PREVALENCE AND CD4 CELL COUNT PATTERN OF TB CO-INFECTION AMONG HIV INFECTED INDIVIDUALS IN NEPAL

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ABSTRACT

Background: Mycobacterium tuberculosis (TB) and Human Immunodeficiency Virus (HIV) infections are two major public health problems in many parts of the world, particularly in developing counties like Nepal. The objective of the study is to find out prevalence and clinical presentation of the TB co-infection among HIV infected individuals and pattern of CD4 cell count in relation to types of TB and response of ART.

Methodology: This is a cross-sectional study carried out in three VCT clinics from Dharan and Kathmandu from April 2010 to March 2011. The appropriate samples, 313 HIV individuals were taken as study sample.

Results: The study revealed that more than 36% of individuals were co-infected with TB. Among them, nearly 65% had pulmonary TB, more than one-forth had gland TB. There is significant association of TB co-infection among male compared to females (P=0.021). Fever, weight loss and cough were found to have significant symptoms associated with TB-HIV co-infection. The average CD4 count among TB co-infected population was significantly less compared to uninfected ones just before starting ART (P=0.022) and even after six months (P=0.001). After one year of ART continuation, there was no significant association on average CD4 count among the two groups. But then, the mean CD4 count became more in TB co-infected individuals compared to those who had no TB co-infection.

Conclusion: TB-HIV co-infection is an emerging medical issue in Nepal. More than one third of HIV patients are co-infected with TB. Consideration of TB need to be made while caring patients with HIV infection and vice versa. ART plays very important role in increasing CD_4 cell count among TB-HIV co-infected patients.

Key words: HIV, TB co-infection**,** CD4 cell count, Clinical features, ART

INTRODUCTION

The United Nations Joint Programme on HIV/AIDS (UNAIDS, 2009) report estimated that 33.4 million people are living with Human Immunodeficiency Virus (HIV) in worldwide, and one third of them are co-infected with tuberculosis (TB). HIV infection increases susceptibility to TB and is the most potent factor in transferring latent or recently acquired TB infection to active clinical diseases. In addition, TB in high HIV prevalence populations is a leading cause of morbidity and mortality. TB patients have been suggested to be an important population for finding of HIV infections. Therefore, prevention and control of co-infection is vital to reduce the epidemic of TB and HIV/ AIDS.[1]

An estimated 2 million deaths have been attributed annually to HIV/AIDS, with approximately 250,000

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pediatric deaths.[2] In infants and young children, immune system immaturity and high viral loads lead to a high risk of rapid disease progression.[3]

Since the detection of the first AIDS case in 1988, the HIV epidemic in Nepal has evolved from a low prevalence to concentrated epidemic. As of 2009, national estimates indicate that approximately 63,528 adults and children are infected with the HIV virus in Nepal, with an estimated prevalence of about 0.39% in the adult population.[4]

Mycobacterium tuberculosis and human immune deficiency virus infections are two major public health problems in many parts of the world, particularly in many developing counties.[1] Co-infection with HIV may worsen the course and complicate the diagnosis and management of TB. Overall, HIV-infected patients have 60% higher risk of acquiring TB in comparison to 10% in non HIV group and this risk remains elevated throughout the course of HIV disease.[5] Prompt diagnosis and treatment are essential to improve drug-resistant TB outcomes, but TB diagnosis in patients with HIV co-infection is challenging, particularly in resource-limited settings. HIV-infected TB patients have higher rates of extra-pulmonary disease, atypical clinical presentations, and normal chest radiographs.[6]

Tuberculosis and HIV control programmes clearly have mutual concerns: the prevention of HIV infection and the treatment of HIV/AIDS should be components of tuberculosis control, and tuberculosis care and prevention should be priorities in the management of HIV/AIDS.[7] TB is the most frequent life-threatening opportunistic disease among people living with HIV and remains a leading cause of mortality, even among persons receiving antiretroviral therapy (ART). Clinical trials have shown that isoniazid preventive therapy (IPT) dramatically reduces the incidence of TB among people living with HIV. A 2004 Cochrane Review found that IPT reduced the risk of TB by 33% overall and by 64% when targeted to people living with HIV who had a positive tuberculin skin test. A recent retrospective study also showed that IPT significantly reduced the incidence of TB even among people living with HIV and receiving ART.[8]

