Surveillance of Tuberculosis among HIV infected persons in three different regions of Nepal

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ABSTRACT

Tuberculosis itself is a major public health problem in Nepal. The emergence of HIV has caused sharp increase in TB incidence in the community. Surveillance of TB/HIV co-infection helps in developing effective TB/HIV control strategies. The objective of this study was to measure prevalence of TB among HIV/AIDS patients in the selected regions. Between December 2006 and May 2008, a cross-sectional study was conducted in three different settings namely Tribhuvan University Teaching hospital, Kathmandu; Regional Tuberculosis Centre, Pokhara and Shree Siddhanath Science Campus, Mahendranagar. After taking informed consent pre-structured questionnaire was administered. Sputum specimen was collected from HIV/AIDS patients to investigate tuberculosis by culture and microscopy. Data analysis was done using SPSS 11.5. Of the 394 HIV infected persons, 225 (57.1%) were male and 169 (42.9%) female. The overall prevalence of TB was found to be 8.1%. Clinical signs and symptoms were significantly lower in those patients undergoing ART (χ^2 value ranging from 4.19 to 9.13). However, development of tuberculosis is independent of ART status (χ^2 value 1.14) and CD4 level (χ^2 value 3.25). TB case detection rate by cultural technique was found to be twice as superior as direct microscopy. It can be concluded that smear negative TB constitute the significant proportion of TB cases in HIV infected persons.

Keywords: HIV/AIDS, Nepal, Surveillance, Tuberculosis

INTRODUCTION

Human immunodeficiency virus (HIV), the causative agent of acquired immunodeficiency syndrome (AIDS), and *Mycobacterioum tubrculosis*, the causative agent of tuberculosis (TB), have been described as the 'Diabolical Duet' because the two go together synergistically.[1] HIV infection, by weakening the body's immune response, is the greatest risk factor for TB. HIV infection elevates the risk of rapid progression from primary tubercular infection to active TB disease. In addition, it also increases the recurrence rate of active TB from latent TB infection through endogenous reactivation.[2] HIV infection is the greatest challenge for National TB control Programmes (NTPs) because even the effective implementation of directly observed treatment short-course (DOTS), which is based on passive case detection and treatment of active disease, is insufficient to control TB in high HIV prevalence area. So, preventing HIV associated TB means going beyond the full implementation of DOTS. Control of tuberculosis in this

situation will require new public health strategy that apply epidemiologically based interventions to detect undiagnosed cases so as to reduce susceptibility to disease. A high standard of care is essential to restore the health of individuals with tuberculosis, to prevent the disease in their families and others with whom they come into contact, and to protect the health of communities.[3]

HIV epidemic is contributing significantly to the upward trend in TB mortality and morbidity. Up to 60 percent of the purified protein derivative (PPD) positive patients with HIV/ AIDS develop active TB during their lifetime compared to 10 percent PPD positive HIV negative individual. So, the HIV epidemic is contributing greatly to the deteriorating TB situation in an increasing number worldwide, particularly in South East Asia and Africa. Similarly, TB is considered as the biggest killer of people who are infected with HIV accounting one- third of AIDS death globally, 40 percent of AIDS mortality in South East Asia and another 40 percent in Africa. Furthermore, increasing TB cases in people living with HIV/AIDS (PLWHA) augment the risk of TB transmission to the general population of the community whether or not HIV infected.[2] TB/HIV co-infection rate varies with geographical regions of Nepal. In a study conducted in Tansen (western Nepal) during 2001-2002, it was observed that out of 260 suspected patients analyzed for the presence of both TB and HIV, 28 (10.76%) were found to be positive for both, whereas in Kathmandu (central Nepal), Prevalence of TB among HIV infected persons was 23% in 2005.[4,5] A study conducted in eastern Nepal showed that among 300 newly diagnosed

TB patients, 14 (4.7%) patients were HIV positive.[6] Sentinel surveys conducted in 2006-2007 showed 2.4% prevalence of HIV among diagnosed TB patients.[7]

These few scientific studies on TB/HIV were conducted in different regions of Nepal by individual researchers in their own way and are based on limited sample size which may not represent the national scenario of TB/HIV co-infection. So, this extensive study was conducted with representative sample size and sufficient catchments areas as per recommendation of previous studies. The objective of this study was to document the prevalence of TB among HIV/AIDS patients in the three selected regions which is necessary for formulating national policy and guidelines for TB/HIV control in the country.

