HIV/Aids-Tuberculosis (Pulmonary and Extra Pulmonary) Co- Infection: Sputum Positivity and Cd4 Correlation

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Abstract- The present study aims to find a correlation between sputum positivity and CD4 cell count in patients with HIV/AIDS-Tuberculosis co infection. It was as a retrospective hospital based observational study. Data was collected over a period of one year in the ART CENTRE, Department of Medicine, Osmania General Hospital. We included 350 HIV/AIDS infected patients on ART with Tuberculosis co infection.

Index Terms- Human Immuno Deficiency Virus, Tuberculosis, CD4 Count, opportunistic infection.

I. INTRODUCTION

Tuberculosis is the most common opportunistic infection in HIV/AIDS and is the most common cause of death in HIV/AIDS patients. Early diagnosis and treatment can decrease the mortality and morbidity. HIV enters the body when an individual comes in contact with infected blood, semen and/or vaginal secretions. The CD4 receptor is the principal target site for HIV. [(1)]

A normal CD4 count in a healthy, HIV-negative adult can vary but is usually between 500 and 1500 CD4 cells/mm3 (though it may be lower in some people).[(2)]

The principal impact of HIV infection on the immune system is destruction of the CD4 T-lymphocytes. During primary infection, HIV and HIV-infected cells reach the lymph nodes and other lymphoid tissues. The virus rapidly disseminates during this early phase of HIV infection. As a result, there is a significant fall in CD4 cells and viral levels, may be as high as 106-107 viral copies/ml. The next stage is down regulation of viraemia.

This coincides with a robust, intense immune response by the host . Both effective cellular immune response mediated by HIV specific cytotoxic T-lymphocytes (CTLs) and humoral response mediated by complement fixing and neutralising HIVspecific antibodies comes into play. As a result, the viraemia drops and CD4 levels bounce back to values slightly lower than the normal levels. However, active and continuous virus replication continues in the lymph nodes and lymphoid organs.In active phase of infection, CD4+ loss can be up to 2 million cells per day. Sometime loss of non-infected cells can be more than that of infected cells. In the initial phases of infection, enormous loss does not reflect as an immediate, proportionate drop in their blood count, due to compensatory proliferation of precursor cells.

CD4+ counts start dropping, when the virus kills lymphoid precursor cells and replenishment of lost cells becomes increasingly inadequate. Even non infected cells suffer 'accelerated apoptotic death' (AAD), induced by excess, prolonged activation. Molecular basis of AAD is not clear. Non-infected cells, carrying viral antigens on the surface, are sequestered by anti-viral IgM/IgG antibodies and killed by cytotoxic lymphocyte (CTL) T-cells. Opportunistic infection (OI) is a disease caused by microbial agent(s) in hosts with defects in humoral and cell mediated immunity. Immuno compromised secondary to human immunodeficiency virus (HIV) infection, use of immune modulatory agents (including steroids and anticancer drugs) are emerging predisposing factors to OI.

II. MATERIAL AND METHODS

It was as a retrospective hospital based observational study. Data was collected over a period of one year in the ART CENTRE, Department of Medicine, Osmania General Hospital. We included 350 HIV/AIDS infected patients on ART with Tuberculsois co-infection.

Investigations:

Complete blood picture, serum creatinine, Blood urea, serum electrolytes, Liver function tests, Sputum for Acid fast bacilli smear, Chest radiography, CD4 cell Count, Fine needle aspiration and biopsy (if necessary), Magnetic Resonance imaging (if necessary), Computerized Tomography (if necessary), Colonoscopy (if necessary).

III. RESULTS

Out of 350 patients, 228 were male and 122 were female of which most of them are falling between age groups 20-29 years

[males-42 (12%), females-33 (9.4%)], 30-39 years [males-86 (24.6%), females-55 (15.7%)], 40-49years [males-72 (20.6%), females-29(8.3%)]. Total 71 (20.3%) cases were sputum positive. Sputum negative cases included both sputum negative pulmonary tuberculosis and extra pulmonary which included 279 cases(79.7%)of which sputum negative pulmonary tuberculosis cases 111(39.8%),extra pulmonary tuberculosis cases are 168(60.2%).

CD4 cell count in sputum positive cases with CD4 cell Count< 200/mm3 -37(52.1%), 200-400 cells / mm3-23(32.4%), >400cells / mm3-11 (15.5%). In sputum Negative Pulmonary tuberculosis cases, CD4 cell count <200 cells/cumm -80 (28.7%), 200-400cells / cumm-26 (9.3%), > 400cells / cumm- 5 (1.8%). Extra pulmonary tuberculosis cases with CD4 cell count < 200 cells/cumm-111 (39.7%), 200-400 cell/cumm-41 (14.4), >400 cells/cumm-16 (6.1%).

