Original Research Article

Impact of CD4 count in the development of mycobacterium tuberculosis in patients with HIV infection in a tertiary care centre

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ABSTRACT

Background: Patients with Human Immunodeficiency Virus (HIV) infection are predisposed to numerous opportunistic infections due to decreased cell mediated immunity, Tuberculosis being most common. Low CD4 count is associated with low immunity and higher risk of tuberculosis.

Methods: Author conducted a retrospective study in the department of Pulmonary medicine in a tertiary care teaching hospital during January to December 2017. Author collected data of all the patients with HIV diagnosed with Tuberculosis from the ART centre. Author collected demographic details including age, sex, symptoms at presentation, details of diagnosis of TB including type of tuberculosis, CBNAAT results, CD4 count at the diagnosis of TB, details of ART therapy and ATT therapy and outcomes of treatment.

Results: Eighty one patients with HIV-TB co- infection were included in the study. Males (70.37%) were more affected than females. Mean age of the study group was 39.97 ± 10 years. Sixty one patients (75.4%) were diagnosed with Pulmonary Tuberculosis and 20 (24.6%) patients were diagnosed with extra pulmonary TB. Mean CD4 counts of the cohort was $226\pm110/\mu l$. Eighty percent of patients developed Tuberculosis with CD4 count $<250/\mu l$.

Conclusions: Author found in this study higher proportions of tuberculosis (80.2%) in patients with HIV infection with CD4 count $<200/\mu l$. Author also found higher proportion of pulmonary Koch's in patients with low CD4 count (CD4 $<200/\mu l$).

Keywords: Coinfection, CD4 count, HIV-TB, Pulmonary TB

INTRODUCTION

Patients with Human Immunodeficiency Virus (HIV) infection are predisposed to numerous opportunistic infections due to decreased cell mediated immunity. Prevalence of HIV in India is estimated to be 0.26% in 2015 and there is steady decline.[1] Tuberculosis (TB) is the most common opportunistic infections seen in HIV patients that contribute to significant morbidity and mortality throughout the world, especially in developing countries like India. Overall, HIV patients have 8 fold higher risk of TB than non HIV people.[2] It is estimated that around 60-70% of patients with HIV infection develop TB in their lifetime.[3]

HIV-TB co-infection has become huge hurdle for achieving Tuberculosis control in India. In 2015, there were an estimated incidence 10.2 million cases globally and HIV-TB coinfection contributed 1.2 million (11%).[4] The diagnosis of TB in HIV infected patients is challenging, due to atypical presentation, frequent negative smear microscopy due to lack of caseous necrosis.[5] Clinical presentation and clinical forms of TB in HIV patients partly depends on CD4 counts. So, it is

METHODS

Author conducted a retrospective study in the department of Pulmonary medicine in a tertiary care teaching hospital during January to December 2017. Author collected data of all the patients with HIV diagnosed with Tuberculosis from the ART centre. Author collected demographic details including age, sex, symptoms at presentation, details of diagnosis of TB including type of tuberculosis, CBNAAT results, CD4 count at the diagnosis of TB, details of ART therapy and ATT therapy and outcomes of treatment.

CD4 counts were done by flowcytometry using Facs count machine using Facscount reagent. HIV testing was done in NACO approved government laboratory using immunochromatohraphy technique. TB detection was done by Xpert MTB/RiF assay, manufactured by Cepheid-Sunnyvale-USA. Single, early morning sputum specimen was taken in a sterile falcon tube and was processed according to the GeneXpert system operator manual given by Central TB division, Government of India. Bloody specimens were rejected.

Statistical analysis

Descriptive data are presented as frequencies (percentages) for discrete variables and as means (SDs) for continuous variables. All statistical tests were 2-tailed, and factors were considered statistically significant at p <0.05. IBM SPSS version 22 and CDC Epi Info version 7 was used for analysis.

RESULTS

Eighty one patients with HIV-TB co-infection were included in the study. Males (70.37%) were more affected than females. Mean age of the study group was 39.97±10 years. Cough (92%) and fever (90%) were the most common symptom, followed by weight loss (85%) and fatigue (82%).

