Spectrum of Tuberculous Infection in Patients Suffering from HIV/AIDS and Its Correlation with CD-4 Counts: A Retrospective Study from Sikkim

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Abstract To determine the spectrum of Tuberculous Infection in Patients suffering from HIV/AIDS and its correlation with CD-4 cell counts. A retrospective analysis of data of all the patient suffering from HIV/AIDS who are registered in the Sikkim State AIDS control society register during the past 7 years to look for tuberculosis as a opportunistic infection and its correlation with CD4 cell counts. Out of 268 patient registered, 51 were suffering with tuberculosis as co-infection, Amongst which cervical tuberculosis was common. There was significantly relation with CD4 cells count. Tuberculosis is one of the commonest opportunistic infection and chances of developing tuberculosis increases with decrease CD4 cell count.

Keywords HIV/AIDS · Tuberculosis · Co-infection · CD4 cell count

Introduction

Tuberculosis is the leading cause of death and morbidity worldwide with approximately 9.4 million incident cases and 1.3 million death annually [1]. India has the highest burden of TB cases in the world accounting for nearly 1/5th of the global burden. Tuberculosis is also one of the most common opportunistic infection in HIV infected individuals in developing countries. About 1.8 million new cases of tuberculosis are occurring annually in India, whereas the pool of HIV-infected individual is quite large (~2.5 million). Therefore there is always a propensity for deadly synergistic interactions between HIV and tuberculosis [2]. HIV infection is the most important known risk factor that favours progression to active TB from latent infection by suppressing the immune response against tuberculosis. Exogenous reinfection is also common in HIV infected individuals. The World Health organization (WHO) reported in 2007 that the African region accounted for most HIV-Positive tuberculosis cases (79 %) followed by southeast Asia region (mainly India), which has 11 % of the total cases [2]. Sikkim a small hilly north eastern state is encircled by Republic of China, Kingdom of Nepal and Bhutan and state of West Bengal and has a population of 7 lakhs. The state is comprised of four districts east, west, north and south Sikkim with its capital at Gangtok. RNTCP was launched on 1st march 2002 in the state achieving full coverage of all the districts. Since then the annual new smear positive case detection rate per lakh population in the state was around 110–120 cases, this figure is considerably high than the countrys figure which range between 60 and 70 new cases. Hence the burden of tuberculosis is higher in the state. The co existence of HIV/AIDS increases the morbidity and mortality in this patients [3]. The clinical presentation of tuberculosis varies depending

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on the severity of immunosuppression. In the early stages of HIV infection pulmonary involvement is most common; with progressive immunosuppression, extra pulmonary involvement presenting as lymphadenitis is most common [4]. In patients with Tuberculous lymphadenitis without pulmonary manifestation the possibility of tuberculous infections often is ignored in the differential diagnosis of lymphadenopathy, resulting in a significant delay of appropriate treatment [5]. Other organs involved in tuberculosis with advanced HIV disease include central nervous system, soft tissue, bone marrow, liver and other viscera. Extra pulmonary tuberculosis (EPTB) which usually account for about 15–20 % of the total TB cases, is now being increasingly reported due to the rise in the HIV pandemic and better diagnostic facilities [1]. Recent studies have suggested that the sites of EPTB may vary according to geographic location and population. [1] It is estimated that 60–70 % of HIV-Positive persons will develop tuberculosis in their lifetime. [2]

The study is important in view of the high prevalence of tuberculosis both pulmonary, extra pulmonary and other opportunistic infection in HIV infected persons. Sikkim being the smallest state of the country with low prevalence of HIV/AIDS and with high prevalence of tuberculosis. No study has been undertaken to study the various manifestation of HIV infection in these small state of the country.