CD4 T cells are critical in the control of *M. tuberculosis* infection, as quantitative and qualitative deficiencies of these effecter cells in HIV-infected individuals increase the rates of both primary and reactivation disease. While the lifetime risk of developing active TB is approximately 10% for immune-competent persons following initial infection, for persons with HIV co-infection the annual risk can exceed 10%, and the risk of TB reactivation rises as the CD4cell count declines.[2] HIV-infected persons are at risk of TB throughout their course of disease, even after they respond to ART.[9]

In Nepal, the first case was demonstrated in 1988 and the concept of treating HIV infection with highly active antiretroviral treatment (HAART) was introduced quite later.[10] Among those with HIV infection, the CD4+ T-lymphocyte count is the major indicator of immunodeficiency, a main factor in deciding whether to initiate HAART, and an important parameter in monitoring treatment response. Despite current recommendations to start HAART at CD4+ counts of 350 cells/mm3 or greater, the reality is that many patients, even in developed countries, are still being diagnosed and initiate treatment late in the course of their HIV infection.[11]

Treatment of tuberculosis patients in resource-limited countries with concurrent epidemics of Hepatitis C Virus (HCV), Hepatitis B Virus (HBV), and HIV may be associated with significant hepatoxicity. Serologic screening of tuberculosis patients for HBV, HCV and HIV or using behavioral algorithms to identify patients in need of intensive monitoring during anti-tuberculosis therapy may reduce this risk.[12]

The present study is focused to find out prevalence of TB among HIV infected individuals, clinical features and ART response on CD_4 cell count.

METHODOLOGY

Setting: The study was carried out in three different places viz. BPKIHS, Dharan; SPARSA Nepal, Kathmandu and Sukhra Raj Tropical and Infectious Disease Hospital, Teku, Kathmandu (TEKU Hospital) from April 2010 to March 2011. It was done with due privacy in their respective VCT Clinic by face to face interview with the HIV infected individuals based on pretested semi-structured questionnaire. Also, an address was given to the past medical documents, for better

authenticity of the information, which most of them had themselves.

Study subjects: The target population of the study was the HIV infected persons visiting the VCT Clinic either for taking medications or for follow-up of regular check up during 1 year period. Among those who gave supportive consent, an approach was made to include all individuals whether they were already taking medications or about to start. A total of 313 HIV infected individuals were interviewed.

Study design and sample size: This is a cross sectional, descriptive study which includes primary and secondary data. Based on the prevalence of TB co-infection among HIV individuals (33.3%)[1], the required sample size was calculated as 315 based on the precision of 5.33 (16% of prevalence) at 95% confidence limit after adding 5% for non-response. Two individuals disagreed to participate in the study.

Exclusion criteria: Those who didn't give consent and who couldn't report CD_4 count were excluded. The CD_4 count was done by the patients themselves.

Statistical analysis: The data was entered into Microsoft Excel 2007 and analyzed in SPSS 17.0. Mean, median and standard deviation were calculated. Mann-Whitney Test and Chi square test were applied to find out statistical significance in numeric and categorical data respectively. Probability of significance was set at 5% level of significance. Odds Ratio (OR) and its 95% confidence interval (CI) were also calculated to examine strength of association between the categorical variables and its' limit.

Ethical consideration: Ethical consent was taken from institutional review board BPKIHS, Dharan; SPARSA NEPAL, Kathmandu and Sukhra Raj Tropical and Infectious Disease Hospital (Teku, Kathmandu). Verbal consent was also taken with the individuals who were diagnosed to be HIV infected prior to interview. Privacy of participants was maintained during interview with due consideration of the emotional aspect.

