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Research Article

CHANGES IN THE CD4 COUNTS, HEMOGLOBIN AND WEIGHT IN PATIENTS WITH HIV ALONE AND HIV- TB CO-INFECTION.

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ABSTRACT

Objectives: To assess the changes in the CD 4 counts, hemoglobin and weight in patients co-infected with HIV/Tb receiving anti-retroviral therapy and anti-tubercular therapy.To compare the changes of these parameters between the group receiving ART alone and the group receiving ART and ATT.

Methodology: Retrospective data was collected from the ART centre, Chigateri Hospital, Davangere, Karnataka. Patients on any one HAART regimen for atleast six months were compared against patients receiving both HAART and ATT. Changes in the CD4 counts, hemoglobin levels and weight were analyzed with statistical tests.

Results: Data from the records of 506 HIV patients were analyzed out of which 90 had tuberculosis. There was a significant improvement in the CD4 counts of both the groups with treatment (HIV:p=0.0001; co-infection:p=0.0001) but the mean improvement did not vary in either groups (HIV:138.71 cells; co-infection:138.58 cells). The hemoglobin did not improve significantly in either group (HIV:p=0.2485; co-infection:p=0.2966) but the mean hemoglobin improvement in the HIV alone group was better (HIV:2.69g%; co-infection:0.41g%). There was an improvement of weight in both the groups with treatment (HIV:p=0.042;co-infection:p=0.0004) but the mean weight improvement was better in co-infection group (HIV:1.86kgs; co-infection:3.36kgs).

Conclusion: In our study all the parameters improved in both the groups. Presence of Tb did not influence the improvement in CD4 counts. The weight improved significantly in both the groups, which was very significant in the co-infection group. The rise in the hemoglobin levels was not statistically significant.

Keywords: HIV-TB coinfection, CD4 counts, Hemoglobin, Body Weight.

INTRODUCTION

The acquired immune deficiency syndrome (AIDS) is caused by the human immunodeficiency virus (HIV). HIV-1 was initially identified by Luc Montanier at the Institute Pasteur, Paris, in 1983 and was then more fully characterized in 1984 by Robert Gallo in Washington and Jay Levy in San Francisco. A second virus, HIV-2, was isolated from West African patients in 1986. Since its discovery almost 70 million people have been infected with the HIV virus and about 35 million people have died of AIDS. An estimated 0.8% of adults aged 15-49 years worldwide are living with HIV, although the burden of the epidemic continues to vary considerably between countries and regions. Sub-Saharan Africa remains most severely affected, with nearly 1 in every 20 adults (4.9%) living with HIV and accounting for 69% of the people living with HIV worldwide [1].

The first case of HIV/AIDS was reported in India in Tamil Nadu in 1986. Since then the virus has spread from the high-risk groups to the general population very fast.The total number of people living with HIV/AIDS (PLHA) in India is estimated at 23.9 lakh (19.3 – 30.4 lakh) in 2009.India has the third largest number of people living with HIV/AIDS. As per the 2008-09 HIV estimates, there are an estimated 23.9 lakh people currently living with HIV/AIDS (Acquired Immunodeficiency Syndrome) in India with an adult prevalence of 0.31 percent in 2009[2].

India has the highest number of patients diagnosed with tuberculosis in the world with 40% of population infected, 1.9 million new cases occurring every year of which about 0.8 million are sputum positive[3].

The high prevalence of both Tuberculosis and HIV diseases in our country increases the chances of co-infection as patients infected with HIV have decreased chemotaxis, defective granuloma formation and maintenance, impaired antigen processing and presentation as well as generalized loss of CD4+ T cells and selective clonal depletion of Mycobacterium tuberculosis specific CD4+ T lymphocytes. All these factors result in either activation of latent tubercular infection or make the patients susceptible to a new infection. Unlike other opportunistic infections which have a selective range of CD4 in which the disease occurs, pulmonary TB occurs throughout the course of HIV but the occurrence of extra-pulmonary tuberculosis (Lymphatic > meningitis > disseminated) is seen when the CD4 counts drop progressively lower[4].

A HIV positive person co-infected with MTB has 50-60% life time risk of developing TB disease, as compared to an HIV negative person who has a 10% life-time risk of developing TB disease.Thus TB mortality could well be influenced by the MTB/HIV co-infection[3]. Despite the existence of affordable medications, too few people living with both HIV and tuberculosis are receiving treatment for both conditions. This situation contributes to substantial, avoidable morbidity and mortality.In comparison to tuberculosis patients without HIV infection, tuberculosis patients who are living with HIV have lower treatment success rates, primarily due to an increased risk of death[5,6]. This is probably because the CD4 counts were not known to improve in tuberculosis and HIV co-infected patients as well as in people with HIV alone in response to HAART [7].

