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Prevalence of Human Immunodeficiency Virus Infection among Tuberculosis Patients in Nepal

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ABSTRACT

Background: National Tuberculosis Program has envisioned to provide human immunodeficiency virus testing for all tuberculosis patients. However, human immunodeficiency virus testing coverage among notified tuberculosis patients is very low in Nepal. Hence, it is difficult to reflect the prevalence of human immunodeficiency virus infection among tuberculosis patients based on the information available from the routine system. Hence National Tuberculosis Program carried out sentinel surveillance to assess the prevalence of human immunodeficiency virus infection among tuberculosis patients and its associated factors in Nepal.

Methods: This study was cross-sectional study type, conducted at six sentinel sites across the country. This study lasted for six months starting from March 2017 to August 2017. The sample size was calculated using Epiinfo STATCAL application assuming confidence interval at 95%, 85% power and 5% non-response rate. The required sample size was 1672 tuberculosis patients. Ethical approval was obtained from Nepal Health Research Council. All types of tuberculosis patients who were equal or above 15 years were included in the study. Human immunodeficiency virus testing was performed among tuberculosis patients as per the testing algorithm recommended by national guideline.

Results: The study was carried out among 1664 tuberculosis patients registered for tuberculosis treatment during the study period. More than two thirds of tuberculosis patients (67%) were male. The median age of tuberculosis patients was found 32 years. During human immunodeficiency virus testing, 41 out of 1664 tuberculosis patients were found human immunodeficiency virus positive resulting seroprevalence of human immunodeficiency virus infection among tuberculosis patients to 2.5%. Prevalence of human immunodeficiency virus infection was significantly associated with age ($P=0.002$), caste/ethnicity ($P=0.025$), religion ($P=0.015$) and occupation ($P=0.014$) of tuberculosis patients.

Conclusions: Prevalence of human immunodeficiency virus infection among tuberculosis patients was found 2.5%. Information and access to tuberculosis and human immunodeficiency virus services need to be increased to address tuberculosis-human immunodeficiency virus co-infection in Nepal.

Keywords: HIV; prevalence; TB; TB-HIV coinfection.

INTRODUCTION

World Health Organization (WHO) estimated around 45,000 new tuberculosis (TB) cases in Nepal in 2016.¹ However only 32,056 cases equivalent to 71% of estimated TB cases were notified by the National Tuberculosis Program (NTP).² Finding missing TB cases have been a major challenge for NTP. Meanwhile, concentrated epidemics of human immunodeficiency virus (HIV) in Nepal have augmented the risk of tuberculosis. TB and HIV co-infection is the leading cause

of mortality among TB patients and people living with Human Immunodeficiency Virus (PLHIVs). Moreover, the prevalence of HIV among TB patients also indicates the spread of HIV into the general population. Despite the provision of HIV testing for all TB patients, routine information system shows very limited coverage of HIV testing among TB patients in Nepal.² Hence, based on the available information, it is difficult to reflect its actual burden. Hence, NTP carried out sentinel surveillance at various DOTS Center to assess the prevalence of HIV among TB patients in Nepal.

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METHODS

A cross-sectional study design was adopted for this sentinel sero-prevalence survey. The survey was conducted at six sentinel sites namely Mahakali Zonal Hospital, Kanchapur, Western Regional Tuberculosis Center (WRTC), Kaski, National Anti-tuberculosis Association (NATA), Morang, United Mission Nepal (UMN), Palpa, National Tuberculosis Center (NTC), Bhaktapur and TB Nepal, Banke. These sites were selected based on the number of TB patients registered for anti-tuberculosis therapy (ATT). These treatment centers, with high caseload of TB patients, were assumed to have greater population coverage representing all geographical regions and socio-demographic characteristics like caste, ethnicity, religion and culture. Under NTP, these sites have been serving as a referral treatment centers providing advanced TB treatment and care services. This study continued for six months starting from March 2017 to August 2017.

