Original article

Human Immuno-Deficiency Virus co-infection in suspected TB patients

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Introduction: Tuberculosis is one of the major public health problems in Nepal and HIV has become the most potent risk factor for the progression of TB infection as HIV-positive people are more likely to develop TB when newly infected or reinfected with *Mycobecterium tuberculosis.* Our main aim was to determine TB/HIV co-infection cases visiting DOTS center and Research center.

Materials and Methods: The study was conducted in DOTS center of TUTH, Maharajgunj and Infectious and Tropical Disease Research and Prevention Center, Tripureshwor. We included a total of 300 patients with the respiratory tract symptoms and cough more than 3 weeks suggesting the symptom of pulmonary tuberculosis and having risk behaviour towards HIV infection. They were interviewed with a structured questionnaire during October 2006 to July 2007. All of them were screened for tuberculosis by sputum microscopy, AFB culture, radiology and HIV infection by standard ELISA method.

Results: Among 300 suspected TB patients, 79 were diagnosed as pulmonary TB positive patients and 34 as HIV seropositive. The coprevalence of TB/HIV was 4.33 percent (13/300) among total patients among which 12 males and 1 female were found to be coinfected with TB/HIV.

Conclusion: HIV co-infection in pulmonary TB positive cases was 16.46 percent (13/79), which revealed it as an alarming situation in developing countries, like Nepal. More cases were found in young adults aged range from 21-40. Males were found to be more infected than female.

Key words: TB, HIV, Co-infection, DOTS, ELISA

Introduction

Tuberculosis (TB) is the world's most serious public health problem in spite of the availability of effective diagnosis and treatment measures. It is a disease of great antiquity and contributing to more morbidity and mortality than any other bacterial infection[1]. TB remains one of the deadliest threats to public health. Roughly, one third of the world's population is infected and more and more bacterial strains have developed resistant to drugs.

TB primarily attacks the most economically productive group of the society (people aged 15-45 years); the community injury that it causes extends far beyond individual disease and death[2].

Almost 9 million new TB cases occurred in 2004, 80% of them in 22 countries[3]. Ten percent of the infected people, who are immunosuppressive e.g:- with HIV/AIDS, develop active TB disease as HIV weakens the cellular immunity. It is estimated that 6 out of 10 adults in Nepal are infected with TB and 80,000 Nepalese populations have active TB disease. Every year, 40,000 people develop active TB of whom 20,000 have infectious pulmonary disease.

DOTS is the strategy for improving treatment outcome to control tuberculosis by giving drugs to the patients under direct observation of health workers. The treatment success rate in DOTS is now 88%. Nationally, in the year 2005/ 2006, over 34,000 TB patients have been registered and are being treated under the NTP. However, due to rise in HIV epidemic and emergence of drug resistance, DOTS is found to be insufficient to control TB in such condition which is resulting in an immediate need to adopt the new strategy going beyond DOTS that includes intensified case detection of active TB through quality assured bacteriology[4]. Introduction of treatment by DOTS has already reduced the number of deaths; however, 5,000-7,000 people continue to die every year form this disease[5].

Today, Tuberculosis and HIV infection have important and bi-directional interactions that impact on the epidemiology, natural history, clinical presentation and management of each pathogen[6]. HIV infection increases the risk that a latent TB infection will reactivate and that new infection or re-infection with *M. tuberculosis* will progress to active disease. The natural history is accelerated with progression form infection to disease occurring within 3 months. The accelerated natural history leads to rapid spread of strains that are circulating in the population including those that are drug resistant. TB also accelerated the course of HIV disease by activating viral replication and increasing the rate of decline of CD4 T cell counts and also activates cells harboring latent HIV infection and promoting viral replication[7].

HIV infection is the greatest single risk factor for developing tuberculosis ever identified. It is estimated that one third of the 40 million people living with HIV worldwide are co-infected with TB. People living with HIV are up to 50 times more likely to develop TB in a given year than HIV negative people. Furthermore, without proper treatment, approximately 90% of those living with HIV die within months of contracting TB. In Nepal, 75% of AIDS patients have had pulmonary tuberculosis. In case of Nepal, estimated prevalence of HIV in new adult TB cases is 2.9% and estimated incidence of TB in HIV positive adults aged 15-49 years is 0.9(thousands).

People living with HIV are more susceptible to multidurg resistant TB (MDR-TB) through nosocomial transmission, malabsorption of TB medication, acquired rifampicin resistance and other type of poor response to TB treatment. However, coinfected patients are also less likely to transmit resistant strains owing to the high mortality in MDR-TB/ HIV patients.

HIV and TB form a lethal combination. HIV positive individuals do not have the internal immune-system resources to keep the mycobacterium TB in check As a result; they succumb to the disease at an alarming rate. Currently, over 12 million people are co-infected and rising.