This is an effort in our institution to see the outcome of the co-infection between HIV and Tuberculosis in patients receiving HAART with respect to the changes in hemoglobin, weight and CD4 counts.

METHODOLOGY

A retrospective observational study was designed and CD 4 counts, Hemoglobin and Weight were considered for analysis as they are commonly evaluated in the follow up of HIV patients on treatment as per NACO guidelines[6]. Ethical clearance was obtained (No: JJMMC/IEC-10/2011-12) from the local ethical committee and a permission was obtained from the Anti-Retroviral Therapy (ART) medical officer of the Chigateri Government District hospital, Davangere for data collection. Data of patients who had completed six months of treatment by the time the ethical clearance was given were collected.

Inclusion criteria

- Patients diagnosed to have HIV infection and were on a fixed ART regimen for six months preceding the beginning of the data collection.
- Patients diagnosed to have tuberculosis along with HIV and were started on ATT along with ART and had no changes in ART regimen for the entire period of receiving ATT.

Exclusion criteria

- Patients who have had a change in the regimen, for any reason, in the study period.

Patients on any one HAART regimen were included in one group (Group A). Patients who received both HAART and ATT were included in the second group (Group B). The baseline CD4 counts, hemoglobin and weight of the eligible patients were recorded and the values of these parameters after six months were also recorded for comparison.

RESULTS

Of the records taken in the year 2012 from July to December, a total of 501 patients were eligible as per the inclusion criteria. Of these 411 were on anti-retro-viral therapy alone and formed one group (Group A). Of the patients who had tuberculosis 90 were on a stable regimen for six months and they formed the other group (Group B). The patients were on various HAART regimens (**Table 1**) but they were not differentiated according to the regimen when the results were compared as some of the regimens had too few patients to be statistically significant.

Table 1: Number of patients receiving various regimens

Patient Group	Regimens			
	ZLE	ZLN	SLE	SLN
No. of patients receiving ART (Group A)	52	245	25	89
No. of patients receiving ART & ATT (Group B)	41	19	25	05

Z – Zidovudine, L – Lamivudine, N – Nevirapine, E – Efavirenz, S – Stavudine

Changes in the CD4 counts, hemoglobin and weight both before and after treatment in the individual groups were analyzed using the paired 't' test. A p value of 0.05 was considered significant. Online Graphpad software was used for statistical analysis of the study.

The mean CD4 counts in the patients of group A before treatment was 217.07 cells and after six months of treatment was 355.78 cells. The mean change was an improvement of 138.71 cells and the change was significant with a p value of 0.0001. In the group B the mean count before treatment were 170.69 cells and the counts after treatment were 309.27 cells. The mean change was an improvement of 138.58 cells and it was significant with a p value of 0.0001 **(Fig 1)**.

The mean hemoglobin of patients before treatment in group A was 10.531g% and after six months of treatment it was 13.219g%. The mean change was an improvement of 2.69g%. With a p value of 0.24, the improvement seen was not significant. In group B, mean hemoglobin before treatment 10.081g% and after treatment it was 10.486g%. The mean change was an improvement of 0.41g% which was not significant statistically (p=0.29) **(Fig 2)**.

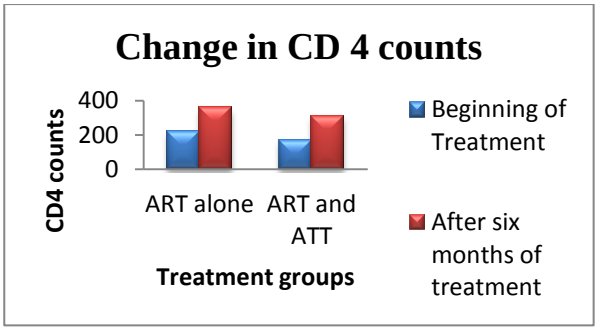

Fig.1

ART-anti-retroviral therapy, **ATT**-anti-tubercular therapy**. Group A(n)**:416, **Group B(n)**: 90.**Mean change of CD4 counts:Group A**: 138.71(p=0.0001) and **Group B**: 138.58(p=0.0001).