The sample size was calculated by using Epi-info STATCAL application assuming a two-sided confidence level at 95%, 80% power (1-B) of the study. The proportion of HIV among TB patients was assumed to be 1.1%, based on the finding from the similar sentinel surveillance conducted by NTP on fiscal year 2013/14.³ The required sample size for the study to monitor the trend of HIV prevalence among TB patients came to be 1,672 TB patients assuming 5% non-response rate. The number of samples from each sentinel sites were selected proportionately considering TB caseloads at respective sites. Consecutive sampling method was used; every patient who meets the eligibility criteria at the particular site was included in the study until the required sample size was reached. Based on the objectives of the study, a structured questionnaire was prepared and finalized by Technical Working Group (TWG) for the sentinel survey comprised of HIV, TB and Laboratory specialists. Statistical Package for Social Science (SPSS version 20) was used for analysis.

Ethical approval for this survey was obtained from Nepal Health Research Council (NHRC). All types of TB patients (smear positive, smear negative, extra-pulmonary) who are equal or above 15 years of age at the time of TB treatment at selected sentinel sites were eligible to take part in the study. TB patients not meeting above inclusion criterions were excluded from the sampling frame. However their right to know the serological status was protected through counselling and referring them to appropriate treatment and testing site. Informed consent, both verbal and written, from each eligible TB patient was obtained prior the participation in the

survey. Similarly participants were informed about their voluntary participation in the survey as well as assured them their right to leave survey at any time for any reasons. All eligible respondents who gave their consent for the participation in the survey were counselled prior (pre-counselling) and after (Post-counselling) testing for HIV infection. Information obtained from all the eligible TB patients who went through the HIV testing were kept confidential and secured at the respective sentinel sites.

Health workers at treatment centers (Laboratory Technician, Survey Coordinator, Counselor) were provided one day orientation, prior the survey, to build their capacity for HIV testing as well as proper recording in the questionnaire. HIV testing was performed as per the testing algorithm recommended by national consolidated guidelines for treating and preventing HIV in Nepal 2014 for the diagnosis of HIV.⁴ The standard national strategy for HIV testing is based on the serial HIV testing algorithm using three different HIV test kits (Determine HIV ½, Uni-Gold HIV and HIV ½ Stat-Pak test kits). Similarly socio-demographic information of the TB patients was also collected through face-to-face interviews using a structured questionnaire. Collected information by health workers were reviewed by Provincial TB Coordinators for the possible errors. Once the information from the respondents was collected in sufficient number, data entry and analysis was assigned to third party to minimize possible biases. The data were entered directly into Statistical Package for Social Science (SPSS version 20) and were analysed for the statistical analysis. The association between socio-demographic characteristics with outcome variable i.e. HIV status were explored using bivariate logistic regression analysis. Value of $P < 0.05$ was considered significant where the confidence interval was set at 95% (95% CI).

RESULTS

The study was carried out among 1664 TB patients registered for the treatment at six sentinel sites during the study period (Table 1). Although the required sample size for the study was 1672 TB patients, 8 eligible TB patients didn't express their willingness to participate in the study. The overall acceptance rate among registered TB patients for HIV testing was 99.5%. Among the total TB patients screened for HIV, 1242 (74.6%) were Pulmonary TB, 422 (25.4%) were extrapulmonary TB. During HIV testing, a total of 41 TB patients were found to be HIV positive resulting HIV seroprevalence among tuberculosis patients to 2.5%. While prevalence of HIV among pulmonary TB cases was 2.8% and among extrapulmonary TB cases, it was 1.7% (Table 2).

Table 1. Detail information regarding the sentinel sites.

Sentinel Sites	Location	Province	Study sample size (%)
Mahakali Zonal Hospital	Mahendranagar, Kanchanpur	Sudurpaschim Province	267 (16.0)
Regional Tuberculosis Center	Pokhara, Kaski	Gandaki Province	330 (19.8)
NATA-Morang	Biratnagar, Morang	Province 1	216 (13.0)
UMN Hospital	Tansen, Palpa	Province 5	177 (10.6)
National Tuberculosis Center	Thimi, Bhaktapur	Province 3	498 (29.9)
TB Nepal-Banke	Nepalgunj, Banke	Province 5	176 (10.6)
Total			1664 (100.0)

Table 2. HIV co-infection among TB patients.

