STUDY OF CD4 COUNT IN HIV PATIENTS ON HAART THERAPY

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ABSTRACT

BACKGROUND

HIV infection has evolved into greatest pandemic in human history with more than 60 million humans currently affected by HIV virus. CD4 cell dysfunction is the hallmark of HIV disease. CD4 count is important for initiation and monitoring of ART and opportunistic infection prophylaxis, we have conducted a study on 100 HIV patients on HAART therapy whose CD4 count is < 350/MI, follows for 6 months.

MATERIALS AND METHODS

Inclusion Criteria - (1) HIV confirmed cases with CD4 count < 350/mL > 18 yrs. of age, patients irrespective of CD4 count in clinical stage III and IV. CD4 count assay is done with whole blood stained and analysed by FACS count cytometry using LASER.

RESULTS

Improvements of CD4 count by a mean of 180.28 cells/mm3 was observed. Improvement of CD4 count is slightly more in females. CD4 count was not significant in patients aged > 60 yrs. in those with CD4 count of < 350 cells/mm3, most mode of transmission is heterosexual (94%). HIV incidents are observed more commonly in non-agricultural labourers (41%), 46% has co-existence illness of these tuberculosin was common (pulmonary and extrapulmonary).

CONCLUSION

1. CD4 count is mandatory in all patients who are confirmed as HIV/AIDS, irrespective of clinical stage since the clinical stage and CD4 count could not correlate. 2. HAART therapy decreases the incidence of opportunistic infections. 3. HAART therapy has improved BMI.

KEYWORDS

HIV Disease, CD4 Count, HAART Therapy.

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BACKGROUND

Human Immunodeficiency Virus (HIV), the cause of AIDS was first described in 1981. The HIV virus itself was discovered after 2 years, during which time various causes were considered including lifestyle factors and chronic drug abuse. The HIV epidemic spread rapidly and silently before the testing and effective management became available during the early part. HIV type 1 is the aetiologic agent of most cases of AIDS.[1,2] HIV infection has evolved to become greatest pandemic in human history with more than 60 million humans currently infected by the virus.[3] HIV disease has claimed more than 25 million lives worldwide.[4] The recent estimate done by National AIDS Control Organisation reports 2.4 million HIV infected people in India. India has the second highest HIV burden in the world next to South Africa.[5] It is an acquired disease for which no permanent cure has been found till date, and consequently has a great impact on the quality of life of a patient. HIV/AIDS infection results in diverse clinical manifestations from asymptomatic carriage to life-threatening opportunistic diseases due to ongoing viral replication, producing a sequential decline in and ablation of cell-medicated immunity. There is a specific decline in the CD_4 + helper T cells, resulting in inversion of the normal CD_4/CD_8 T-cell ratio and deregulation of B-cell antibody production.[6] Immune responses to certain antigens begin to decline and the host fails to adequately respond to opportunistic infections and normally harmless commensal organisms. Because the defect preferentially affects cellular immunity, the infections tend to be non-bacterial (Fungal, viral). The acquired immune deficiency syndrome is the advanced stage of this illness, in which the infected host can no longer control opportunistic organisms or malignancies that rarely cause illness in immune competent individuals.

Rates of disease progression in HIV infected individuals are highly variable.[7] HIV subverts the immune system infecting CD_4 + T-cells that normally orchestrate immune responses and by activating the immune system and inducting a cytokine milieu that the virus uses to its own explicative advantage.

The lack of recognisable correlates of protective immunity in HIV infection continues to hamper vaccine development and immunotherapeutic approaches. It remains unclear why HIV infected patients experience inexorable immunodeficiency and disease progression despite the presence of robust cytotoxic CD_8 T-cell response and production of neutralising antibodies and antiviral immune responses. HIV reduces ability of thymus gland to replace lost CD_4 cells.

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The progress that has been made to date in understanding the pathogenesis of HIV infection is unparalleled.[8] CD_4 T-cell dysfunction is a major hallmark of HIV disease. CD_4 count is important for initiation and monitoring of ART and opportunistic infections prophylaxis. Government of India launched ART programme on 1st April 2004. Combination of at least three antiretroviral drugs from different groups (Highly Active Anti-Retroviral Therapy) HAART/c ART (Combined ART) is the current standard of care.

Development of newer generation antiretroviral has extraordinary clinical benefits for patients in terms of efficacy, simpler regimens with few toxicities. Since drug therapy is life long, improving patient's commitment and adherence by counselling, regular monitoring is essential for better outcomes.