The normal oral or ear temperature is 37° C but may range between 35.8°C and 37.2°C.[13] The temperature more than this was considered to be fever. Diarrhea was defined as 2 or more loose or watery stools per day for more than 2 consecutive days.[14] Chronic diarrhea was defined as diarrhea persisting for more than 14 days.[15] Tuberculosis co-infection was ascertained by past medical records and history of taking anti-tubercular therapy. HBV and HCV infection were considered positive with respect to serological tests as per medical records. Individuals who gave history of use of syringes for self administration of drugs were considered intravenous drug users (IDU). Most of IDU, but not all, had multiple scar marks on their forearm. The threshold for starting ART was considered to be CD_4 count to be less than 250/μL. Weight loss may be due to lack of food intake (anorexia, dysphasia or vomiting), mal-absorption of nutrients, or a systemic effect of important diseases such as cancer (within or outside the gastrointestinal tract), inflammatory bowel disease or chronic infections such as TB (within or outside the gastrointestinal tract).[16] Weight loss in HIV infected patients can be due to HIV wasting syndrome or due to chronic infections like tuberculosis. HIV wasting syndrome has been defined by the Centre for Disease Control (CDC), USA, as involuntary weight loss greater than 10% of baseline weight associated with either chronic diarrhea for at least 30 days or chronic weakness or documented fever for at least 30 days in the absence of a concurrent illness or condition other than HIV infection that could explain findings (e.g., tuberculosis, cryptosporidiosis, or other specific enteritis).[17] We were mainly focused on weight loss due to tuberculosis.

RESULTS

The mean age of the individuals was 33.7 years which ranged from 2 years to 67 years. Around one-third were males. Almost 40% of males and 25.3% of females had TB co-infection. In the study sample, 72.8% were married, 8% were unmarried, 14.1% were single, 5.1% was widow/widower. Of the total sample 65.5% were IDU and 34.5% were non-IDU. Majority of them (94.2%) were receiving ART and 5.8% were to start ART or not taking ART. The study revealed that 36.1% persons were co-infected with tuberculosis. About 5.75% had HBV and 41.53% had HCV infection (Table 1).

There was significant association of TB co-infection among male compared to females

Table 1. Socio-demographic profile of HIV infected individuals in three VCT centers who volunteered for the study. (n=313)

Variables		Frequency	%
Sex	Male	234	74.8
	Female	79	25.2
Marital Status	Married	228	72.8
	Unmarried	25	08.0
	Single	44	14.1
	Widow	6	01.9
	Widower	10	03.2
Living with (for consideration of social support)	Family	193	61.7
	Rehabilitation center	67	21.4
	Alone	51	16.3
	Friends	2	00.6
Reason for First Recognition of Having acquired HIV Infection	Increased Severity of Presenting Illness	180	57.5
	Accidental Examination of Blood	65	20.8
	Spouse Being HIV positive	49	15.6
	Deliberate Checkup for HIV	12	03.8
	Presence of Risk Behavior(s)	7	02.2
TB Co-infection	Yes	113	36.1
	No	200	63.9
IDU	Yes	205	65.5
	No	108	34.5
ART	Being Taken	295	94.2
	Not Being Taken	18	05.8
Hepatitis Co-infection	HBV	18	5.75
	HCV	130	41.503.0
VCT Centers Visited	BPKIHS	65	20.8
	SPARSA Nepal	95	30.4
	TEKU HOSPITAL	153	48.9

(OR=1.95, CI=1.06-2.37, P=0.021). Regarding the clinical feature of HIV individuals, 53.8% had fever, 46.5% experienced weight loss, 41% suffered from chronic diarrhea, 37.2% had cough, 34.4% had rashes, 28.5% had headache, 23.6% used to get fatigue easily, 12.8% had oral lesions, 7.6% had blurred vision, 3.8% genital lesions and 2.8% had night sweats (Table 2). Around two third had pulmonary TB, 25.7% had gland TB, 5.3% had spinal TB, 2.7% had abdominal TB and 1.8% had tuberculosis of Meninges (Figure 1).
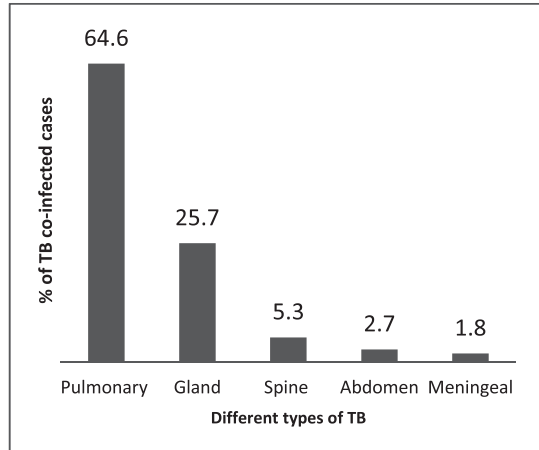

Figure 1. Different types of TB co-infection (%) among HIV positive individuals in three VCT centers. (n=113).