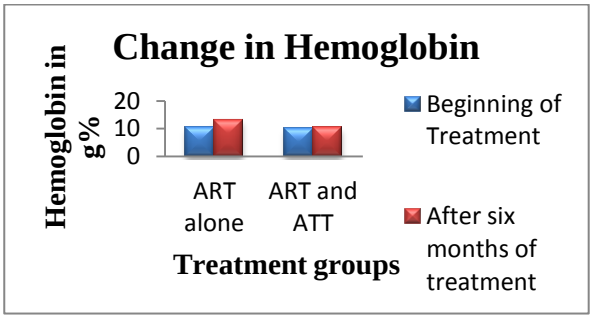

Fig.2

ART-anti-retroviral therapy, **ATT**-anti-tubercular therapy**. Group A(n)**:416, **Group B(n)**: 90.**Mean change of hemoglobin:Group A**: 2.69 g%(p=0.24) and **Group B**: 0.41 g%(p=0.29).

In group A, the mean weight before and after six months of treatment was 48.88kgs and 50.54kgs respectively. The change observed was an improvement of 1.86 kgs with a p of 0.04.The group B had a mean weight of 43.78kgs before the treatment and after the treatment it was 47.15kgs. The mean change was an improvement of 3.36kgs which was statistically significant (p=0.0004) **(Fig 3)**.

DISCUSSION

According to the WHO clinical staging of HIV/AIDS for adults and adolescents, presence of pulmonary tuberculosis indicates a clinical stage 3 of HIV/AIDS and extra-pulmonary tuberculosis indicates a clinical stage 4 of HIV/AIDS. WHO recommends treatment of patients who are diagnosed to have HIV and Tb co-infection with ART along with ATT to all patients with extra-pulmonary tuberculosis and to all those with pulmonary tuberculosis unless CD 4 counts are greater than 350 cells/mm^3 (**Table 3**).

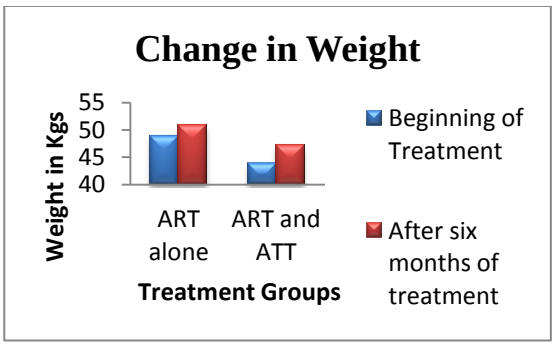

Fig.3

ART-anti-retroviral therapy, **ATT**-anti-tubercular therapy**. Group A(n)**:416, **Group B(n)**: 90.**Mean change of body weight:Group A**: 1.86 Kgs(p=0.04) and **Group B**: 3.36 Kgs(p=0.0004).

Table 3: WHO guidelines for starting ART in patients diagnosed with tuberculosis (followed by RNTCP).

CD4 cell count (cells/mm^3)	Timing of ART in relation to initiation of ATT	ART recommendations
CD4 < 200	Start ATT first, Start ART as soon as ATT is tolerated (between 2 weeks to 2 months)	Recommended ART (EFV based regimens)
CD4 between 200 – 350	Start ATT first; start ART after 8 weeks	Recommended ART
CD4 > 350	Start ATT first; re-evaluate patient for ART at 8 weeks and at the end of ART	Defer ART
CD4 not available	Start ART 2 – 8 weeks after ATT initiation	Recommended ART

EFV –Efavirenz, ART – Anti-Retro Viral Therapy, ATT – Anti – Tubercular therapy.

If a patient with active Tb is diagnosed with HIV and requires ART, the first priority is to start ATT according to RNTCP guidelines. ART may be started later if the patient are tolerating the pill burden and are compliant with ATT with adequate counseling and precautions for drug interactions[7].

The three parameters chosen as variables in this study are preferred in most ART centres to evaluate the prognosis of the patients in their follow up.The CD4 counts can predict the patient's susceptibility to various opportunistic infections and thereby increasing mortality in People Living with HIV/AIDS (PLHA). Hemoglobin can be a predictor of morbidity and rarely mortality that is independent of CD4 counts. A decrease in hemoglobin is one of the most common presentations of HIV. The treatment with anti HIV drugs can also result in anemia. So to monitor the treatment or its adverse effects, hemoglobin becomes one of the important prognostic factors [8].Bodyweight is also independent of CD4 cell count as a prognostic measure; bodyweight changes reflect changes in the rate of viral replication, and bodyweight is affected by severe opportunistic infections or malignant diseases[9].

Apart from the viral load, the CD4 count is the most important predictor of mortality for a patient infected with HIV and is on treatment [6]. Whalen et al., in the year 1995 published their study in which they conclude that there is an increased risk of death in HIV patients co-infected with active tuberculosis even when the patients were matched with compliant ARV treatment and CD4 counts[10]. Also it has been noted that the lower the counts of CD4, the harder it is to improve the count[11]. Since 1995, when their study was published, the treatment of both HIV patients and tuberculosis patients has evolved a lot. With the availability of HAART regimens for HIV, the mortality has significantly come down and the outcome of patients with both HIV and Tb co-infection has also significantly improved with the advances in both ATT and ART [13]. Even in severely immune compromised patients with Tb, the initiation of HAART will reduce the mortality and disease progression [10].