Sixty one patients (75.4%) were diagnosed with Pulmonary Tuberculosis and 20 (24.6%) patients were diagnosed with extra pulmonary TB (Table 1). All patients were subjected to upfront CBNAAT testing. CBNAAT was positive in all patients with suspected pulmonary koch's. For extra pulmonary koch's it was positive only in half of the patients and rest were clinically diagnosed. Two patients were positive for rifampicin resistance. All except two were new cases of Tuberculosis. All patients were initiated on DOTS and followed by ART therapy after 2 weeks, but one patient died before initiation of treatment.

Mean CD4 counts of the cohort was 226±110/µl. Eighty percent of patients developed Tuberculosis with CD4 count <250/µl (Figure 1). Author found two cases of MDR TB and their CD4 counts were 80/µl and 150/µl. Author found Pulmonary koch's more common than extra pulmonary Koch's in patients with CD4 count <200/µl (Table 2).

Table 1: Table depicting type of the specimen subjected to CBNAAT and yield of CBNAAT in patients with HIV infection.

Type of sample	Site of sample	Number of positive CBNAAT result, n (%)
Pulmonary samples	Sputum	61
	Bal	0
	Gastric aspirate	0
Extra pulmonary samples	Pleural fluid	5
	Ascitic fluid	0
	Synovial fluid	0
	Pus	3
	Cerebro spinal fluid	2

Table 2: Table depicting distribution of pulmonary and extra pulmonary TB with levels of CD4 count.

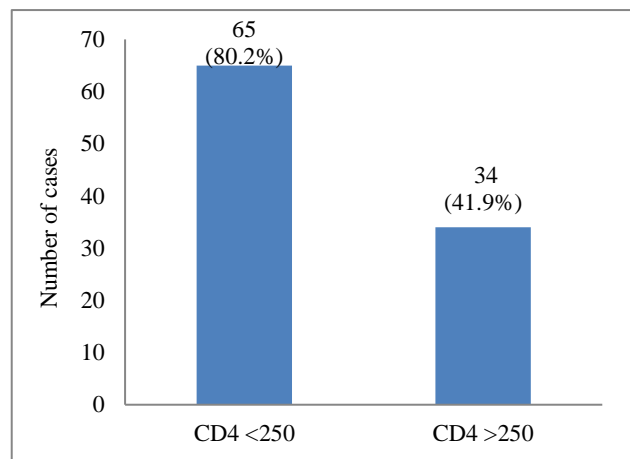| CD4 count	Pulmonary n (%)	Extra pulmonary
CD4 count <200, n= 48	39 (81.2%)	9 (18.75%)
CD4 count >200, n= 33	22 (66.6%)	11 (33.3%)
Mean CD4 count, n=226/µL	61	20

Figure 1: Proportion of HIV infected patients acquired with tuberculosis with respect to levels of CD4 count.

DISCUSSION

Tuberculosis remains the most common cause of death in patients with HIV infection globally. Patients with HIV infection have 10% per year risk of acquiring TB in contrast, to patients with Non-HIV infection have 10% risk in life time.[6] Author found in this study that patients with HIV- TB co-infection with low CD4 count are at a

higher risk of developing Tuberculosis. Author also found pulmonary koch's was more common than extrapulmonary koch's in patients with CD4 count <200/µl.

TB-HIV co-infection is associated with poor prognosis than when either disease present alone. HIV infection predisposes the patient to severe forms of TB such as disseminated TB and drug resistant TB. Tuberculosis in turn increases the viral load leading to higher mortality and morbidity in those patients.[7] Hence it is very important to diagnose and treat TB early in those patients. Low CD4 counts can be used as a marker for suspicion of severe forms of TB. CD4 cells are the T helper lymphocytes involved in cell mediated immunity. These help to coordinate the immune response by stimulating other immune cells such as macrophages, B lymphocytes and CD8 T lymphocytes which are mainly involved in fighting off infections.[8] In HIV infection, HIV virus gains entry into CD4+ T cell via attachment to CD4 receptor and brings about conformational change in gp120 allowing HIV virus to bind to coreceptors expressed on host cell and enter the cell membrane and merge with RNA resulting in replication of viral progeny.[9]

