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Risk for developing tuberculosis among intravenous drug users with human immunodeficiency virus (HIV) infection

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Approximately one third of people living with human immunodeficiency virus (HIV) infection are co-infected with tuberculosis (TB), and TB accounts for up to a third of deaths from AIDS worldwide. Injectable drug use is an important factor in epidemiology of both TB and HIV. This study was carried out to assess the risk of intravenous drug use for developing TB in HIV infected patients. A cross-sectional study was conducted from January, 2009 to December, 2011. Equal numbers of HIV seropositive patients with and without history of intravenous drug use (IVDU) attending Department of Microbiology, BP Koirala Institute of Health Sciences for CD4 cells counting were enrolled to study the prevalence of pulmonary tuberculosis. Three early morning sputum specimens on consecutive days were collected from all participants and processed for microscopy (Auramine-O and Ziehl-Neelsen staining) and culture on Lowenstein-Jensen (L-J) media. Observation was noted. Of a total of 336 subjects enrolled in our study, group I and group II comprised HIV patients with IVDU (n = 168) and without IVDU (n = 168), respectively. In group I, *Mycobacterium tuberculosis* was detected in 40 (23.8%) patients. There was no statistical association between duration of intravenous drug use and finding of *M. tuberculosis* positivity (p > 0.05). In group II, *M. tuberculosis* was detected in 32 (19%) patients. Univariate analysis revealed that TB in HIV seropositive patients appeared with higher frequency in intravenous drug users (odds ratio (ORa) = 1.3; CI 95%, 0.786 to 2.242) than the non-users. Average CD4 cells count among HIV positive patients in group I and II was 248.6 and 292.7, respectively; with 47 patients (27.9%) in group I and 40 patients (23.8%) in group II having counts below 200. Rate of TB is high in intravenous drug user populations infected with HIV.

Key words: HIV seropositive, intravenous drug users, pulmonary tuberculosis.

INTRODUCTION

Tuberculosis (TB) and human immunodeficiency virus (HIV) infection both remain a very serious public health problem. Despite the fact that TB is a preventable, treatable and curable disease, it is a major infectious disease

with high prevalence. One of the reasons behind the failure to control TB burden is the impact of HIV on TB. World Health Organization (WHO) has estimated 9.27 million incident cases of TB where 1.37 million (14.8%) were HIV- seropositive (Guelar et al., 1993). Persons co-infected with HIV and *Mycobacterium tuberculosis* are at much greater risk of developing active TB than HIV-seronegative individuals (Guelar et al., 1993). Synergistic action of HIV and TB is defined in such a way that HIV infection weakens the immune system of a person and tubercle bacilli can grow more easily resulting in active TB disease in persons with recently acquired or latent TB infection (WHO Regional Strategic Plan on HIV/TB SEA/TB/261. SEA/AIDS/140, 2003). The life time risk of developing TB in HIV negative is 5.0 to 10.0% but the risk may increase up to 60% in HIV positives (Dhungana et al., 2008).

A metaphor is apt: this is a time when oil (HIV) is poured into the fire (TB-infected persons) in Asia (Vermund and Yamamoto, 2007). The synergy of HIV and TB takes several forms: *M. tuberculosis* infection increases viral load; immunosuppression from advancing HIV disease increases the risk of tuberculosis, new as well as re-infection (quiescent *M. tuberculosis* will reactivate) (Selwyn et al., 1989). Preventive therapy with isoniazid (INH) can be initiated if co-infected individuals are identified as soon as possible.

Although Center for Disease Control and Prevention (CDC) has reported high rates of TB among HIV-seropositive intravenous drug users (IVDUs) (Centers for Disease Control and Prevention, 2005), clear differentiation has not been defined among IVDUs and non-IVDUs with HIV seropositivity. Therefore, we aimed to determine the prevalence of people infected with tuberculosis (PTB) among HIV seropositive IVDUs attending BP Koirala Institute of Health Sciences, Dharan, Nepal.