In the present study, the mean CD4 counts in group A was 217.07 cells when the patients were started on HAART and after six months of treatment it was 355.78 cells. The difference of means was an improvement of 138.71 cells. In group B, the mean count was 170.69 cells before the start of the treatment with ATT and concomitant ART. After six months the mean count was 309.27 cells. The mean difference was an improvement 138.58 cells. On comparison of the improvement in both the groups, there is no difference implying that tuberculosis on adequate treatment did not increase the mortality in the study population reflected here by the equal increase of mean CD4 counts in both the groups. Though the mean CD4 counts are lesser in the co-infection group, a combined ART and ATT has improved the counts as well as the other group receiving only ART.

Harris RJ, Sterne JA et al reported from their study that anemia at baseline in a HIV patient was independently associated with higher mortality. According to them baseline anemia continued to be a predictor of mortality and to a lesser extent progression to AIDS too[15]. Amanda Mocroft, Ole Kirk et al in a study conducted in Europe that included 6725 HIV patients found out that 1 g% decrease in the hemoglobin increased the hazard of death by 57% (relative hazard), a drop in 50% of the CD4 counts increased the hazard by 51%. This indicates that hemoglobin is a more important prognostic factor in a patient with HIV[12].

Anemia is a frequent complication of both HIV and tubercular infections and in both infections it is associated with increased morbidity and mortality. However very few studies have emphasized anemia in HIV-Tb co-infection. One study conducted in Tanzania by E. Saathoff, E. Villamor in a large population (750 females and 1693 males) of co-infected patients concluded that among Tb infected individuals, anemia is strongly associated with HIV co-infection independent of socio-economic status[13]. The treatment with anti HIV drugs can also result in anemia. So to monitor the treatment or its adverse effects, hemoglobin becomes one of the important prognostic factors[6]. In our study population, the hemoglobin improved in both the groups. The group A showed a better mean improvement of 2.69 g% as compared to the improvement seen in group B which had an improvement of 0.41 g%. By this observation, we can probably infer that a HIV patient if infected with tuberculosis is more susceptible to anemia that is difficult to improve with ATT and ART alone. So these patients might require additional nutritional supplementation to decrease the mortality and morbidity due to anemia. Also, a confounding factor in this study was that most of the patients were on zidovudine based regimens which by itself can cause anemia[8].

Lovett Lawson, Mohammed A. Yassin et al in a study in Africa found that weight loss and low BMI were the most common symptoms when the patients were diagnosed to have HIV- TB co-infection[14]. In a brief report published by Society of Infectious Diseases of America in the year 2000, the authors have found that the wasting of >10% was seen in 58% of patients and 50% of them were on HAART[11]. In patients with HIV infection, loss of metabolically active tissue results in an increase in mortality, accelerated disease progression, impairment of strength and functional status. Although a loss of 10% body weight has been considered for suspicion of HIV, even a loss of 5% has been associated with increasing morbidity and mortality[9] and hence AIDS is also called the 'slim's disease'. Initially it was thought that HIV enteropathy and diarrhea was the cause of loss of body weight, autopsy of such patients revealed disseminated tuberculosis which could have resulted in loss of weight[15].

In our study population, the mean body weight in the co-infection group was 5.10 Kgs lesser than the other group before initiation of treatment.This shows the increased susceptibility of HIV patients to loss of body weight if co-infected with tuberculosis. After treatment there was a significant improvement of body weight seen in both the groups. In group A, a mean improvement of 1.86 Kgs was noted and in group B the improvement was 3.36 Kgs and the mean difference after six months of treatment reduced to 3.59 Kgs from 5.10 Kgs. It can also be noted that on treatment with ART along with ATT, the increase in body weight was much more than the increase in the patient who did not have tuberculosis further emphasizing the effect of tuberculosis in decreasing the body weight of the patient.

The increase in the CD4 counts, hemoglobin and body weight in both the groups in our study corroborates with the finding in earlier studies. One important confounder in our study is the unavailability of the details of nutritional supplementation given to the patients which might have had a big impact on the parameters.

CONCLUSION

Tuberculosis though is an important opportunistic infection, timely and adequate interventions if taken, does not increase the mortality in the People Living with HIV/AIDS.

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CONFLICT OF INTEREST

No conflict of interest among the authors.