Though the co-epidemic is rising and being common threat to the control programme, most of DOTS centers and TB health centers have no policies for detection of HIV in TB patients. So, the study, concentrated in DOTS center and Research center, where patients suspected to have TB infection visiting for their check up, were included as study population. The study was conducted to access the prevalence of HIV infection is suspected TB patients coming to TB centers, which may help to access the impact of HIV on tuberculosis epidemic. Estimation of HIV in TB patients visiting the TB center can act as early warning system for the spread of TB due to HIV.

Material and Methods

The study was conducted in Health Research Laboratory, Institute of Medicine, Tribhuvan University Teaching Hospital, Maharajgunj during October 2006 to July 2007. Altogether, 300 TB suspected cases, showing sign and symptom suggesting TB were included by periodic visit to DOTS center of TUTH, Maharajgunj and Infectious and Tropical disease research and prevention center, Tripureshwor. Informed/oral consent was taken and each was questionnaired to collect personal information, medical history and other variables related with TB and HIV infection. From each patient 3 sputum specimens was collected after counseling the patient; first specimen on the spot (during their first visit in clinic), second specimen in the early morning on next day and third specimen on spot during their visit in center next day. Blood sample from each patient was also collected and serum was separated. Sputum sample was processed for smear microscopy by Ziehl-Neelsen staining technique and result was reported according to WHO/IUATLD positively grading system[8]. Sputum samples were cultured in solidified L-J media after processing of sample by modified petroff's method followed by incubation at 37^0C from 6-8 weeks. Serum samples were processed for detection of HIV infection by using sandwich ELISA method. Data and result obtained were entered and analyzed using SPSS and Excel.

Results

Among 300 cases enrolled in the study, as shown in (Table1), 205 (68.33%) were male and 95 (31.67%) were female. The majority of them were in age group 21-30 followed by

51-60 years (20.67%). Statistical analysis showed that mean age as 40.7 years and median age as 39.4 years.

Table 1: Age and Gender Distribution of studied population

Age group	Male		Female		Total	
	No	Percentage	No	Percentage	No	Percentage
11-20	9	4.39	6	6.32	15	5
21-30	49	23.90	29	30.53	78	26
31-40	42	20.49	17	17.89	59	19.67
41-50	34	16.59	15	15.79	49	16.33
51-60	40	19.51	22	23.16	62	20.67
61-70	27	13.17	6	6.32	33	11
71-80	4	1.95	0	0	4	1.33
Total	**205**	**100**	**95**	**100**	**300**	**100**

Out of 300 suspected tuberculosis cases, 79 of them were diagnosed to be TB positive by smear microscopy, AFB culture and radiology. Highest prevalence of tuberculosis patients were found in the age group 21-30 years (18/79) which constitute 22.78% followed by 51-60 years (17/79). More male patients were found to be TB infected which was found to be significant (c^2= 11.47, P<0.01) as shown in table no 2.

Table 2: Age and Gender Distribution of total TB positive patients

Age group	Male		Female		Total	
	No	Percentage	No	Percentage	No	Percentage
11-20	1	1.51	0	0	1	1.27
21-30	15	22.73	3	23.08	18	22.78
31-40	11	16.67	4	30.77	15	18.99
41-50	12	18.18	3	23.08	15	18.99
51-60	15	22.73	2	15.38	17	21.52
61-70	12	18.18	1	7.69	13	16.46
Total	**66**	**100**	**13**	**100**	**79**	**100**

All 300 patients tested for HIV infection, 11.33% (34/300) were found to be HIV sero-positive in which 21 sero-positive cases were reported in whom TB infection was not found. Out of 34 HIV sero-positives (Table 3), higher number of male i.e, 70.59% (24/34) were found to be HIV sero-positive than female i.e, 29.41% (10/34) (Table 3-4).

Table 3: Distribution of patients tested for HIV

	Male	Female	Total
HIV positive	24	10	34
HIV negative	181	85	266
Total	**205**	**95**	**300**

Table 4: Age and Gender Distribution of HIV positive patients

Age group	Male		Female		Total	
	No	Percentage	No	Percentage	No	Percentage
11-20	0	0	1	10	1	2.94
21-30	7	29.17	1	10	8	23.53
31-40	10	41.67	5	50	15	44.12
41-50	5	20.83	2	20	7	20.59
51-60	2	8.33	1	10	3	8.83
Total	**24**	**100**	**10**	**100**	**34**	**100**

Among 300 patients included, 4.33% (13/300) were found to be TB/HIV co-infected cases in which highest co-infected cases were reported in age group 31-40 years followed by 41-50 years (Table 5). TB/HIV co-infected patients were ranged in age from 25 years to 55 years. Highest prevalence of co-infected patients 38.46% (5/13) were reported in age group 31-40 years followed by 41-50 years with 30.77% (4/13).