The prevalence and morbidity due to opportunistic infections can be controlled by improving the general condition and immune status of the individual.[9] Early HAART initiation is the rule except in Tuberculosis and cryptococcal meningitis, where it is deferred until 4 - 8 weeks of specific treatment if CD_4 counts are > 50/mm^3. In this study, the individual and group wise benefit of antiretroviral therapy on CD_4 + T-cell count is evaluated in patients suffering from HIV/AIDS at Government General Hospital, Anantapuramu, Andhra Pradesh.

MATERIALS AND METHODS

This study is conducted on the patients who attended the ART Centre at Government General Hospital, Anantapuramu between the period from 1st January 2015 to 31st December 2015. A total of 100 patients are included in the study.

Inclusion Criteria

1. All the patients with confirmed adult HIV/AIDS and with CD4 counts < 350/microlitre (According to WHO guidelines, 2010).
2. Patients irrespective of the CD_4 count in clinical stage III and IV.
3. Patients above the age of 18 years.

Exclusion Criteria

1. All the patients with confirmed adult HIV/AIDS and with CD_4 counts > 350/microlitre.
2. Patients who lost for followup.
3. Patients below the age of 18 years.

A chart was prepared with detailed pre- and post-therapy CD_4 counts, opportunistic infections at the time of presentation, type of HAART therapy and the pre- and post-therapy body weight.

Confirmation of HIV/AIDS

All patients who attended the ART Centre at Government General Hospital, Anantapuramu between January 2015 and December 2015 were screened for HIV, and the HIV positive status was confirmed according to NACO guidelines. The blood sample collected at one time was tested with the first kit (Coomb-AIDS). If it was reactive, it was then retested sequentially with the second (ASPEN) and third kits. (Single HIV).

CD_4 Count Assay

Blood was collected in heparinised bottles for flow cytometry analysis. The heparinised blood of about 100 µL of whole blood is stained and analysed for CD_4 by FACS count cytometry using Laser. CD_4 count was repeated after 6 months.[10]

Investigations Considered

1. Measurement of Weight/BMI.
2. HB%, TC, DC, ESR.
3. Blood Urea.
4. Serum Creatinine.
5. Urine Analysis.
6. Chest x-ray.
7. Other relevant investigation wherever necessary.
8. Liver Function Tests.

After obtaining the consent from the patient, he/she was included in the study.

RESULTS

Total number of 100 patients were analysed. Both the initial CD_4 count and CD_4 count after 6 months of highly active antiretroviral therapy were obtained as follows.

Age Group	Male		Female		Total	
	No. of Patients	%	No. of Patients	%	No. of Patients	%
13 - 20	-	0%	1	1%	1	1%
21 - 30	14	14%	16	16%	30	30%
31 - 40	23	23%	12	12%	35	35%
41 - 50	16	16%	9	9%	25	25%
51 - 60	4	4%	2	2%	6	6%
> 60	2	2%	1	1%	3	3%
Age and Sex Distribution						

	No. of Patients	Mean Age
Male	59	38.4
Female	41	33.3
Mean Age and Sex Distribution		

Among the 100 patients studied, males were more commonly affected (59%) when compared to females (41%).

Mode	No. of Cases	Percentage
Heterosexual	94	94%
Unsafe Injection	2	2%
Men having Sex with Men	4	4%
Mode of Spread		

Among the 100 patients analysed heterosexual transmission was the most common mode of transmission (94%) with men having sex with men constituting 4% and unsafe injection constituting 2%.

Occupation	Number of Patients	Percentage
Agricultural Labour	16	16%

Non-Agricultural Labour	41	41%
Services/Employees	11	11%
Business	16	16%
Housewife	5	5%
Transport	11	11%
Occupation Distribution of Patients		

Regarding occupation 41% are Non-Agricultural Labourer, 16% Agricultural Labourer, 16% are in Business, 11% are Employees, 11% are in Transport field and 5% are housewives.

Income Category	No. of Patients	Percentage
Low	30	30%
Middle	47	47%
High	23	23%
Total	100	100%
Income Category of Patients		

Among the 100 patients studied, 47% of the patients were earning between Rs. 2,000 to 5,000 per month, so it seems middle income socioeconomic status is playing a role in altering sexual behaviour patterns. But this could also be because of a sampling bias; 30% were earning less than Rs. 2,000 per month and 23% earning more than Rs. 5,000 per month.

