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A PROSPECTIVE STUDY TO COMPARE THE EFFECT OF DIFFERENT HAART REGIMENS ON CD4 COUNTS OF HIV PATIENTS WITH TUBERCULOSIS

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ABSTRACT: Introduction: AIDS is one the most dreaded diseases of human race in the present times. More than two- third of HIV infected individuals have an associated infectious pulmonary disease. Mycobacterium tuberculosis is considered as more virulent compared to other opportunistic pathogen causing latent infection. Cure of AIDS is still an unsolved mystery but some of the drugs have been developed to decrease the mortality and morbidity of the disease. These are called as Highly Active Anti-Retroviral Therapy (HAART). This work has been conducted in order to know the role of various anti-retroviral regimens in the treatment of patients of Acquired Immuno Deficiency Syndrome (AIDS) in terms of changes in CD4 count as well as in CD4/CD8 ratio. **Material and Methods:** A total of 3078 patients screened for the study. Those who were diagnosed with HIV were enrolled. Pretreatment parameters like Haemogram, CD4, CD8 + lymphocyte count and their ratio etc. were recorded. Patients were divided into four groups and were started with different HAART regimens. Their CD4 count and CD4/CD8 ratio were monitored regularly. **Results:** The prevalence of HIV sero-positivity in our study was 3.60%. Tuberculosis was the most common diagnosis among the seropositive cases. Baseline CD4 count was <50 cells/ µl in 31.67% of the patients. The mean CD4 count was 134.25 ± 99.44 cells/µl. Out of them 50% were having CD4/CD8 count <0.20. Out of 60 patients who were monitored for CD4 count, only 42 revisited for follow up. They were divided into 4 groups and started with HAART regimens. The mean CD4 count and CD4/CD8 ratio were observed to be increase after 3, 6, & 9 months of HAART in all the groups. But when this increase was compared between different groups, it was not significant (ANOVA test; p value >0.05). **Conclusion:** After starting on HAART regimens, 74.4% showed significant improvement in symptoms. The mean CD4 count and CD4/CD8 ratio observed to be increased after 3, 6, & 9 months of HAART in all the groups. When compared between different groups, the difference was not significant (ANOVA test; p value >0.05).

INTRODUCTION: AIDS, the Acquired Immuno Deficiency Syndrome, is a modern pandemic [1]. It is one the most dreaded diseases of human race in the present times. More than two- third of HIV infected individuals have an associated infectious pulmonary disease.

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Mycobacterium tuberculosis is more virulent than most of other opportunistic pathogen causing latent infection and hence, is often first endogenous infection to reactivate CD4 lymphocyte and macrophages dysfunction in HIV patient placing them at a high risk for both primary and reactivation tuberculosis [2]. The initial phase of the disease may be known as serocomversion illness. The next phase is known as asymptomatic HIV infections or AIDS related complex [3].

AIDS is fatal disease characterized by defective immunity that results from a progressive deficiency of the subset of CD4 T lymphocytes also known as

helper T cells, leading to the patients at higher risk of developing a variety of other opportunistic infections [4]. Cure of AIDS is still an unsolved mystery but some of the drugs have been developed to decrease the mortality and morbidity of the disease. These are called as Highly Active Anti-Retroviral Therapy (HAART) [5]. HAART can reverse many of the immunological deficiencies associated with untreated HIV infection. This is most apparent in terms of increased peripheral CD4+ T cell count.

Previous studies have shown that immunologic and virologic response to HAART was stronger in individuals who had no prior experience with the antiretroviral therapy agents [6]. According to studies, baseline CD4 count was a better predictor of virologic suppression induced by triple combination therapy than the baseline viral load [7]. This work has been conducted in order to know the role of various anti-retroviral regimens in treating patients of AIDS in terms of changes in CD4 count as well as in CD4/CD8 ratio.

Aim and Objectives:

- To compare the increase in CD4 count by different HAART regimens.
- To compare the change in CD4/CD8 ratio by different HAART regimens.

MATERIAL AND METHODS: The study was started after the approval from Institutional Ethics Committee (IEC).

All the patients were recruited after filling the Informed Consent Form.

Study population: A total of 3078 patients screened for the study. Patients were taken from:

- Those attending out-patient department and admitted as indoor patients in the department of Tuberculosis and Respiratory diseases.
- High risk patients from Obstetrics & Gynecology, Skin & VD, Pathology and Blood Bank.

Study Duration: Study was conducted for a period of 18 months.

Lab Studies: HIV positive patients were subjected to following Tests:

- Haemogram
- Sputum smear for AFB
- Urine examination- Routine & Microscopic
- PPD skin test
- X- ray chest, PA view
- CD4, CD8 + lymphocyte count and their ratio
- Immonocomb Assay test for HIV in all admitted cases and in cases which were highly suspicious having AIDS by clinical features.
- ELISA test of HIV in those who were positive immunocomb or immunocomb negative but with highly suspicious clinical features.

