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Evaluation of CD4 count response in HIV subjects with antiretroviral treatment protocol

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ABSTRACT

Introduction: The present study was undertaken to evaluate the CD4 count responses in subjects who are on long term first line antiretroviral treatment (ART).
Materials and Methods: A total of 200 People Living with HIV/AIDS (PLHIV), on first line ART for five years seen in the ART centre were included in the study. Patients were interviewed and details entered as per the proforma. Proforma included various details such as serial CD4 counts and Opportunistic infection pre and post ART.
Results: Mean CD4 count pre ART was 171.32 ± 65.23 per mm^3 and one year after ART was 374.56 ± 159.12. There was significant rise in CD4 count one year after the initiation of ART (p = 0.000) The mean CD4 count at the time of collection of data was 545.23 ± 259.11 as compared to mean CD4 count pre ART of 171.32 ± 65.23 per mm^3. The rise was significant.
Conclusions: National AIDS Control. Organization (NACO) suggested first line regimens outcome in vigorous immunologic response that is continued over a mean period of over six years in a majority (84%) of the subjects and consequence in significant decline in opportunistic infections.

1. Introduction

Human Immunodeficiency Virus (HIV) demolishes CD4 cell count, which consequence to an augmented plasma HIV RNA levels and experience an Acquired Immune Deficiency Syndrome (AIDS) in the long-run. Worldwide, a whole of 36.7 million individuals are living with HIV from whom 2/3 are from low and middle-income countries. Sub-Saharan Africa holds the maximum weight of the diseases, 71% of the worldwide total, but only about 12% of the world's residents.[1]

CD4 counts are utilized as predictive markers of HIV illness sequence. Untreated HIV-infected individuals have a steady reduction in CD4 cell levels, leading to augmented risk of AIDS-defining illnesses and death. Mixture antiretroviral therapy (ART) has been extremely effectual in preventing HIV disease sequence and restoring CD4 cell levels as well as dropping viral duplication and lowering rates of HIV linked morbidity and mortality.[2,3]

The chief objective of ART is to decrease HIV connected morbidity and mortality, extends survival, perk up the quality of life, reinstate and protect immunologic purpose and avert HIV-transmission. The level of CD4 cell counts is regularly utilized for monitoring retort to ART in HIV-infected subjects. According to the CD4 cell count criteria, a subject would be qualified when his/her CD4 cells counts fall under a specified threshold value.[4,5] The WHO 2013 guideline advocate that ART be begin for all subjects with CD4 count 500 cells/mm^3 or fewer. In 2015, WHO suggested HIV-treat all approach based on 2 clinical trial outcomes. Nevertheless, numerousre searches are against previous beginning of ART in subjects who have elevated

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CD4 cell counts. This is because premature experience to ART may impetuous premature development of struggle and superfluous side-effects.[6]

Following the initiation of mixture ART and normally within six months of believer therapy, around 80% of HIV-positive subjects have untraceable plasma HIVRNA viral loads. The inhibition of HIV replication facilitates immune reconstitution. The general immunological response to treatment for the majority of subjects is categorized by comparatively quick increases in CD4 cell counts through the first two years of treatment, followed by lesser but steady increases through 3–6 years of treatment.[7]

Elder age, male gender, elevated baseline viral load, confrontation to drugs, poor adherence, connections with other medications, co-infections like Hepatitis C, HTLV 1 and 2, anaemia, substance abuse and depression are a few of the factors other than the first low CD4 count which can power immunological revival and management outcome.[8]

Over the past three decade there has been a incredible augment in our understanding of molecular biology and the viral structure and pathogenesis of the illness. This information has lead to the growth of a number of new antiretroviral drugs and management protocols. While ART does not treat HIV infection, the diminish in the viral load and the development in immunological grade bring about by the utilize of these drugs have resulted in a obvious diminish in the mortality and morbidity linked with the illness.[9]

Clinical trials have recognized the effectiveness of antiretroviral therapy with triple-drug regimens for persons infected with the human immunodeficiency virus (HIV), but the efficiency of these regimens in the residents of subjects enrolled outside clinical trials is unidentified. A cross-sectional study was undertaken to approximate the CD4 count responses in subjects who are on long term first line ART.

2. Materials and Methods

Present is cross-sectional study. The study was done for the period of one year. The ethical institute was informed about the study and the ethical clearance certificate was obtained prior to the study. The included patients were informed about the study and the consent was obtained prior to the inclusion in the study.