MATERIALS AND METHODS

Between December 2006 and May 2008, a cross sectional study was carried out by three distinct collaborative organizations located in different regions of Nepal. They were Tribhuvan University Teaching Hospital (TUTH), Kathmandu (Central region), Regional TB center (RTC), Pokhara (Western region) and Shree Siddhanath Science Campus (SSC), Mahendranagr (Far western region). Accordingly, three distinct study settings were set up. They were Department of Microbiology, TUTH (Central region), Mycobacteriology Research Laboratory, RTC, Pokhara (Western region) and Department of Microbiology, SSC, Mahendranagar (Far western region). Research approval/ ethical clearance were obtained from three distinct research/ funding organizations namely Development Partnership in Higher Education (DelPHE), Nepal Health research council (NHRC) and University Grants commission (UGC). Altogether 394 HIV infected persons (both symptomatic and asymptomatic were included in the study. Among these, 150 were seleted from Central region (TUTH HIV/ AIDS unit, Navakiran Plus HIV/AIDS Care home, Sparsha Nepal HIV/AIDS care home, Youth Vison Crisis Centre), 180 from Western region (Friends of Hope, Community Support Group, Nauloghumti and Paluwa) and sixty from far western region (Mahakali Zonal Hospital, National Nepal Social welfar association and Nawa Aasa). The interviewer went to these centers to take the interview and collected the sputum specimens of HIV positive subjects. Participants were selected by random sampling method using the

Table-1: socio-demographic feature of respondents

Socio-demographic features		Male Number (%)	Female Number (%)	Total Number (%)
Age group (in years)	1-10	2(0.9)	2(1.2)	4(1.0)
	11-20	7(3.1)	2(1.2)	9(2.3)
	21-30	79(35.1)	85(50.3)	164(41.6)
	31-40	100(44.4)	63(37.3)	163(41.4)
	41-50	36(16.0)	12(7.1)	48(12.2)
	51-60	1(0.4)	5(3.0)	6(1.5)
Occupation	Unemployed	79(35.1)	79(46.7)	158(40.1)
	Farmer	53(23.6)	61(36.1)	114(28.9)
	Business	45(20.0)	15(8.9)	60(15.2)
	Volunteer	26(11..6)	6(3.6)	32(8.1)
	NGO/INGO	20(8.9)	7(4.1)	27(6.9)
	Student	2(0.9)	0	2(0.5)
	Teacher	0	1(0.6)	1(0.3)
Education	Illiterate	50(22.2)	105(62.1)	155(39.3)
	primary	96(42.7)	42(24.9)	138(35.0)
	Lower secondary l	2(0.9)	0	2(0.5)
	Secondary	70(31.1)	21(12.4)	91(23.1)
	Higher Secondary	7(3.1)	1(0.6)	8(2.0)
Mode of HIV infection	Sexual	118(52.4)	161(95.3)	279(70.8)
	IDU	101(44.9)	5(3.0)	106(26.9)
	Mother to child	4(1.8)	3(1.8)	7(1.8)
	Blood transfusion	2(0.9)	0	2(0.5)
Antiretroviral therapy (ART) status	With ART	87(38.7)	63 (37.3)	150 (38.1)
	Without ART	138(61.3)	106(62.7)	244(61.9)
Total		225 (100)	169(100)	394 (100)

The overall prevalence of TB was found to be 8.1%. Males showed slightly higher prevalence rate than females as shown in table 2.

patients' lists available in these centers. After taking written informed consent, study participants were interviewed using questionnaire, which collected data on socio-demographic, behavioral and clinical features. Then, three sputa specimens (first spot, early morning, and second spot) were collected and transported to the respective study settings for processing. All three sputa specimens were processed for Acid Fast Bacilli staining using Ziehl Neelsen method.[8] In addition, early morning sputum were subjected to modified Petroff's method for decontamination and then inoculated into 2 sets of 3% Ogawa medium followed by incubation at 37^0C for 6-8 weeks[8]. Appearence of brown, granular colonies (sometimes called "buff, rough and tough") in Ogawa Medium was recorded as positive for *M. Tuberculosis.* Data obtained from laboratory result and field visit were entered into statistical package for social sciences (SPSS 11.5 version) and analyzed.

RESULTS:

Of the 394 PLWHA volunteers, 225 (57.1%) were male and 169 (42.9%) female. Majority (83%) of the respondents were in the age group 21-40 years. 40.1% of the respondents were unemployed followed by farmers (28.1%) and businessmen (15.2%). Many of them are illiterate (39.3%) and acquired HIV infection by sexual means (Table-1). The overall prevalence of TB was found to be 8.1%. Males showed slightly higher prevalence rate than females as shown in Table-2.