Materials and Methods

The study is a Retrospective analysis of all patients Diagnoses as HIV/AIDS from all over the state and registered in the Sikkim State AIDS control register, Gangtok Sikkim during the period of past 7 years. The study was conducted after taking approval from the ethical committee, and after taking permission from the project director of Sikkim State AIDS Control Society (SSACS), Gangtok, The data were collected from the State AIDS control register. A total of 268 patients have been registered having HIV/AIDS out of which 51 patients have report to be suffering from tuberculosis as a co infection along with HIV/AIDS. The records of all HIV-infected patients registered in the Antiretroviral treatment(ART) centre were evaluated. All the patients registered were diagnosed as having HIV-infection using three antigenically different rapid kits as per the national HIV testing policy (ELISA/Rapid/Simple) and CD4 cell counts were determined by flow cytometry technique using Facs count machine with Facs count reagents. For the diagnosis of tuberculosis radiological investigation, Ziehl–Neelsen (ZN) staining for acid fast bacilli from a given specimen, histopathological demonstration of typical caseous granuloma and pleural/ascitic fluid analysis and response to Anti tubercular therapy (ATT) were evaluated.

ART was started for all the HIV-Infected patients and the response to it was guided by baseline and 6 monthly CD4 counts in accordance with ART guidelines.

The data obtained were compiled, tabulated and analysed using SPSS version 16.00. The results of the study were reported in the forms of tables along with the *p* value by the side of the table. *P* value of <0.05 was taken to be significant.

Aims and Objective

To determine the spectrum of tuberculosis in a patient having HIV/AIDS and its correlation with CD4 cell counts.

Results and Observation

Table 1 shows the baseline characteristics of the population studied, a total of 268 patients suffering from HIV/AIDS formed a part of the study population among which 159 (59.3 %) were male and 109 (40.7 %) were female, 105 (39.2 %) of the population were in the age group of 31–40 years followed by 95 (35.4 %) in the age group of 21–30 years, which together forms 74.6 % of the total population and they belong to the economically productive age group. The dependent population in our study comprised 10 % of the study population. 207 (77.2 %) of the population were from middle class families. 240 (89.6 %) had heterosexually transmitted HIV/AIDS and 13 (4.9) had transmission through blood and blood products, vertical transmission of HIV was seen only in 10 (3.7 %) of the population and the rest 5 (1.9 %) acquired through other mode of transmission. 51 (19 %) of the study population was also suffering from tuberculosis out of which 23 (8.6 %) were suffering from cervical lymphadenopathy.

Table 2 shows the relationship between status of tuberculosis in patients suffering from HIV/AIDS with CD4 cells count before the start of anti retroviral treatment. After analysing the data it has been seen that 51 (19 %) of the total study population were suffering from tuberculosis out of which 43 (16.04 %) had CD4 cells counts below 300 cells and 4 (0.014 %) each have CD4 cells counts in the range of 300–400 cells and above 400 cells and this relationship was found to be statistically significant on Chi square test.

Table 3 shows the relationship between status of tuberculosis in patients suffering from HIV/AIDS with CD4 cells count after 6 months after the start of anti retroviral treatment. The results shows improvement in CD4 cells count after start of anti retroviral treatment. 12 (0.044 %) patients suffering from tuberculosis and 32 (0.119 %) patient without tuberculosis with CD4 cells

Table 1 Baseline characteristics of the population studied

Socio-demographic variables	Total studied population (N = 268)	Percentage (%)
Gender		
Male	159	59.3
Female	109	40.7
Age group (years)		
1–10 years	12	4.5
11–20 years	08	3.0
21–30 years	95	35.4
31–40 years	105	39.2
41–50 years	33	12.3
>50 years	15	5.6
Address		
East Sikkim	192	71.6
West Sikkim	17	6.3
North Sikkim	09	3.4
South Sikkim	50	18.7
Socio-economic status		
Upper class	17	6.3
Middle class	207	77.2
Lower class	44	16.4
Mode of transmission of hiv/aids		
Heterosexually	240	89.6
Vertical transmission	10	3.7
Blood and blood products	13	4.9
Others	5	1.9
Status of tuberculosis		
Tuberculosis present	51	19.0
Tuberculosis absent	217	81.0
Type of tuberculosis		
Tuberculosis absent	217	81.0
Pulmonary tuberculosis	16	6.0
Cervical lymphadenopathy	23	8.6
Others	12	4.5

count below 300 cells showed improvement in cell counts 6 months after start of anti retroviral treatment, however this relationship was not statistically significant.