Literacy Status	No. of Patients	Percentage
Illiterate	30	30%
Primary Education	15	15%
Secondary Education	38	38%
Inter	7	7%
Degree	10	10%
Literacy Distribution of Patients		

There were 30 Illiterates (30%) and 75 Literates in the study group. Among the literates 15% were educated up to primary school level, 38% up to high school level, 7% studied intermediate and 10% studied up to college level.

Locality	No. of Patients	Percentage
Rural	40	40%
Urban	60	60%
Residence/Locality		

Geographically, 60% were from urban area and 40% from rural area.

History of Smoking	No. of Cases	Percentage
Yes	22	22%
No	78	78%
Smoking Correlation to Sexual Behaviour		

Among the 100 patients studied, 22 cases (22%) have history of smoking.

History of Alcohol Intake	No. of Cases	Percentage
Yes	25	25%
No	75	75%
Alcoholism Correlation to Sexual Behaviour		

Among the 100 patients studied, 25 cases (25%) have history of Alcohol intake. Overall 15 patients out of 100 patients were both alcoholic and smoker showing risk attitude among HIV patients.

Disease	No. of Cases	Percentage
Pulm TB	11	11%
Extra-Pulm TB	12	12%
Diabetes Mellitus	6	6%
Hypertension	5	5%
Anaemia	9	9%
Hepatitis-B	5	5%
CAD	1	1%
Associated Illness/Disease Configuration		

Among the 100 patients studied, 46 patients had co-existing illness. Extrapulmonary tuberculosis was present in 12 patients, pulmonary tuberculosis in 11 patients and Diabetes Mellitus in 6 patients, Hypertension in 5 patients, 9 were anaemic, 2 patients had Hepatitis-B infection, 1 patient had history of CAD. So tuberculosis was the most common opportunistic infection in the study population. The associated illness was diagnosed at the time of the initial diagnosis of HIV and it seems HAART decreases the incidence of significant opportunistic infections.

CD4 Count	Male	Female	Total
< 50	10	5	15
51 – 100	15	4	19
101 – 150	11	5	16
151 – 200	8	5	13
201 – 250	6	7	13
251 – 300	5	7	12
301 – 350	3	7	10
> 350	1	1	2
CD_4 Cell Count Comparison			

CD_4 Cell Count	Mean ± SD
Pre-ART	164.96 ± 107.33
Post-ART 6 months followup	345.24 ± 184.69

Among the 100 patients analysed for the impact of HAART on CD_4, the mean CD_4 count at the time of presentation is 164.96 and increase of 180.28 cells/mm3 was noted after 6 months of HAART at 345.24, which was statistically significant when analysed by paired 't' test which showed the 'P' value of < 0.001.

CD_4 Cell Count	Male
Pre-ART	139.97 ± 93.29
Post-ART 6 months followup	309.78 ± 179.44
Comparative Analysis of Initial and Followup CD_4 Count in Males	

In the male subgroup, mean CD_4 count at the time of presentation was 139.96 and after 6 months ART followup was 309.78 with rise of 169.81 cells/mm^3.

CD_4 Cell Count	Female
Pre-ART	200.93 ± 116.82
Post-ART 6 months followup	396.27 ± 182.24
Comparative Analysis of Initial and Followup CD_4 Count in Females	

In the female subgroup, mean CD_4 count at the time of presentation was 200.93 and after 6 months ART followup was 396.27 with rise of 195.34 cells/mm^3.

Initial CD_4 Count Group	No. of Patients	Pre-ART CD_4 Count	Post-ART CD_4 Count
< 50	15	24.2±16.12	160.07±81.51
51 – 100	19	75.79±15.25	222.89±92.40
101 – 150	16	121.31±16.80	308.31±97.61
151 – 200	13	181.15±12.55	420.08±161.57
201 – 250	13	222.69±13.76	396.46±192.09
251 – 300	12	282.17±13.87	491.17±185.54
301 – 350	10	321±16.53	537.6±145.68
> 350	2	453±141.42	535±190.92
Group Wise Analysis of Initial and Followup CD_4 Count			

Age Group	No. of Patients	Pre-ART CD_4 Count	Post-ART CD_4 Count
13 – 20	1	334	502
21 – 30	30	195.5±114.26	388.37±195.32
31 – 40	35	157.74±106.04	325.66±195.65
41 – 50	25	125.48±85.79	312.96±162.30
51 – 60	6	114±75.94	298±167.38
> 60	3	288.33±69.83	452±122
Age Wise Analysis of Initial and Followup CD_4 Count			