Table1:CD4 CELL COUNT IN SMEAR POSITIVE PULMONARY TUBERCULOSIS

GENDER	CD4<200	CD4 BETWEEN 200-400	CD4>400	TOTLAL
FEMALE	12(16.9%)	6(8.5%)	3(4.2%)	21(29.6%)
MALE	25(35.2%)	17(23.9%)	8(11.3%)	50(70.4%)
TOTAL	37(52.1%)	23(32.4%)	11(15.5%)	71(100%)

Table2:CD4 CELLCOUNT IN SMEAR NEGATIVE PULMONARY TUBERCULOSIS

GENDER	CD4<200	CD4 BETWEEN 200-400	CD4>400	TOTAL
FEMALE	28(25.2%)	9(8.1%)	1(0.9%)	38(34.2%)
MALE	52(46.9%)	17(15.3%)	4(3.6%)	73(65.8%)
TOTAL	80(72.1%)	26(23.4%)	5(4.5%)	111(100%)

Table3:CD4 CELLCOUNT IN EXTRA PULMONARY TUBERCULOSIS

GENDER	CD4<200	CD4 BETWEEN 200-400	CD4 >400	TOTAL
FEMALE	45(26.8%)	12(7.1%)	5(3%)	62(36.9%)
MALE	66(39.3%)	29(17.3%)	11(6.5%)	106(63.1%)
TOTAL	111(66.1%)	41(24.4%)	16(9.5%)	168(100%)

IV. DISCUSSION

Opportunistic infections (OIs) may serve as indicators of underlying HIV infection. Mortality among HIV-infected individuals is due to improper awareness and consequent poor clinical management of OIs. HIV load increases in the presence of ongoing OIs, thus accelerating progression to clinical acquired immunodeficiency syndrome (AIDS). The incidence of Oppurtunistic Infections(OI) range from 10.7 to 69.7 /100 patient years.

Among 28 OIs—tuberculosis (65%), candidiasis (57.5%) and diarrhoeal diseases (40%) are the most common OIs found in Indian patients.[3]

According an estimate of World Health Organisation (WHO),TB has become one of the leading causes of death among HIV –infected persons.[4]

The risk of developing TB after an infectious contact has been estimated to be 5-15%/year in HIV -1 infected patients (compared to 5-10% during life time of non HIV-1 infected patients [5]

In India the incidence of TB is around 40% in the general population; however, it has been estimated that around 25-30% more cases of TB may be added due to HIV infection.[6]

Active TB is the commonest OI among HIV infected individuals and is also the leading cause of death in PLHA. Surveys in India shows 1-13% HIV among TB patients.[7]

Even in HIV infected patients.Pulmonary TB is the most commonest form of TB. [8]

Changes in the CD4 lymphocyte count occur with the institution of highly active antiretroviral therapy (HAART).

A critical marker of immunologic integrity is the CD4 cell count,and the clinical manifestations of tuberculosis vary with the CD4 cell count in HIV-positive patients with tuberculosis.[9]

Patients with tuberculosis manifest significant immunologic abnormalities including anergy and failure of T-lymphocytes to proliferate and produce IFN-alpha in resposnse to mycobacterial antigens.[10]

CD4 cell counts in HIV-negative patients with tuberculosis have been reported to be normal or low, and no clear relationship has been noted between the clinical presentation and CD4 cell count. [11-15]

Tuberculsosis can occur at any CD4 cell count.Pulmonary tuberculosis is more common at CD4 counts between 200-500/microL. Miliary and extra pulmonary tubercuosis at less than 200 cells/microL. MAC at Less than 50 cells/microL.

HIV infected smear positive patients tend to excrete significantly fewer organisms per ml of sputum than HIV-negative patients which can lead to AFB being missed if the appropriate number of sputum samples as well as high power fields is not examined by microscopy.[16]

The Sputum negativity tends to increase as the HIV disease and immnune suppression progresses. Diagnosis of TB is based on clinical impression and relevant investigations including chest radio graph, sputum examination, tissue /blood culture for Mycobacterium tuberculosis and biopsy when deemed necessary. HIV serological testing is performed using ELISA method and confirmed by Western Blot. Absolute CD4 lymphocyte counts are quantified. Severe immune suppression is defined as CD4 cells <200/cumm. [17]

Treatment:

Patients were treated based on RNTCP and NACO Guidelines. Anti tuberculosis therapy (ATT) must be administered according to the directly observed treatment-short course (DOTS) regimen. Institution of Highly active Anti-retroviral therapy (HAART) is recommended 10-14 days after institution of ATT in patients with CD4 counts less than 200 cells/mm3. In patients with CD4 counts over 200 cells/mm3 HAART may be commenced 2-8 weeks after the institution of ATT. As rifampicin is known to enhance the metabolism of protease inhibitors and nevirapine., efavirenz based antiretroviral therapy(ART) is recommended while patients are on rifampin.

V. Conclusion

- In our study we conclude that male sex under Age group (20 – 29) are more common, sputum negativity incidence is 79.7% and sputum positivity 20.3% CD4 cell count < 200 in sputum positive cases 52%, sputum negative pulmonary tuberculosis in 28%, extra pulmonary tuberculosis in 39.7%.
- Even though sputum positivity did not correlate well with CD4 cell count, sputum negativity increased with decrease in CD4 cell count. With arbitrary cut off of CD4 cell count of <200, the incidence of extra pulmonary tuberculosis was higher.

VI. LIMITATIONS OF STUDY

- It is a retrospective study.
- Survival rates were not assessed in the patients who are started on early HAART in CD4 count between 0 - 200.
- Patients were not followed up.

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