When we compared between the type of tuberculosis in patients suffering from HIV/AIDS with CD4 cells count before the start of antiretroviral treatment we found that 19 (0.07 %) patients were suffered from cervical tuberculosis, 14 (0.05 %) patients with pulmonary tuberculosis and 9 (0.03 %) patients with other form of tuberculosis (meningitis, disseminated tuberculosis, abdominal tuberculosis and pleural effusion) when the CD4 cells counts was below 300 cells however this association was not statistically significant and was only by chance (Table 4).

Table 5 shows the relationship between the type of tuberculosis in patients with HIV/AIDS with CD4 cells counts 6 months after the start of antiretroviral treatment, there was improvement in the cell counts after the administration of the therapy but there was no statistically significant relationship of the tuberculosis type with that of improvement in CD4 cells count.

Discussion

The study is a retrospective analysis of 268 patients diagnosed as suffering from HIV/AIDS from all over Sikkim who are registered in the Sikkim state AIDS control register, Gangtok, Sikkim during the period of past 7 years. This patients suffer from variety of opportunistic infection and tuberculosis has always been one of the common opportunistic infection to develop in HIV positive individuals which can occur at any stage of the disease. This patients can develop both pulmonary and extra pulmonary tuberculosis (EPTB). EPTB can occur in isolation or in combination with pulmonary focus or can involve multiple sites as in disseminated disease [1].

Our study consists of 268 patients suffering from HIV/AIDS where we found that 35.4 and 39.2 % patient in the age group of 21–30 years and 31–40 years are suffering from HIV/AIDS which is the economically productive age group. Extremes of age in our study were comparatively less affected which accounts for 7.5 % below 20 years and 5.6 % above 50 years. Similar study done by Jaryal et al.

Table 2 Status of Tuberculosis in patients suffering from HIV/AIDS and its correlation with CD4 cells counts before start of anti retroviral treatment (ART)

CD4 cells count before start of ART	Status of tuberculosis		Total	χ^2 , df, p
	Present	Absent		
<300 Cells	43	140	183	$\chi^2 = 7.48$, df = 2, p = 0.024*
300–400 Cells	4	40	44	
> 400 cells	4	37	37	
Total	51	217	268	

* p value <0.05 is considered as significant

Table 3 Status of tuberculosis in patients suffering from HIV/AIDS and its correlation with CD4 cells counts 6 months after start of anti retroviral treatment (ART)

CD4 Cells count 6 months after start of ART	Status of tuberculosis		Total	χ^2 , <i>df</i> , <i>p</i>
	Present	Absent		
<300 cells	31	108	139	$\chi^2 = 4.268$, <i>df</i> = 2, <i>p</i> = 0.118
300–400 cells	10	34	44	
>400 cells	10	75	85	
Total	51	217	268	

* *p* value <0.05 is considered as significant

Table 4 Type of tuberculosis in patients suffering from HIV/AIDS and its correlation with CD4 cells counts before start of anti retroviral treatment (ART)

Type of tuberculosis	CD4 Cells count before start of ART			Total	χ^2 , <i>df</i> , <i>p</i>
	<300 cells	300–400 cells	>400 cells		
No evidence of TB	140	40	37	217	$\chi^2 = 8.045$, <i>df</i> = 6, <i>p</i> = 0.235
Pulmonary tuberculosis	14	1	1	16	
Cervical lymphadenopathy	19	2	2	23	
Other type of TB	9	1	2	12	
Total	183	44	41	268	

* *p* value <0.05 is considered as significant

Table 5 Type of tuberculosis in patients suffering from HIV/AIDS and its correlation with CD4 cells counts 6 months after start of anti retroviral treatment (ART)

Type of tuberculosis	CD4 Cells count 6 months after start of ART			Total	χ^2 , <i>df</i> , <i>p</i>
	<300 cells	300–400 cells	>400 cells		
No evidence of TB	109	34	75	218	$\chi^2 = 8.738$, <i>df</i> = 6, <i>p</i> = 0.189
Pulmonary tuberculosis	11	1	4	16	
Cervical lymphadenopathy	14	5	3	22	
Other type of TB	05	4	3	12	
Total	139	44	85	268	

* *p* value <0.05 is considered as significant

[2] in Shimla showed higher prevalence of HIV/AIDS 31–40 years which accounted for 65.61 %. In a study conducted by Kulkarni et al. [6] the mean age of patients suffering from HIV/AIDS was 34.6 and 33 years in male and female respectively.