Type of TB	HIV Testing Result		Total (%)
	HIV Negative	HIV Positive	
Pulmonary TB	1208	34	1242 (74.6%)
Extrapulmonary TB	415	7	422 (25.4%)
Total (%)	1623 (97.5%)	41 (2.5%)	1664 (100%)

Table 3. HIV co-infection among TB patients at different Sentinel sites.

Sentinel Sites	Number (n)	HIV Testing Result	
		HIV Negative (%)	HIV Positive (%)
Mahakali Zonal Hospital, Kanchanpur	267	99.6	0.4
Regional Tuberculosis Center, Kaski	330	97.3	2.7
NATA-Morang	216	95.4	4.6
UMN Hospital, Palpa	177	93.8	6.2
National Tuberculosis Center, Bhaktapur	498	98.6	1.4
TB Nepal- Banke	176	98.3	1.7
Total (%)	1664 (100%)	1623 (97.5%)	41 (2.5%)

Table 3 shows the detail information regarding the prevalence of HIV among TB patients at the selected

sentinel sites. Table 4 demonstrates the socio-demographic characteristics of TB patients as well as their association with the prevalence of HIV. More than two third of TB patients (67%) in the study were male. The median age of tuberculosis patients was 32 years with the range of (15-97) years. Majority of the respondents (42%) belonged to age group category of (25-44) years. However, around 9.9% (164) TB patients chosenot to disclose their age. Nearly two out of five TB patients were Janajatis (40%), followed by Brahmin/Chhetri (28%), Dalits (20%), Madhesi/Muslim (12%) respectively.

Table 4. Association between demographic characteristics of TB patient and prevalence of HIV.

Characteristics	Number (n)	HIV status		P value
		Negative (%)	Positive (%)	
		n=1623	n=41	
Age group **				
Less than 25	374	98.9	1.1	0.002
25-44	692	96.7	3.3	
45 and above	434	98.8	1.2	
Age missing (age not disclosed)	164	94.5	5.5	
Sex				
Female	548	97.6	2.4	0.0866
Male	1116	97.5	2.5	
Caste/Ethnicity *				
Dalit	334	97.9	2.1	0.025
Janajati	671	98.2	1.8	
Madhesi/Muslim	198	94.4	5.6	
Brahmin/Chhetri/other	461	97.6	2.4	
Religion *				
Hinduism	1291	97.5	2.5	0.015
Buddhism	280	98.9	1.1	
Islam/Christian	93	93.5	6.5	
Marital status				
Ever married	1267	97.3	2.7	0.302
Unmarried	397	98.2	1.8	
Literacy status				

Illiterate	1139	97.3	2.7	0.717
Literate	525	97.6	2.4	
Occupation *				
Agriculture	649	98	2	0.014
Labourer	233	95.3	4.7	
Housewife	236	95.8	4.2	
Job	133	98.2	1.8	
Others	323	99.3	0.7	

*Significant ** Highly significant

The prevalence of HIV among male TB patients (2.5%) was found comparatively higher than among the female TB patients (2.4%). However, the difference was not statistically significant ($P=0.866$). Similarly, the prevalence of HIV was found significantly ($P<0.01$) higher among the TB patients who choose not to disclose their age (5.5%) than in TB patients belonging to (25-44) years age group (3.3%) and was found lowest among less than 25 years TB patients (1.1%). Prevalence of HIV was found significantly higher among Madhesi/Muslim TB patients (5.6%, $P<0.05$), among Christian/Islam TB patients (6.5%, $P<0.05$) and among the labour (4.7%, $P<0.05$) respectively. Although the prevalence of HIV was found comparatively higher among married (2.7%) and illiterate (2.7%) TB patients, but the association was not found statistically significant.

DISCUSSION

Prevalence of HIV among TB patients was found 2.5%. The prevalence has increased sharply in comparison to the findings from the similar study conducted by NTC in 2013 (i.e. 1.1%).³ However, it has increased slightly in comparison to the study conducted in 2011 (i.e. 2.4%).⁵ Similar studies conducted in different neighbouring countries in Asia have found different results (0.5% in Guangxi, China, 1.0% to 13.8% in different districts of Eastern India, 0.34% in Sindh, Pakistan) which could be due to different socio-geographical, economic context as well different epidemics of HIV and TB.⁶⁻⁸ It was observed that the prevalence of HIV was found more prominent in pulmonary TB patients than extrapulmonary TB patients. In this study, pulmonary TB patients were 1.58 times more likely to have co-infection with HIV than extrapulmonary TB patients. Several other studies conducted in India and China have also found the similar association between TB classification types and HIV status.^{6,9,10} However, this finding contrasts with studies conducted in India and Pakistan which have shown higher prevalence of HIV infection among extrapulmonary TB cases.^{11,12}