But among TB co-infected ones the presenting clinical features were quite different. Around 83% had fever, 69% experienced weight loss, 59.3% had cough, 31% suffered from chronic diarrhea, 29.2% had headache, 21.2% used to get fatigue easily, and 4.4% had night sweats (Figure 2.)
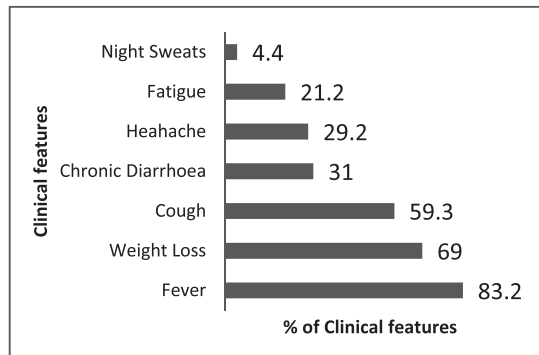

Figure 2. Clinical presentation HIV infected individuals co-infected with of TB in three VCT centers. (n=113).

Fever was found to be significantly associated with TB co-infection (OR=11.27, CI=6.11-20.99, P<0.001). Weight loss was also found to be significantly associated with TB co-infection (OR=5.73, CI=3.36-9.81, P<0.001). Similarly, cough had significant relation with TB co-infection (OR=5.83, CI=3.39-10.05, P<0.001) (Table 2.).

Table 3 shows the average CD4 count among those individuals who had TB co-infection was found to be significantly less compared to the individuals who didn't have TB co-infection in case of just before starting ART (P=0.022). Similarly, after six months, the mean CD_4 count was significantly

associated among them (P=0.001). But after one year of starting ART, there was no significant association on average CD4 count among the two groups. However, data shows a slight increment in average CD4 count among TB co-infected persons than not infected persons. Similar association was observed after 1.5 years, 2 years, 2.5 years, 3 years and 3.5 years.

Table 4 demonstrates those population who were taking ART, had mean CD4 count of 180.16 (SD=98.97 and median CD4 count= 168) just

before starting ART compared to mean CD4 count of 447.78 (SD=166.05 and median =425) in the individuals who were not taking ART. Mean CD4 count was in increasing pattern without any decline for two and half years among the population taking ART. But in succeeding six months' duration, the mean CD4 count decreased to 379.39 (SD=147.69 and median =376.5). In subsequent six month the mean CD4 count increased to 410.28 (SD=168.47 and median CD4 count=376.5). The mass not taking ART had falling pattern of mean CD4 count for one and half year.

Table 2. Clinical features in HIV infected people along with tuberculosis co-infection. (n=113)

Variables Yes(n=113) %		Presence of TB Co-infection		Total (n=313)	OR (CI)	χ^2 value	P value
		No(n=200) **%**					
Clinical features	Fever	83.2	34.9	155	11.27 (6.11-20.99)	80.18	<0.001
	Weight loss	69.0	32.0	134	5.73 (3.36-9.81)	49.64	<0.001
	Cough	59.3	22.9	107	5.83 (3.39-10.05)	49.55	<0.001
	Chronic diarrhea	31.0	47.4	118	0.63 (0.38-1.06)	3.41	NS
	Headache	29.2	28.0	82	1.27 (0.73-2.20)	0.83	NS
	Fatigue	21.2	25.1	68	0.96 (0.52-1.74)	0.02	NS
	Night sweats	4.4	1.7	8	3.04 (0.62-16.39)	1.44	NS
Sex	Male	39.7	60.3		1.95 (1.06-2.37)	5.329	0.021
	Female	25.3	74.7				
NS-not significant							