MATERIALS AND METHODS

A cross-sectional study was conducted during three year period (January, 2009 to December, 2011). Equal numbers of HIV seropositive patients with and without history of IVDU attending Department of Microbiology, BPKIHS for CD4 cells counting were enrolled to study the prevalence of PTB. The nature and purpose of the study were explained to all the participants and they were assured of their confidentiality and anonymity. Written consent was obtained from all the participants. The participants were provided standard sputum containers and instructed to collect early morning sputum specimens on three consecutive days. The specimens were transported to laboratory and processed for microscopy [using Auramine-O fluorescent staining for screening of acid fast bacilli, and Ziehl-Neelsen (Z-N) staining for their confirmation] and culture (World Health Organization, 1998). At least 100 oil immersion fields were on Lowenstein-Jensen (L-J) media. Acid fast bacilli (AFB) detected on the smear were graded according to WHO guideline (World Health Organization, 1998). About 300 OIF were examined to declare a slide negative. Growth on L-J media was identified.

Research ethics

Ethical clearance for conducting the study was obtained from the Institutional Review Committee of BP Koirala of Institute of Health Sciences, Dharan, Nepal.

Statistical analysis

The data obtained from questionnaire and CD4 cells counting were entered in Microsoft Excel and analyzed using SPSS version 16.0 software. Frequency of demographic variables was calculated. Association of CD4 cells count and *M. tuberculosis* positivity was determined using chi-square test.

RESULTS

Of a total of 336 HIV positive patients divided into two groups in our study, group I comprised of patients with IVDU (n = 168) and group II without IVDU (n = 168). Gender wise, group I included159 males and 9 females while there were 121 males and 47 females in group II. Mean age of the subjects in these groups were 29.1 and 39.3 years, respectively. Frequency of demographic variables is presented in Table 1. In Group I, *M. tuberculosis* was detected in 40 patients (23.8%). Acid fast staining demonstrated AFB positivity in the smear from only 37 patients, while culture revealed positivity even in additional 3 patients.

There was no statistical association between duration of intravenous drug use and finding of *M. tuberculosis* positivity ($p > 0.05$) as shown in Table 2. Group II exhibited positivity of *M. tuberculosis* in 32 patients. Both acid fast staining and culture revealed the presence of the bacilli with equal sensitivity. Univariate analysis revealed that tuberculosis in HIV seropositive patients appeared with higher frequency in IVDUs (ORa = 1.3; CI 95%, 0.786 to 2.242) than non-IVDUs. Average CD4 cells count among HIV positive patients in Group I and II was 248.6 and 292.7, respectively; with 47 patients (27.9%) in group I and 40 patients (23.8%) in group II having counts below 200. Table 3 shows positivity of *M. tuberculosis* among HIV patients with (group I) and without (group II) intravenous drug use and their $CD4^+$ cell counts.

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Table 1. Demographic variables.

Categories	Variables	Group I	Group II
Age	20-30	67	41
	30-40	82	65
	>40	19	62
Occupation	Unemployed	74	84
	Social worker	25	18
	Business	23	37
	Employed	44	29
Education	Illiterate	-	-
	Literate	5	12
	Primary	41	29
	Secondary	93	71
	Higher secondary	29	56

Table 2. Duration of intravenous drug use and finding of *M. tuberculosis* positivity.

Duration (years)	*M. tuberculosis*		P value
	Positive	Negative	
< 5	13	39	
5-10	19	60	0.932
>10	8	29	