Source of data: A total of 200 PLHIV, on first line ART for five years in the ART centre or admitted in the Medicine wards of Medical College and associated Hospital.

2.1. Inclusion criteria

1. Adult patients diagnosed with HIV infection and on first line ART for 5 years.

2.2. Exclusion criteria

1. Patients on drugs likely to cause CD4 cytopenia.

Subjects were interviewed and details entered as per the proforma. Proforma included details such as age, gender, educational status, co-morbidities, history of smoking or alcohol use, duration of HIV, duration of treatment, ART regimens, opportunistic infections before and after ART, hospitalizations before and after ART, weight before and after ART and serial CD4 counts. Data was entered and analysed in the SPSS statistical program. Descriptive statistics were collated.

3. Results

A total of 200 subjects were incorporated in the research. There were 134 males and 66 females. The male to female ratio was found to be 2:1. Out of total 200 patients 69% were between 35 and 50 years of age, extremes of age were lesser in number. The mean age was 44.5 ± 5.29 years. The mean duration of disease in females was 5.20 ± 3.24 years and in males 5.34 ± 6.18 years. The dissimilarity was statistically significant, of the total 200 patients there were 174 patients with presence of symptoms at the time of diagnosis of the disease, whereas there were 26 patients who were symptoms free. Candidiasis was the most common opportunistic infection occurring in 134 out of the 200 patients studied, that was followed by Tuberculosis found in 86 patients, PCP was found in 74 patients, and Cryptococcal meningitis was seen in six patients.

The pre- ART CD4 counts ranged from 6 to 345 per mm^3. The mean pre-ART CD4 count was 171.32 ± 65.23 per mm^3. In males the mean CD4 count was 162.62 ± 77.23 per mm^3 and in females it was 179.28 ± 77.22 per mm^3. The difference was not significant, majority of study population required hospitalizations prior to initiation of ART. Ninety two subjects were admitted one time, 48 subjects were admitted twice, 34 subjects were admitted thrice, 12 patients were admitted four times and 4 of them required five hospitalizations. Only 10 patients were not hospitalized prior to ART. The mean duration of ART in the study subjects was 5.87± 2.34 years.

After the start of ART protocol out of 200 patients, weight gain was seen in 154 patients, whereas weight loss was seen in 38 patients. In only 8 patients no loss of weight or any type of change was seen. After the treatment regime of six months of ART, the opportunistic infections were seen in the following patients: Candidiasis was seen in 56 patients, 38 patients were diagnosed with Tuberculosis, 30 patients had PCP, and Cryptococcal infections were seen in four patients. Few patients had other opportunistic infections after the initiation of ART. Among the other OIs diarrhoea was most common that was followed by recurrent LRTI (Lower respiratory tract inection).

Mean CD4 count pre ART was 171.32 ± 65.23 per mm^3 and one year after ART was 374.56 ± 159.12. There was significant increase in CD4 count one year after the initiation of ART ($p = 0.000$) The mean CD4 count at the

time of collection of data was 545.23 ± 259.11 as contrast to mean CD4 count pre ART of 171.32 ± 65.23 per mm^3. The rise was significant. There was significant increase in CD4 count following the initiation of ART. But in few patients after the initial rise there was drop in CD4 count. In few patients the CD4 count response plateau and remained same. The mean CD4 counts rose progressively till 5 years of treatment. The mean CD4 was higher at a mean duration of ART of 6.03 ± 1.64 years as compared to the values at 5 years but the maximum CD4 value was higher and the minimum CD4 value was lower, indicating that in some patients the CD4 counts continued to rise even after 5 years and in some patients it had started falling.

Table 1: Opportunistic infection after 6 months of ART

Opportunistic Infection	Pre ART	After 6 months
Candidiasis	134	56
Tuberculosis	86	38
PCP	74	30
Cryptococcal infections	6	4

Table 2: CD4 response at the time of study

Time	Pre ART	Current
Mean CD4	171.32 ± 65.23	545.23 ± 259.11

Table 3: CD4 response after one year of ART

Time	Pre ART	1 year
Mean CD4	171.32 ± 65.23	374.56 ± 159.12

4. Discussion

Two hundred consecutive patients satisfying the inclusion criteria were included in the study. Out of these 134 were males and 66 were females. This data is in concordance with NACO annual report 2011-2012. In India among the people living with HIV 61% are men and 39% are women. A male preponderance (77%) was also documented in a study done by Goel et al.,[10]

The disease duration varied from 5 years to 19 years. This is expected as the study was designed to look at long term CD responses and only patients on ART for at least 5 years were included in the study. Males were found to have a significantly longer duration of disease. Similar findings were documented in a study done by Neogi et al.,[11] the disease duration varied from 4 to 15 years. Both these studies reflect the long term survival that is possible with ART.