DISCUSSION

Prior to Treatment

Fall in CD_4 count that happens in asymptomatic phase of HIV infection follow three types of patterns. These are the rapid, typical and slow patterns. In rapid decliners with CD_4 cell crash, the counts fall by approximately 50 per month from a normal value of 800 - 1200 cells/mm^3. In typical situation, the fall is around 50 - 100 cells per year. In slow progressors, the counts continue at higher level for years without significant fall. This is usually not in relation with rise in viral load that happens over a period of time.

On Treatment

The elevation in CD_4 cell count is commonly used to assess the response to ART. But anti-retroviral drugs per se have no effect on CD_4 cells. They modify or inhibit various stages of viral replication, then viral levels in the body are reduced, CD_4 cell depletion gets arrested leading to rise in CD_4 cell count. Thus, fall in HIV viral loads and rise in CD_4 cell count should occur in a predictable inverse relationship.

To improve treatment outcome, ART adherence counselling should target specific personal barriers to ART adherence like lack of family support, health and sexual life concerns, desire to have children and family instability.

Factors such as the impact of hepatitis, TB co-infection or pregnancy and anaemia on antiretroviral therapy choice, toxicity and regimen change should also be examined before initiation of antiretroviral therapy.

Reconstitution of CD_4 T-cells during viral suppression generally follows a biphasic pattern, typically showing burst of increase of 50 - 120 cells/mm^3 during first three months followed by a second slower phase of T-cell repopulation with average rate of increase of 2 to 7 cells/mm^3 per month.

The Aim of Current study is to primarily evaluate the impact of ART on change in CD_4 count. (A total of 1144 (Male 561 + Female 583) patients were confirmed HIV positive between 1st January 2015 to 31st December 2015 in ART centre at Government General Hospital, Anantapuramu. Antiretroviral Therapy was initiated in 903 (Male 438 + Female 465) patients with WHO/NACO eligible CD_4 count/stage including previously diagnosed patients). Among 1144 patients confirmed HIV positive from January 2015 to December 2015, 100 patients having CD_4 counts < 350 or WHO Stage III and IV irrespective of CD_4 count were included in the study and after six months followup repeat CD_4 count was done.

These patients' CD_4 counts pre- and post-anti-retroviral therapy are analysed and represented in the study; 398 patients were lost to follow-up for various reasons (Male 223 + Female 175).

Prevalence of HIV infection is more in low and middle income groups with 30% and 47% respectively in current study, most of them being agricultural and non-agricultural labourers. Predominant mode of transmission is heterosexual (94%) in current study. Social stigma may be the cause for under disclosure/reporting of MSM and female sex worker status.

There were sex related changes in composition of the subjects with respect to age. Male, female ratio being 3:2. Most common age group affected in males was 31 - 40 years and among females it was 21 - 30 years' age group. Young adults account for much of HIV burden. The change in CD_4 count in most of the subjects has been noticed. Male and female subjects showed statistically significant improvement by 169.81 and 195.34 cells/mm^3 after 6 months ART with females having slightly better increments in CD_4 counts.

In this study, it was found that the mean age of seeking medical advice is 33.3 years in females and 38.4 years in males. There is male preponderance probably due to risk behaviour. In current study > 60 years' age group showed less significant improvement in CD_4 count post 6 months ART. Downregulation of the immune system with advancing age could be the reason for less significant growth in CD_4 count in above 60 years' age group. The subjects above 50 years' age group are low in number when compared to younger age groups.

Some of the previous studies evaluated the increase in CD_4 count with relation to sex and also to viral load. With the available resources the study involves evaluation of age, gender and initial CD_4 count group wise impact of ART on change in CD_4 count. Most of the patients seeking medical therapy occurred in a range of low CD_4 count between 0 - 100 (34% in current study). The clinical and epidemiological importance of this finding is that lower the CD_4 count more likely are the patients to develop opportunistic infections like Pneumocystis Carinii pneumonia. CD_4 count is important in approaching management of HIV infection like opportunistic infections prophylaxis.

From the statistics, it understood that the mean CD_4 count at the time of presentation was 139.97 in males and 200.93 in females. This when compared to the normal CD_4 count is much less. The mean increase of the count when the total subjects are taken is also significant ($P < 0.001$). The mean count after therapy was 309.78 in males and 396.27 in females.

