substance use history was vital only incident (newly diagnosed) cases were included thereby eliminating recall bias. Case to control ratio was 1:1 as the effort for obtaining information from cases and controls was same. The controls were selected from same population as cases to minimize the information bias between the cases and controls. This was an unmatched case control study as socio-demographic characteristics were also considered as risk factors under evaluation.

However the controls who were, those tested HIV negative at ICTC, who represent the same socio sexual characteristics as the cases. As substance use history was vital, only incident cases were included there by eliminating recall bias. Testing for HIV for this study was done using NACO approved national protocol.(11)

CONCLUSION

Smokeless tobacco use and alcohol dependence was associated with HIV infection. Smoking and other non injectable substances were not associated with HIV infection

Limitations: This was hospital based case-control study thus the results might not be generalizable to population. Differential misclassification of 'cases in window period' as 'controls' could not be eliminated due to lack of resources. Information on details of substance use, multiple sexual partners, premarital sex, etc. are based on the history revealed by the subjects. Other factors like psychosocial factors/ personality traits which could also play a role in HIV transmission are beyond the scope of this study. A matched case control study with a larger sample size covering wide geographical area may be done to assess the role of substance use and dependence for generalizability.

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