All the subjects received the standard NACO regimens consisting of two NRTI's plus one NNRTI.ZLN [Zidovidine, Lamivudine and Nevirapine] was the most commonly used ART regimen, in 130 patients. Eighteen were on SLN [Stavudine, Lamivudine and Nevirapine], 26 were on ZLE [Zidovidine, Lamivudine and Efavirenz] and 6 were on SLE [Stavudine, Lamivudine and Efavirenz]. In two subject TLE [Tenofovir, Lamivudine and Efavirenz] was administered. In a study done by Rohit et al.,[10] out of 1248 patients, 501 patients were on Zidovidine based regimen, 747 patients were on Stavudine based regimen. 25 In a study done by Ghate et al.,[12] in 2011 at Pune, among the 142 patients the initial ART regimens were as follows; ZLN 43.7%, SLN 38%, SLE 12% and ZLE 6.3%. In all the studies majority of the patients were on standard NACO recommended regimens.

Mean CD4 counts; showed that the CD4 counts increased progressively through a mean duration of 5 years. However, the minimum value was lower and the maximum value higher in the last CD4 count, as compared to the five-year values indicating that at a mean ART duration of 6.03 ± 1.64 years, in some patients the CD4count had continued to rise whereas in some it had started falling. Sixty percent attained normalization of their CD4 counts.

The best possible answer to ART is indicated by a median rise of CD4 count of 50/mm^3 towards the end of 6 months or 100/mm^3 at 1 year of management. 34 researches performed in diverse countries have documented dissimilar levels of rise in CD4 counts following the management. Present findings on increase in CD4 counts are comparable to that observed in various researches in India as well as in various countries. In a study done by Devi et al., mean baseline CD4 and peak CD4 cell count during therapy was 156.43 ± 85.83/mm^3 and 401.11 ± 273.3/mm^3. In the study done by Goel et al.,[10] there was a significant improvement in CD4counts from before (122.78 ± 70.06/mm^3) to after therapy (305.37 ± 147.39/mm^3).

In our study 84 patients showed steady rise in CD4 count. Tar water et al., reports that the boost of CD4 cell count in the primary two years was sustained in spite of the CD4 cell count at which strong ART was started, nevertheless, the increase levelled off following2 years. Research performed by Rajashekaran et al.,[13] on augment in CD4 counts among 2 and 3.5 years following the beginning of ART at 2 years, the absolute and percentage CD4 cell count alter from the baseline median CD4 cell count for the subjects whose CD4 cell counts were <100, was 393 and 819% correspondingly.

The study described that numeral opportunistic infections reduce once patients were on ART. At baseline, Ninety seven percent of the patients had single or multiple opportunistic infections with candidiasis being the most common. Nevertheless, as the management progressed, the number of subjects with documented OIs decreased to 67 per cent. These are infections that have occurred six months post ART till the time of inclusion in the study, a mean ART duration of 6.03 ± 1.64 years.

Candidiasis reduced from 67% to 28%, Tuberculosis from 43% to 19%, PCP from 37% to 15%, CMV from 9% to 6% and Cryptococcal infections from 3% to 2%. There was

a definite reduction in these HIV related OIs. The reduction in other infections which included diarrhoea and respiratory infections were not much; from 44% to 41%. It is difficult to interpret this finding as the post ART infections have been documented from the completion of 6 months of ART till the time of the research. The mean number of opportunistic infections reduced from 2.03 ± 0.81 before ART to 1.06 ± 1.11 post-ART. The difference was statistically significant ($p = 0.000$).

5. Conclusions

NACO suggested primary line regimens consequence in vigorous immunologic retort that is constant over a mean phase of over six years in a mainstream (84%) of the subjects and consequence in significant lessening in opportunistic infections.

6. Acknowledgments

None.

7. Conflict of Interest

None.

8. Source of Funding

None.

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