Hence CD4 counts reflect the level of immunity and also risk for opportunistic infections can be acquired. A study done by Ajay et al found severe forms of TB with CD4 <200 mcg/dl.[10] A prospective study done by Ackah et al found increased risk of mortality in HIV patients with severe immune deficiency (i.e. CD4 <200) when they were coinfected with Tuberculosis.[11] Another South African population based study found 61% of patients with TB had CD4 count of <200/µl similar to this study.[12] There are several limitations in this study. First, author had a small sample size hence the results cannot be generalized to population so there is a need for larger studies to confirm the findings. Second, author did not have data of viral load of these patients, so author could not correlate the risk of Tuberculosis with viral load and compare with CD4 counts. Third, there was no data available on comorbidities of those patients as diseases like diabetes, itself can increase risk for development of tuberculosis.

CONCLUSION

Author found in this study higher proportions of Tuberculosis (80.2%) in patients with HIV infection with CD4 count <200/µl. Author also found higher proportion of pulmonary Koch's in patients with low CD4 count (CD4 <200/µl).

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REFERENCES

1. National AIDS Control Organization. HIV Facts and Figures. Available at http://naco.gov.in/hiv-facts-figures. Accessed on Feb 15, 2018.
2. National AIDS Control Organization. Search Result. Available at http://naco.gov.in/goisearch?search_key=risk+of+Tb+in+HIV+. Accessed Feb 15, 2018.
3. Swaminathan S, Ramachandran R, Baskaran G, Paramasivan CN, Ramanathan U, Venkatesan P, et al. Risk of development of tuberculosis in HIV-infected patients. Int J Tuberc Lung Dis Off J Int Union Tuberc Lung Dis. 2000;4(9):839-44.
4. WHO. Tuberculosis and HIV. Available at http://www.who.int/hiv/topics/tb/en/. Accessed on 2 Feb 15, 2018.
5. Arora D, Jindal N, Bansal R, Arora S. Rapid Detection of Mycobacterium tuberculosis in Sputum Samples by Cepheid Xpert Assay: A Clinical Study. J Clin Diagn Res JCDR. 2015;9(5):DC03-DC05.
6. WHO. IRIS: Global tuberculosis control: WHO report, 2011. Available at http://apps.who.int/iris/handle/10665/44728. Accessed on Feb 15, 2018.
7. Padmapriyadarsini C, Narendran G, Swaminathan S. Diagnosis and treatment of tuberculosis in HIV co-infected patients. Indian J Med Res. 2011;134(6):850-65.
8. AIDS info. CD4 T lymphocyte definition. Available at https://aidsinfo.nih.gov/understanding-hiv-aids/glossary/113/cd4-t-lymphocyte. Accessed on Feb 15, 2018.
9. Wilen CB, Tilton JC, Doms RW. HIV: Cell Binding and Entry. Cold Spring Harb Perspect Med. 2012;2(8).
10. Jaryal A, Raina R, Sarkar M, Sharma A. Manifestations of tuberculosis in HIV/AIDS patients and its relationship with CD4 count. Lung India Off Organ Indian Chest Soc. 2011;28(4):263-6.
11. Ackah AN, Digbeu H, Daillo K, Greenberg AE, Coulibaly D, Coulibaly IM, et al. Response to treatment, mortality, and CD4 lymphocyte counts in HIV-infected persons with tuberculosis in Abidjan, Cote d'Ivoire. Lancet. 1995;345(8950):607-10.
12. Gupta RK, Lawn SD, Bekker L-G, Caldwell J, Kaplan R, Wood R. Impact of HIV and CD4 count on tuberculosis diagnosis: analysis of citywide data from Cape Town, South Africa. Int J Tuberc Lung Dis Off J Int Union Tuberc Lung Dis. 2013;17(8):1014-22.