Table-2: Distribution of respondents by TB status and sex

TB status	Male Number (%)	Female Number (%)	Total Number (%)
With TB	22(9.8)	10(5.9)	32(8.1)
Without TB	203(90.2)	159(94.1)	362(91.9)
Total	225	169	394

87.5% of the TB/HIV co-infected persons were in the age group of 21- 40 years (table 3)

Table-3: Distribution of respondents by TB status and age group

Age group (in years)	With TB Number (%)	Without TB Number (%)	Total Number (%)
1-10	0	4(1.1)	4(1.0)
11-20	0	9(2.5)	9(2.3)
21-30	12(37.5)	152(42.0)	164(41.6)
31-40	16(50.0)	147(40.6)	163(41.4)
41-50	4(12.5)	44 (12.2)	48(12.2)
51-60	0	6(1.7)	6(1.5)
Total	32(100)	362(100)	394(100)

Clinical signs and symptoms are significantly lower in those patients undergoing ART. However, development of Tuberculosis is independent of ART status (Table-4).

Table-4: Distribution of respondents by Clinical presentation/TB and ART status

Clinical signs and symptoms Clinical signs and symptoms	With ART	Without ART	□² value
Yes	49	105	
No	101	139	
Yes	38	90	
No	112	154	
Yes	34	83	
No	116	161	
Yes	20	54	
No	130	190	
Yes	39	100	
No	111	144	
Yes	15	17	
No	135	227	

At the time of specimen collection 270 participants had known CD4 count. Among the patients with CD4 count less than 200, 13.22% (1600/121) had co-infected with TB where as only 6.71% (1000/149) of the patients with CD4 count 200 and above were co-infected with TB. However, χ^2 test shows that development of Tuberculosis is independent of CD4 level (Table-5).

Table-5: Distribution of respondents by TB status and CD4 level

CD 4 range	With TB	Without TB	Total	□² value
Less than 200	16	105	121	
200 and above	10	139	149	
Total	26	244	270	

Among 32 TB cases, 16 were smear negative TB cases i.e all the 32 cases were culture positive, but AFB was detected in sputum for only 16 cases (Table-6).

Table-6: Case detection rate of TB: cultural technique versus direct microscopy

Methods of diagnosis	No. of TB cases detected	Inference
Culture	32	
Direct microscopy	16	

DISCUSSION

One of the major findings of this study is the documentation of 8.1% TB prevalence in HIV infected persons in Nepal. A similar study carried out in United Mission Hospital, Tansen during 2001 and 2002 showed 10.76% TB/HIV co-infection rate.[4] Our previous study carried out during 2005 in Kathmandu demonstrated 23% TB prevalence

in HIV infected persons.[5] More recent studies carried out during 2008-2009 in admitted HIV/AIDS patients in Seti Zonal Hospital, Dhangadi documented 27.3% TB prevalence in HIV/AIDS patients.[9] Unlike this study, majority of our samples were from outdoor patients (both symptomatic and asymptomatic). This could be one of the reasons for obtaining lower prevalence rate. Similar studies conducted in other countries have further corroborated our findings. In a TB surveillance among HIV infected persons in Cambodia, it was observed that 9% of the participants were positive for TB.[10] Similarly the prevalence of TB among HIV patients visiting a clinical setting in Cambodia was found to be 16.1%.[11] From Table-4 it is revealed that unlike other clinical symptoms, the development of TB has no any relationship with ART status. A study carried out in United Kingdom has suggested that highly active antiretroviral therapy (HAART) can be effective to prevent TB, but only with very high levels of coverage and compliance. [12] Another study carried out in Burkina, Faso demonstrated that delaying HAART initiation until the CD4 count dropped to < 50 significantly increased TB incidence in the first 3 months after HAART initiation.[13] Table 5 shows that TB can occur even in patients with CD4 count 200 and above. A similar study carried out in Africa has suggested that pulmonary TB occur along the continuum of immunodeficiency and it is not likely to be a marker of the severity of HIV infection.[14] On the basis of table 6 it can be asserted that higher number of TB cases can be detected by inclusion of cultural technique along with direct microscopy. Several studies have demonstrated that smear negative TB constituted the significant proportion of TB cases in HIV/AIDS $_{\text{patients.}}$ 15-18

Higher prevalence of TB among HIV infected persons was observed. However, the rate is lower than the previous studies (which are primarily hospital based with limited sample size). The disease was detected even in HIV patients with higher CD4 count of 200 and above and in both the ART as well non ART subjects. Cultural technique was found to be twice as superior as direct microscopy for the case detection of TB. On the basis of this study it can be recommended special TB programmes for PLWHA was absolutely essential to prevent TB not only in these groups of people but also in the community.

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