Table 3. Change and comparison of CD$_4$ cell count in HIV infected persons six monthly, among those who had TB co-infection and those who hadn't, during the course of ART for three and half years. (n=313)

CD4 Count (Six Monthly)	Presence of TB Co-infection		Total	P value
	Yes	**No**		
Just Before Starting ART (Mean ± SD), Median, No.	(171.65 ± 101.48), 161.00, 113	(209.05±128.95), 182.00, 200	(195.55±120.94), 172.00, 313	0.022*
At 6 Months' Duration (Mean ± SD), Median, No.	(251.42 ± 141.59), 221.00, 106	(281.94±106.63), 268.00, 184	(270.79±121.27), 255.50, 290	0.001*
At 1 Year's Duration (Mean ± SD), Median, No.	**(311.87 ± 180.88), 283.00, 87	(297.61±116.67), 304.00, 142	(303.03±144.24), 293.00, 229	0.576
At 1.5 Years' Duration (Mean ± SD), Median, No.	(344.92 ± 172.20), 305.00, 62	(319.52±129.73), 327.00, 112	(328.57±146.30), 317.50, 174	0.757
At 2 Years' Duration (Mean ± SD), Median, No.	(368.42 ± 187.55), 335.00, 45	(315.82±123.84), 327.00, 76	(342.07±153.81), 330.00, 121	0.084
At 2.5 Years' Duration (Mean ± SD), Median, No.	(433.94 ± 259.33), 385.00, 18	(372.11±158.91), 347.00, 38	(391.98 ± 196.53), 347.00, 56	0.611
At 3 Years' Duration (Mean ± SD), Median, No.	(448.00 ± 226.75), 425.00, 8	(359.79 ± 114.68), 376.00, 28	(379.39 ± 147.69), 376.50, 36	0.446
At 3.5 Years' Duration (Mean ± SD), Median, No.	(474.29 ± 255.59), 617.00, 7	(385.39 ± 121.13), 384.00, 18	(410.28 ± 168.47), 387.00, 25	0.363

P value was calculated by Mann-Whitney Test (non-parametric test)
* Significant value
**After one year of having taken ART, the mean CD4 count became more in TB co-infected individuals compared to those who had no TB co-infection. Then subsequently the mean CD4 count was always at higher level among those who had TB compared to those who hadn't.

Table 4. Change and comparison of CD_4 count in HIV infected individuals six monthly, among those who were under ART and those who weren't, during the course of ART for a period of three and half years. (n=313)

CD$_4$ Count (Six Monthly)	Receiving ART		Total	P value
	Yes	**No**		
Just Before Starting ART (Mean ± SD), Median, No.	(180.16 ± 98.97), 168.00, 295	(447.78 ± 166.05), 425.00, 18	(195.55 ± 120.94), 172.00, 313	<0.001*
At 6 Months' Duration (Mean ± SD), Median, No.	(268.85 ± 120.68), 255.00, 286	(409.00 ± 86.08), 431.50, 4	(270.79 ± 121.27), 255.50, 290	0.013*
At 1 Year's Duration (Mean ± SD), Median, No.	(300.77 ± 143.20), 291.50, 226	(473.33 ± 144.68), 400.00, 3	(303.03 ± 144.24), 293.00, 229	0.026*
At 1.5 Years' Duration (Mean ± SD), Median, No.	(328.21 ± 146.65), 315.00, 173	-	-	-
At 2 Years' Duration (Mean ± SD), Median, No.	(342.07 ± 153.81), 330.00, 121	-	-	-
At 2.5 Years' Duration (Mean ± SD), Median, No.	(391.98 ± 196.53), 347.00, 56	-	-	-
At 3 Years' Duration (Mean ± SD), Median, No.	**(379.39 ± 147.69), 376.50, 36	-	-	-
At 3.5 Years' Duration (Mean ± SD), Median, No.	(410.28 ± 168.47), 387.00, 25	-	-	-

P value was calculated by Mann-Whitney Test (Non-parametric test)
* Significant value
**Sudden decline in mean CD_4 count at the time of three years after gradual increase in preceding two and half years.