Antiretroviral therapy: Different groups of patients were prescribed different ART regimens (Table A) according to following criteria:

- Clinical presentation
- H/O contact to commercial sec workers, drug abuse and blood transfusion
- Immunocomb positive status
- ELISA positive status
- Either CD4 count less than 200cells/µl or patients with AIDS defining illness (WHO Guidelines)

TABLE A: CATEGORIZATION ACCORDING TO HAART REGIMEN

Group I 2 NRTI + 1 NNRTI	Group II 2NRTI + 1NNRTI	Group III 2NRTI + 1NNRTI	Group IV 2NRTI + 1PI
Zidovudine (300 mg bid) + Lamivudine (150 mg bid; 2mg/kg if body wt. <50 kg) + Nevirapine (200 mg OD for 14 days, then 200 mg bid for 14 days; 4mg/kg for 14 days then twice daily for children)	Stavudine (40 mg bid) + Lamivudine (150 mg bid; 2mg/kg if body wt. <50 kg) + Nevirapine (200 mg OD for 14 days, then 200 mg bid for 14 days; 4mg/kg for 14 days then twice daily for children)	Zidovudine (300 mg bid) + Lamivudine (150 mg bid; 2mg/kg if body wt. <50 kg + Efavirenz (600 mg OD)	Zidovudine (300 mg bid) + Lamivudine (150 mg bid; 2mg/kg if body wt. <50 kg + Indinavir (800 mg TDS)

Statistical analysis: It was done using SPSS Software. Paired t test used to assess changes in the mean CD4 count and CD4/CD8 ratio. ANOVA teat was used to compare the efficacy of ART regimens between the groups.

RESULTS: Results are shown here in form of relevant tables showing distribution of clinical features in HIV sero-positive cases (**Table 1),** clinical presentation in HIV sero-positive cases (**Table 2**), distribution of tubercular cases according to site of involvement (**Table 3**), various presentation of tuberculosis lesion (**Table 4**), relationship of symptomatic patients with base line CD4+ count at the time of starting ART (Table 5), mean CD4 count (absolute values) in cases on HAART (**Table 6**), changes in mean CD4 count in cases on HAART (**Table 7**), change in mean CD4/CD8 ratio in cases of HAART (**Table 8**).

TABLE 1: DISTRIBUTION OF CLINICAL FEATURES IN HIV SERO-POSITIVE CASES

Clinical Features	No. of Cases (%)
Fever (> 1 month)	79 (71.67)
Weight Loss (>10% of initial body wt.)	74 (66.67)
Cough	67 (60.00)
Difficulty in deglution (oral thrush)	40 (36.67)
Chest pain	25 (23.33)
Breathlessness	31 (28.33)
Diarrhea (>1 month)	24 (21.67)
Lymphadenopathy (including hilar lymphadenopathy)	22 (20.00)
Repeated episodes of pneumonia	14 (13.34)
Asymptomatic	7 (6.67)

TABLE 2: VARIOUS CLINICAL PRESENTATION IN HIV SERO-POSITIVE CASES

Clinical Presentation	No. of Cases	Percentage
Tuberculosis	80	72.07 %
Nontubucular chest infection	14	12.61 %
Non chest symptom	10	9.09 %
Asymptomatic	7	6.30 %
Total	111	100 %

TABLE 3: DISTRIBUTION OF TUBERCULAR CASES ACCORDING TO SITE OF INVOLVEMENT

Site	No. of Cases	Percentage
Pulmonary tuberculosis only	29	36.25%
Ex. Pulmonary tuberculosis	8	10 %
Both pulmonary and ex. Pulmonary tuberculosis	43	53.75%
Total	80	100 %

TABLE 4: VARIOUS PRESENTATION OF TUBERCULOSIS LESION

Type of Lesion	No of Cases (%)
Cavitory	15 (24.2)
Exudative	36(59.7)
Reticulomodular	18(29)
Old Fibrotic	17(27.4)
Hilar Lymphadenopathy	37(61.3)
Miliary	9(14.5)
Pleural Effusion Including Hydropneumothorax	5(8.1)
Calcification (Including Pleural Clacification)	1 (1.6)

TABLE 5: RELATIONSHIP OF SYMPTOMATIC PATIENTS WITH BASE LINE CD_4 + COUNT AT THE TIME OF STARTING ART

Baseline CD_4 + count (cell/microliter)	Symptomatic	Asymptomatic	Total
<50	19	0	19
51-100	9	0	9
101-150	7	0	7
151-200	6	4	10
201-250	6	0	6
251-300	4	0	4
301-350	2	0	2
>350	3	0	3
Total	56(93.33%)	4(6.66%)	60(100%)