Table 5: Correlation of HIV with gender in TB infected patients

Infection Sex	TB infection Number	TB/HIV Co-infected Number	Percent	Chi Square (X^2)
Male	66	12	18.18	X^2 = 0.67
Female	13	1	7.69	P=0.01
Total	**79**	**13**	**16.46%**	

Among 13 co-infected patients, only one female (7.69%) belonging to age group 31-40 years was found to be co-infected, rest of 12 (92.31%) were males. Significant relationship was found between smoking/alcoholic habit (Table 6) and the subsequent development of TB (c^2=9.52, P<0.05 for smoking habit and c^2=5.297, P<0.05 for alcoholic habit).

Table 6: Correlation of tuberculosis with smoking and alcoholic habit of the patients

Variables	TB positive (79)n(%)	TB negative (221)n(%)	Chi square
Smoking			
Yes	64 (31.84)	137 (68.16)	c^2 = 9.52
No	15 (15.15)	84 (84.85)	P<0.05
Alcohol			
Yes	56 (31.11)	124 (68.89)	c^2 = 5.297
No	23 (19.17)	97 (80.83)	P<0.05

Highest numbers of IDUs 47.06% (16/34) with HIV sero-positive were followed by migrators with 26.42% (10/34). In both TB and HIV infected patients, occupational status (Table 7 and 8) showed majority of them being involved in different service i.e, 22.78% (18/79) and 41.18% (14/34)

respectively.

Table 7: Occupational Status of TB infected persons

Occupation	Number	Percent
Service	18	22.78
Factory employee	16	20.25
Agriculture	12	15.2
Housewife	9	11.39
Unemployed	9	11.39
Business	7	8.87
Driver	4	5.06
Government employee	4	5.06
Total	**79**	**100**

Table 8: Occupational status of HIV infected persons

Occupation	Number	Percent
Service	14	41.18
Business	6	17.65
Factory employee	5	14.71
Housewives	4	11.76
Driver	3	8.82
Agriculture	2	5.88
Total	**34**	**100**

Discussion

The study revealed 4.33% (13/300) of co-infection cases in suspected TB patients enrolled which showed low prevalence among TB patients in comparison to the previous study done by Sherchand et al and UMHT hospital[9]. However, among TB infected patients, the prevalence of co-infection was found to be 16.46% (13/79). Highest co-infected cases were predominantly observed in age group 31-40 years i.e. 5 (38.46%) followed by second highest prevalence 4 (30.77% in 41-50 years. Among 13 TB/HIV co-infected patients, higher infected number was found in males i.e. 12 (92.31%) than female i.e. only one case (7.69%) as shown in table no 3.

In TB infected population, higher prevalence of TB infection was seen in age group 15 years to 60 years which showed the greater effected population is productive age group. So, it is greatly affecting the economic and social status of country. Gender wise distribution of TB infected population showed 83.54% male and only 16.45% to be female which indicated female to be 4-5 times less infected than male. Such gender differentiation was also seen in HIV infection and in TB/HIV co-infection cases. Such differentiation might be due to exposure of male to external environment in case of TB infection and due to risk behaviour of male regarding their sexual character in case of HIV infection. Though these reasons have been seen as direct cause of such differentiation, other reasons like quick and easy access to the clinic/doctor and visiting the health centers independently in case of male have been found to play greater role in diagnosis of infection in male patients than female. Males' and females are almost equally distributed with in the population of our country and with such population distribution between sexes, the low detection of female TB cases remains a troubling public health issue demanding urgent focused study.

The study demonstrated that major risk groups of HIV infection were found to be IDUs, Housewives whose partners were out of hometown for long time in case of work and migrators who were living far from their home and family. It has been reported that in most of the Asian countries, IDUs are the first community to be affected by HIV and Nepal was the first developing country to establish a harm reduction program with needle exchange for IDUs. HIV prevalence among Nepal's estimated 19,850 IDUs varies by location, 22% of IDUs are HIV positive in Pokhara, whereas 52%, 33% and 8% are HIV positive in Morang, Sunsari and Jhapa districts respectively[10]. Since highest percentage of IDUs is still being reported in Kathmandu, this study based on Kathmandu valley might have reported highest number of IDUs i.e. 16/34 (47.06%) with HIV sero-positive. Followed by IDUs, second highest number 10/34 (26.42%) was found in case of migrators. In developing countries like Nepal, both internal and external migration for seasonal and long tern labor range form 1.5 to 2 million[11]. As recorded during questionnaire, occupational wise highest number of both TB and HIV patients were found to be associated with different services followed by factory employee in TB infection and Business in HIV infection. Both alcoholic and smoking habit were found to be major risk in TB development which were fond to have statistically significant relationship with TB infection.

Conclusion

Through this study, TB/HIV co-infection was found to be 4.33% (13/300). Though this problem is currently seem to be small but has been increasing in the alarming rate in developing countries like Nepal that is creating great problem in TB control programmes. Although HIV is considered as concentrated epidemic, there is increasing trend in HIV infection and there could be a substantial increase in TB/HIV co-infected cases in future. So, extensive

study is in immediate need to get more representative data of TB/HIV co-infection to develop national policy regarding this speedily emerging issue.

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