DISCUSSION

Early diagnosis of TB in HIV seropositive people is itself an important achievement, since active TB in HIV people is AIDS defining disease and should receive antiretroviral (ARV) therapy independent of CD4 cells counts. A number of epidemiological factors associate with development and progression of TB among HIV infected people. Moreover, drug users present a challenge among these infected people. In this study, we compared the prevalence of PTB among drug-user and non-user HIV positive people. We found 23.8 and 19% of PTB prevalence among HIV seropositive IVDUs and non-IVDUs, respectively. Evidence suggests that about 30% of HIV infected people are estimated worldwide to have simultaneous infection with *M. tuberculosis* (Getahun et al., 2010). However, a range of figure (14 to 46%) can be seen in different studies conducted in different settings (Corbett et al., 2003; World Health Organization, 2009). The findings of this study is in contrast with the lower rates reported in earlier publications from Nepal (Dhungana et al., 2008; (Sharma et al., 2010; Ghimire et al., 2004). The prevalence seemed to be fairly high (23%) in the capital's (Kathmandu, Nepal) tertiary care center (Dhungana et al., 2008), whereas low prevalence (10.8%) had been reported from the cities with low population outside the capital (Ghimire et al., 2004). High prevalence in our study corresponds to our selection of sample population. Most of the participants were from HIV/AIDS living care homes which may provide the suitable environment for household contact of TB. High occurrence of TB in a setting of HIV prevalence has been reported from various parts of the world: South Africa (17.3%) (Lawn et al., 2011), Cambodia, Thailand, and Vietnam (15%) (Cain et al., 2010) and China (22.9%) (Yu et al., 2009). A Meta analysis (Gao et al., 2010) from china has shown a range of prevalence of TB: 0.5% (Cao et al., 2006) to 35% (Wang et al., 2007) among HIV positive people.

Our finding strongly indicated higher prevalence of PTB among HIV positive IVDUs as compared to HIV positive non-IVDUs. Effects of drug use in human physiology and varieties of risk factors (such as cluster of vulnerable people to acquire infection; smoking and alcohol use; and poor nutrition) may be responsible for high prevalence of TB among drug users. Significant relation of alcohol and smoking with the prevalence of TB has already been reported from the same place where this study was conducted (Gyawali et al., 2013). Deleterious effect of drug use on the immune system has been shown by *in vitro* studies (Friedman et al., 2003; Wei et al., 2003).

In our study, majority of participants in both groups were young (20 to 40 years), unemployed and have completed only secondary level of education. Drug use and intensity of HIV and TB were not observed to go parallel with higher education and employment status. We observed no significant relation ($P > 0.05$) between duration of drug use and finding of TB. However, few studies have reported their positive relations (Brassard et al., 2004; Grimes et al., 2007; Glynn JR., 1998). With the already discussed results, it can be summarized that HIV-induced immune-suppression along with the physiological effect of drug use and the associated risk factors play important role for the high prevalence of TB among IVDUs rather than the single effect of drug use.

Many studies have highlighted that HIV infection increases the risk of tuberculosis by approximately 7-folds, though this may vary with the stage of the HIV epidemic, the prevalence of TB, and the age groups considered (Glynn JR., 1998). And, dually infected individuals develop TB at a rate of 5 to 10% per year (Deiss et al., 2009). These conditions may be due to HIV-TB co-infection with degraded humoral and cell mediated immune responses.

Although higher proportion of TB was observed in group I patients than the group II patients with respect to all three categories of CD4+ cell counts (< 200, 200 to 400 and > 400), significant association was not proved (P

Table 3. Positivity of *M. tuberculosis* among HIV patients with (group I) and without (group II) intravenous drug use and their $CD4^+$ cell counts.

CD4 cell count/µl of blood	Group	*M. tuberculosis*		P value
		Positive	Negative	
<200	Group I	16	31	NS
	Group II	11	29	
200-400	Group I	18	43	NS
	Group II	16	47	
>400	Group I	06	54	NS
	Group II	05	60	

> 0.05). However, the higher prevalence of TB in group I than group II patients in the present study alarms the risk of drug use for development of TB among HIV people. Hence, it demands longitudinal studies to be conducted in the future covering large population setting. Furthermore, drug abuse may increase the chances of cross-infection and it may also become important treatment barrier because of the escaping behaviours of the abusers from social network. Hence the barriers, including poor adherence and limited access to care, pose unique challenges for their treatment. It is a proved fact that treatment failure is the primary risk factor for the development of drug resistance. Thus increased attention should be paid to such group while making policies to control TB and HIV infection.

Conclusion

Drug abuse remains a risk for HIV people to develop TB. Adults of 20 to 40 years age are at risk for both illicit drug use and HIV infection among them. Rate of tuberculosis is high in such drug users infected with HIV. So, to strengthen the health policy to control HIV infection and TB, IDVUs should be screened for both of these diseases.

Conflict of interest

Authors declare no conflict of interest.

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