TABLE 6: MEAN CD4 COUNT (ABSOLUTE VALUES) IN CASES ON HAART

Groups	Baseline Cd4 Count	Mean change after 3 months	Mean change after 6 months	Mean change after 9 months
Groups 1	157.38 ±91.87 n=16	245.31 ±137.95 n=13	320.55139 ±139.88 n=9	456.0 ±69.86 n=5
Groups 2	118.83.3 ±85.82 n=12	213.44 ±148.50 n=8	264.0 ±169.99 n=6	274.0 ±113.68 n=4
Groups 3	123.75 ±99.76 n=8	274 ±130 n=4	318.25 ±89.97 n=4	320.0 ±113.68 n=2

TABLE 7: CHANGES IN MEAN CD4 COUNT IN CASES ON HAART

Groups	Mean change after 3 months	Mean change after 6 months	Mean change after 9 months
Groups 1	92.23	155	275.25
Groups 2	42.25	146.5	171
Groups 3	177	221.75	293
Groups 4	226.75	394	305

TABLE 8: CHANGE IN MEAN CD4/CD8 RATIO IN CASES OF HAART

Groups	Baseline count	Mean change after 3 months	Mean change after 6 months	Mean change after 9 months
Groups 1	0.243±0.191 n=16	0.49±0.233 n = 13	0.713±0.196472 n=9	1.016±0.198957 n=5
Groups 2	0.278±0.185 n=12	0.427±0.270637 n=8	0.748±0.287 n=5	0.824±0.39 n=3
Groups 3	0.273±0.202 n=8	0.803±0.015 n=4	0.605±0.29 n=4	0.78±0.283 n=2
Groups 4	0.232±0.21 n=6	0.505±0.26 n=4	0.79±0.18 n=3	1.0 n=1

DISCUSSION: The prevalence of HIV sero-positivity in our study was 3.60%. Sivaraman (1992) and Arora (1993) reported it to be 2.7 % and 3.4% respectively [8, 9]. The most common clinical feature among the sero-positive HIV cases was fever (in 71.67%) followed by weight loss (in 66.67%) and cough (in 60.00%). Tuberculosis was the most common diagnosis among the seropositive cases with 72.07% cases. Among 80 patients, 8 (10%) had extrapulmonary TB, 29 (36.25%) had pulmonary TB while 43 (53.57%) had both. Dhurat *et al., (*2000) reported 67.5% cases were of Tuberculosis [10].

The most common extrapulmonary site was lymph node in 27.5%. Sircar *et al.,* (1998) showed lymphadenitis in 22.5 % of HIV seropositive cases [11]. According to the type of lesions, hilar lymphadenopathy was most common (61.3%) followed by exudative lesions (59.7%), reticonodular (29%), old fibrotic lesion (27.4%) and military mottling in 14.5% cases.

Out of 111 seropositive cases, 60 received HAART. Baseline CD4 count was< 50 cells/ µl in 31.67% of the patients. The mean CD4 count was 134.25 ± 99.44 cells/µl. Out of them 50% were having CD4/CD8 count <0.20. Out of 60 patients who were monitored for CD4 count, only 42 agreed to revisit for CD4 count follow up. They were divided into 4 groups and started with HAART regimens.

In Group I, the baseline CD4 count was 157.38 ± 91.87 which increased to 456.0 ± 69.86 after 9 months of treatment. Similarly in group II it increased from 118.83 ± 85.82 to 274.00 ± 113.68, in Group III from 123.75 ± 99.76 to 320.00 ± 77.78 and in Group IV from 191.33 ± 42.33 to 445.00. The mean CD4 count was observed to be increased after 3, 6, & 9 months of HAART in all the groups. But when this increase was compared between different groups, it was not significant (ANOVA test; p value >0.05). This could be because of less number of cases and significant dropouts in some of the study groups. G Kaufmann *et al.,* (1998) concluded that after 4 years only 36% of patients receiving HAART reached > 500 cells /µl [12]. Ray *et al.,* found that after 12 weeks of antiretroviral therapy all the children included in the study showed significant rise in CD4 count i.e. from 389 ± 116 to 569 ± 121 cells/µl [13].

CONCLUSION: Out of 3078 patients attending the respiratory medicine department and screened for HIV, 111 (3.60%) were HIV positive by ELISA method Fever, weight loss and cough were the most common symptoms. 72.07% of HIV seropositive cases were of tuberculosis. 60 of the patients were started on HAART. Only 42 of them agreed to undergo CD4 count at follow-up visit.

In Group I, the baseline CD4 count was 157.38 ± 91.87 which increased to 456.0 ± 69.86 after 9 months of treatment. Similarly in group II it increased from 118.83 ± 85.82 to 274.00 ± 113.68, in Group III from 123.75 ± 99.76 to 320.00 ± 77.78 and in Group IV from 191.33 ± 42.33 to 445.00. The mean CD4 count was observed to be increased after 3, 6, & 9 months of HAART in all the groups. But when this increase was compared between different groups, it was not significant (ANOVA test; p value >0.05).

The mean CD4/CD8 ratio was found to be increased after 3, 6 & 9 months of HAART in all the groups but the difference in increases in CD4/CD8 ratio in all the groups was not significant (ANOVA; p value>0.05). This could be because of fewer number of cases and significant dropouts.

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