DISCUSSION

The present study estimated the prevalence of TB co-infection among HIV positive individuals to be 36.1 % in context Nepal which is consistent with worldwide statistics.[1] There was significant association of TB co-infection among male compared to females (OR=1.95, CI=1.06-2.37, P=0.021). Among TB co-infected cases, fever was the commonest clinical feature, followed by weight loss and cough. A night sweat, which was considered as one of the constitutional symptoms didn't have dominant figure in this study.

Other symptoms among the cases were chronic diarrhea (31 %), headache (29.2%), easy fatigue (21.2%) and night sweats (4.4%). However only fever, weight loss and cough were the significant symptom associated with TB co-infection. The clinical presentation of TB in HIV infection is affected by the degree of underlying immune suppression.[5] Our study is consistent with this fact because we found that the mean CD_4 counts of the patients co-infected with TB being much less than in those who were not. Of all symptoms, weight loss can be of utmost important. Studies have repeatedly documented that the existence and magnitude of weight loss predict morbidity and

mortality.[18,19] Correlations have been established between high HIV viral load, low CD4 cell counts, and weight loss. In HAART experienced patients with suppressed plasma viral load, weight loss has been attributed to the persistence of HIV in peripheral blood monocytes and macrophages. The persistence of HIV leads to excessive cytokine activation and dysregulation, and this in turn triggers various metabolic abnormalities that lead to weight loss such as increase in resting energy expenditure, proteolysis, and hypercatabolism.[17] A study reported that as little as 5% of weight loss over 4 months was associated with decreased survival.[20]

We also found that the majority of the patients lived with family .i.e. the major bulk of HIV infected patients had good support from the family as 61.7% lived with their family. Had there been no co-operation from the family, they would not be staying along with the family members. Stay in rehabilitation center counted for second largest population (21.4%). It was due to the reason that they wanted to live with individuals having same disease so that they could share their feelings and learn more about the disease. Also, a good number of populations lived alone (16.3%) which may be indicative of lack of social support. Environmental

social determinants, such as housing conditions, social networks, and social support, are also key drivers for HIV/AIDS, viral hepatitis, STDs, and TB. Kidder et al. conducted a study among housed and homeless individuals with HIV/AIDS and found that homeless people with HIV/AIDS had poorer health status, were less adherent to medication regimens, and were more likely to be uninsured and to have been hospitalized. [21]

There is effect of tuberculosis on mortality in HIV positive people. A Meta-Analysis shows that people living with HIV (PLWH) with TB face an approximately two times higher risk of death from all causes compared to PLWH without TB. The increased hazard of mortality implies that PLWH with TB die earlier compared to PLWH without TB.[22] In our study more than one third (36.1%) persons were co-infected with TB.

Our study revealed that nearly two third (64.6%) of TB infected patients had pulmonary TB followed by gland TB (25.7%) and spinal TB (5.3%). This supports that prime concern of co-infection of TB in HIV positive individuals is that of pulmonary TB followed by gland TB. At CD4+ cell counts greater than 350/µL, TB disease is most often limited to the lungs, histopathologic results are similar to those in HIV-seronegative patients (i.e., granuloma with or without caseation), and extra-pulmonary involvement, when present, usually is nodal or pleural (Burman and Jones, *Semin Respir Infect*, 2003). In advanced HIV infection, pulmonary involvement is still the most common TB presentation; however, extra-pulmonary involvement is observed in approximately 70% of patients with CD4+ cell counts less than 100/µL, and up to 50% of those with CD4+ cell counts greater than 50/µL will have positive TB blood cultures.[5]

With proper treatment, a person with infectious tuberculosis very quickly becomes non-infectious – probably most often in less than two weeks - and so can no longer transmit infection to others.[7] Highly active antiretroviral therapy (HAART) improves the immune function and decreases morbidity, mortality and opportunistic infections in HIV-infected patients. HAART improves immune function by suppressing HIV viral replication and increasing CD4+ T-cell counts. [23]

With respect to our study- before starting ART, the average CD4 count was found to be significantly less among TB-HIV co-infected patients compared to those who didn't have TB co-infection. Similarly, after six months, the mean CD4 count was significantly associated among the two groups. After one year of having taken ART, the mean CD4 count became more in TB co-infected individuals compared to those who had no TB co-infection. Then subsequently the mean CD4 count was always at higher level among those who had TB compared to those who hadn't.