This study found that prevalence of HIV among TB patients differed with different gender. Although the association wasn't statistically significant, male TB patients were more likely to have HIV-TB co-infection than female. Global trends have also shown that incident and mortality of TB occurs more in male than female.^{1,13} Similarly for the developing countries like Nepal, where social structure prefers more male dominance than female, male are more involved in outdoor activities involving risky behaviors (like extramarital sexual activities, intravenous drug injection, alcohol consumption and smoking) which could have put them at increased risk for TB and HIV. Movement as well as migration pattern to India could also have affected the result as such TB and HIV endemic areas of India have been the preferred destination among Nepalese migrants for earnings. Similar studies conducted in Nepal, China have also found no any significant association between gender of TB patients and prevalence of HIV.^{5,6} However a study conducted in India found the association highly significant.⁸ This study found that the prevalence of HIV was significantly associated with the age of TB patients. The prevalence of HIV was 3.00 times higher among TB patients aged 25 to 44 years; 1.09 times higher among TB patients aged 45 years and above in comparison to the TB patients aged below 25 years. In this study, TB patients aged (24-44) years were the most affected age group. It could be due to high prevalence of TB and HIV among people belonging to (25-49) years age group.^{1,2,14} However studies conducted in China and India couldn't detect any significant relationship between age of TB patients and prevalence of HIV.^{6,8} This study found that prevalence of HIV was significantly higher among the Madhesi/Muslim TB patients that TB patients belonging to other caste/ethnic groups (i.e. Brahmin/Chhetri, Dalit, Janajati). This could be due to fact that Madhesi/Muslim population are largely concentrated across Terai region where the epidemic of TB and HIV is high.^{2,14} However, a study conducted in Guangxi China couldn't establish any significant association between caste/ethnicity of TB patients and prevalence of HIV.⁶

This study found the significant relationship between prevalence of HIV and religion of the TB patients. TB patients belonging to Islam/Christian by religion were 5.90 times more likely to have HIV; Hindu TB patients were 2.27 times more likely to have HIV in comparison to Buddhist TB patients. Occupation of the TB patients and prevalence of HIV was also found significantly associated in this study. TB patients who are labourer; who are housewives were more likely to have HIV. However, studies conducted in China and Nigeria found no any significant relationship between occupation of

TB patients and prevalence of HIV.^{6,15} In this study, ever married TB patients were 1.5 times more likely to have HIV than unmarried TB patients. However, this study couldn't find any statistically significant relation between prevalence of HIV and marital status of TB patients. Similar studies conducted in China, Nigeria also couldn't establish marital status as a significant predictor for increased risk of HIV among TB patients.^{6,15} Similarly, this study couldn't find any significant association between prevalence of HIV and literacy status of TB patients. Finding is similar to a study conducted in Nigeria.¹⁵ However the prevalence of HIV was slightly higher among illiterate TB patients than literate.

This study couldn't escape out of limitations. This study was conducted among six selected sentinel sites which couldn't cover all the TB cases notified during the study period as well as lacks adequate geographical representation. Similarly, patients receiving TB diagnosis, treatment and care services from the private sector were missed by this study. Information regarding important predictors for TB and HIV like smoking habit, alcohol consumption, diabetic status was missed in this study, which could have otherwise explored additional evidences to strengthen TB-HIV co-infection program in Nepal.

CONCLUSIONS

Prevalence of HIV among TB patients has increased gradually in Nepal. TB patient characteristics like age, caste/ethnicity, religion and occupation were found significantly associated with the prevalence of HIV. Hence, information on the availability of diagnostic and treatment services as well as access to HIV prevention, diagnosis and treatment services need to be increased in these sub-groups of the population. Similarly, interventions like universal HIV testing among TB patients, TB/HIV collaborative activities are necessary to scale up across the country.

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