The sex distribution of the affected population in our study showed that majority of the study population were male accounting for 59.3 %. In a similar study done by Jaryal et al. [2] the dominant sex was of male accounting for 65.61 %. Majority of the patient belonged to east district of sikkim which accounted for 71.6 % of the total population this is due to high density of population in the east district of the state. 207 patients in our study belonged to middle class family according to kuppuswamy scale of

which majority were driver by occupation followed by labourers, army personals, housewives and unemployed. This finding is similar to the results obtained by Jaryal et al. [2].

In our study Heterosexual mode of transmission was the most common route of transmission of HIV/AIDS which accounted for 89.6 % of the cases. Among the other route vertical transmission and blood and blood products route accounted for 3.7 and 4.9 %. In a study conducted by Jaryal et al. [2] the most common route of HIV transmission was unprotected heterosexual sex which is consistent with that of our study. 51(19 %) of the total patients in our study were suffering from tuberculosis at the time of diagnosis of HIV/AIDS out of which 23 (8.6 %) had

Cervical lymphadenopathy, 12 (4.5 %) had other variety of tuberculosis altogether 13.1 % patients were suffering from extrapulmonary tuberculosis and only 15 (6 %) had pulmonary tuberculosis. A study conducted in Shimla also reveals that extrapulmonary tuberculosis was of higher prevalence in a patients suffering from HIV/AIDS [2]. A study conducted by Attili et al. [7] showed a contradictory result where they found majority of patients suffering from pulmonary tuberculosis followed by extrapulmonary tuberculosis and disseminated tuberculosis.

In our study we show that the chances of HIV/AIDS patient acquiring tuberculosis was higher when the CD4 cells count was less than 300 cells when compared with the cell counts above 300. There is statistical significant of this association with p value of 0.024. Our finding is consistent with the study conducted by Jaryal et al. [2] where tuberculosis was high in patients with CD4 counts <200/cmm. A contradictory result were obtained by Attili et al. [7] in their study where they found that tuberculosis in HIV patients from areas endemic with tuberculosis occurs in patients with wide range of immune status and has a better prognosis than other AIDS defining illnesses. In our study we saw that there is change in the status of tuberculosis with increased cell counts after 6 months of start of ART however this finding is not statistically significant. We also tried to correlate the type of tuberculosis in patients suffering from HIV/AIDS with CD4 cells count. We show that all type of tuberculosis was higher when the CD4 cells counts was <300 cells, there was no advantage of one form of tuberculosis over the other form with the CD4 cells count. The p value was computed to be 0.235 and 0.189 before the start of ART and 6 month after start of ART respectively.

Conclusion

HIV infection affects the economically productive age group. Commoner in patients of low socioeconomic status. Tuberculosis is one of the common opportunistic infection in patients suffering from HIV/AIDS and the chances of developing tuberculosis is more if the CD4 cells count goes down below 300 cells. Cervical lymphadenopathy was the most common form of tuberculosis in the patients with HIV/AIDS followed by Pulmonary tuberculosis. Therefore early diagnosis and start Antiretroviral treatment along with the treatment of opportunistic infection on time helps bring the CD4 cells count back and cut down the burden of opportunistic infection.

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Author's contribution Santosh Prasad Kesari: conceived the idea of the study and guide for conduct of the study, participated in its design and coordination, performed the statistical analysis and helped to draft the manuscript. Bina Basnett: On the spot data collection and drafting the manuscript. Ajay Chettri: participated in design of the study and helped to draft the manuscript.

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Compliance with Ethical Standards

Conflict of interest There are no potential, perceived, or real competing and/or conflicts of interest among authors regarding the article and therefore have nothing to declare.

Ethical Standards The study was conducted after taking prior permission from the ethical committee and the Project director, Sikkim state AIDS control society.

Ethical Approval All the co-authors have seen and approved the final version of the manuscript and it is not currently under active consideration for publication elsewhere, has not been accepted for publication, nor has it been published earlier, in full or in part. All the authors have been personally and actively involved in substantive work leading to the report, and will hold themselves jointly and individually responsible for its content.

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