The risk of TB following *M. tuberculosis* infection is determined mainly by the individual's immune status (and hence HIV infection is a potent risk factor for tuberculosis).[6] It was found that the mean CD_4 count was in increasing pattern without any turn down for three and half years among TB co-infected individuals, but the group which were TB free had fluctuating mean CD4 count. This shows that there is marked increase in CD4 count in TB co-infected individuals despite lower initial CD4 count before starting ART. But after three and half years the variation is somewhat similar. Studies of the kinetics of CD4+ count response post-HAART indicate that the CD4+ count increases rapidly during the first 3-6 months, in part due to release of memory T-cells from lymphoid tissue, and then increases slowly during the next 3-4 years, reflecting reconstitution of the immune system. The magnitude of CD4+ recovery may depend on a variety of factors, including maintenance of virologic suppression, age, and CD4+ count at HAART initiation.[11]

There are no validated markers to differentiate those who will have a more robust CD4 response to ARV from those who will not.[24] Antiretroviral drug concentrations are among the most important determinants of clinical response to a drug accounting for both toxicity and efficacy.[25] We also tried to see pattern of change of mean CD_4 count among different type of TB co-infection. Those people who had pulmonary TB, had mean CD4 count of 157.86 just before starting ART compared to mean CD4 count of 214.21 in the individuals who had TB of gland and 127.17 in the individuals who had TB of spine. The mean CD_4 count of 157.86 for pulmonary TB is quite low as compared to other similar studies. It could have been so because there

was also hepatitis infection among the volunteers of the study. Among TB co-infected individuals, 6.2% had HBV alone, 38.9% had HCV alone and 2.7% had both HBV and HCV infection. Another explanation could be that TB facilitates HIV viral replication to a greater extent in the earlier stages of HIV infection than during advanced illness, when viral replication is already at its peak.[26] We found that the mean CD4 count was in rising pattern without any decline for three and half years among the population with pulmonary TB, but the ones having TB of gland also had rising pattern of mean CD4 count but only for two years. Then the mean CD4 count had falling pattern till three and half years. The mass of people having TB of spine had fluctuating pattern of mean CD4 count as shown in figure 3.
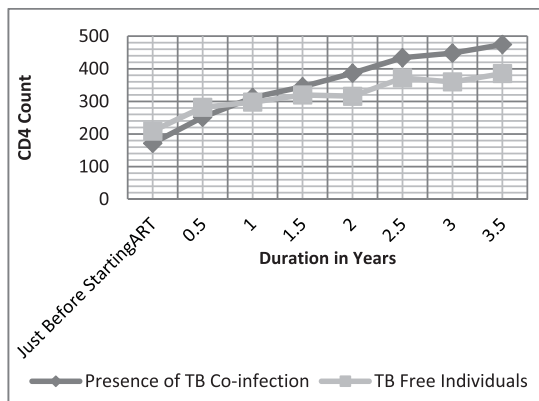

Figure 3. Change and comparison of mean CD_4 cell count in HIV infected individuals six monthly, among those who had TB co-infection and those who hadn't, during the course of ART for a period of three and half years. (n=313).
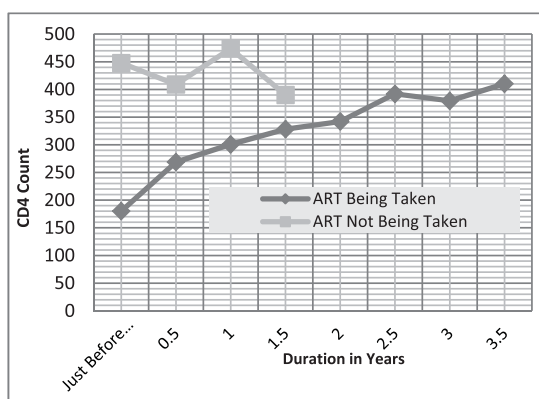

Figure 4. Change and comparison of mean CD_4 cell count in HIV infected individuals six monthly, among those who were taking ART and those who weren't taking ART, during the course of ART for a period of three and half years. (n=313).

The question of whether those initiating HAART will continue to increase their CD4+ count after 4-5 years or will plateau has been debated in the literature, and remains unclear. Some studies have suggested that normalization of CD4+ counts in HIV-infected persons can be achieved if viral suppression with HAART can be maintained for a sufficiently long period of time.[11] Several factors such as age, ethnicity, body weight and patients' immune status may influence antiretroviral drug concentrations.[25] In our study, those who were taking ART had mean CD4 count of 180.16 just before starting ART compared to mean CD4 count of 447.78 in the individuals who were not taking ART. We found that the mean CD4 count was in increasing pattern without any decline for two and half years among the population taking ART whereby the mean CD4 count was 391.98. But in succeeding six months' duration, the mean CD4 count decreased to 379.39. In subsequent six month the mean CD4 count increased to 410.28. The mass not taking ART had falling pattern of mean CD4 count for one and half year (Table 3). In one study, after > 5 years on HAART, patients with viral suppression who started at <200 cells/mm3 had an adjusted annual increase of 32 cells/mm3, attaining an average CD4+ count of 497 cells/mm3. Another study statistically estimating the CD4+ trajectory concluded that those starting HAART at <200 CD4+ cells who remained on therapy would continue to increase through 7 years, although 25% still had <350 cells at 7 years. One small study of 16 patients followed for up to 10 years with strict viral control based on HIV RNA detection using ultrasensitive techniques showed continued positive increases in CD4 + counts, although this study represented a small group of highly selected patients.[11]

On the other hand, other studies report that the average CD4+ count may level off after 4-6 years following HAART initiation, even among patients with viral suppression. Given this leveling off, many patients who start at lower CD4+ counts, even after years on HAART with early CD4+ increases, may fail to reach a normal CD_4+ threshold. In one study of those with sustained viral suppression who started HAART at <200 CD4+ cells/mm3, after 6 years only 42% had > 500 CD4+ cells/mm3, and only 12% had >750 cells/mm3. In another study, 44% of those starting therapy with a CD4+ count <100 cells/mm3 and 25% of those starting HAART

with a CD4+ count of 100–200 cells were unable to achieve a CD4+ cell count >500 cells/mm3 over a mean follow-up of seven years, and many did not reach this threshold by year 10.[11]

Antiretroviral therapy improves survival in HIV-positive patients. In addition, antiretroviral therapy reduces TB rates by up to 90% at an individual level, by 60% at a population level and it reduces TB recurrence rates by 50%. ART should be initiated for all people living with HIV with active TB disease irrespective of CD4 cell count. TB treatment should be started first, followed by ART as soon as possible and within the first 8 weeks of starting TB treatment.[27]

Despite several explanations, the most important aspect is the survival the HIV infected individuals. Death rates in HIV-positive individuals remain elevated compared to those in the general population and it is believed that HIV may play a role in the development of several serious non-AIDS conditions. Thus, combination ART may have a greater positive impact on the health of HIV-positive individuals than anticipated, which may now justify its earlier use.[28]

The dramatic scale-up of ART in resource-limited settings has brought not only TB treatment but also prevention of TB in HIV-infected persons to the forefront. TB prevention strategies with known efficacy include rapid identification and treatment of active TB cases (in source patients), infection-control measures to reduce nosocomial transmission of TB and ART to reduce the incidence of TB among HIV-infected patients. Research priorities in TB prevention center on adapting and improving these known strategies for HIV infection in resource-limited settings.[9]

CONCLUSION

TB and HIV co-infection is an emerging medical issue in Nepal. The prevalence of TB co-infection among HIV cases is found to be 36.1%. Consideration of TB need to be made while caring patients with HIV infection and vice versa. Timely given ART can be of utmost significance so it should be initiated when CD4 cell count falls below the cut off value. Preventive, promotive and curative aspects of TB and HIV should be under-taken hand in hand so that both of these entities are addressed simultaneously.

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