The seropositivity was found to be associated with a low level of literacy. Truck drivers and labourers who migrated for their livelihood were the important occupational groups among the males, who needed awareness in the current preventive programme for AIDS.

Even in the very low initial count, females when compared to males the response to HAART is good for females than in males with less incidence of poor responders. The males also show a rise in count, which is significant. Castagno et al in their study showed that stopping HAART resulted in gradual decline in the number of CD_4 cells. Current study does not include the effect of individual antiretroviral drugs. The drugs are used in combination of individual agents. While analysing the data, it became evident that the number of subjects in the study showed good response to therapy.

These findings show the definitive impact of HAART in increasing CD_4 cells in AIDS patients. The number of new HIV infection is on decline and the life expectancy of the HIV infected person is almost reaching to that of a normal individual. Success achieved by ART has now transformed the HIV infection from being a virtual death sentence to a chronic manageable illness.[11,12]

BMI was missing in patients too weak to stand in our cohort, and thus with poor prognosis. Studies in Africa have assessed the short-term prognostic value of nutritional indicators at HIV diagnosis on survival.[13] These studies showed a correlation between a low BMI at enrolment in HIV care and subsequent treatment outcome.

Life expectancies of patients with baseline CD_4 counts > 200 cells/μL were between 70% and 86% of those in HIV-negative adults of the same age and sex, and life expectancies were increased by 15% - 20% in patients who had survived 2 years after starting ART.[14]

Unrecognised TB at the time of ART initiation resulted in impaired CD_4 recovery compared with TB treated before ART initiation. More vigilant screening with more sensitive and rapid TB diagnostics prior to ART initiation is needed to decrease the risk of ART-associated TB and sub-optimal immune reconstitution. In current study subjects presenting with a very low count initially, often with high WHO stage due to TB co-infection after HAART were among poor responders in the CD_4 count improvement. Patients with no or a small increase in CD_4 counts after 6 months of HAART and low CD_4 levels at initiation of therapy have an increased risk of HIV-related disease. In dually infected patients, it suggests that TB additionally influences the reduction of CD_4 counts in HIV patients.[15]

Routine HIV viral load monitoring is not generally available in national ART programme and treatment failure is frequently suspected by immunological and/or clinical failure. All suspected treatment failure cases are confirmed by viral load assay to determine eligibility of second line ART. Typically, biological failure precedes immunological failure and lastly clinical failure.

Le T et al study "Enhanced CD_4 + T-cell recovery with earlier HIV-1 antiretroviral therapy" – A transient, spontaneous restoration of CD_4 + T-cell counts occurs in the 4-month time window after HIV-1 infection. Initiation of ART during this early period is associated with an enhanced likelihood of recovery of CD_4 + counts. HIV-infected patients with higher baseline CD_4 (+) T-cell counts could result in higher total CD_4 (+) T-cell counts, thereby achieve a better immune recovery. These results support current guidelines to start HAART at a threshold of 350 cells/microl.[16,17] Among HIV-infected Nigerian individuals, HBV confection, especially among those with high levels of HBV replication, was associated with lower CD_4 + T-cell counts at ART initiation, independent of HIV RNA level. Patients with HBeAg-positive status had a slower biological response to ART compared with HBeAg-negative patients. Further work is needed to understand the effects. Higher DNA and detectable HBeAg levels were independently associated with lower CD_4 + T-cell counts at ART initiation, but not with higher HIV loads.[18]

HIV-positive patients who currently smoke have increased mortality and decreased quality of life as well as increased respiratory symptoms, COPD and bacterial pneumonia. These findings suggest that smoking cessation should be emphasised for HIV-infected patients.

Antiretroviral Therapy (ART) adherence is a key to successful treatment of HIV infection and alcohol is a known barrier to adherence. Beyond intoxication, ART adherence is impacted by beliefs that mixing alcohol and medications is toxic participants who endorsed interactive toxicity beliefs were significantly more likely to miss medications on drinking days. Demonstrated significantly poorer ART adherence were less likely to be viral suppressed and more likely to have CD_4 counts under 200/mm^3. Among HIV-infected Indians in primary care, predictors of unprotected sex included alcohol use and desire for children. Prevention interventions for Indian couples should integrate reproductive health and alcohol use counselling at entry into care.[19]

Studies have yielded conflicting results regarding alcohol's influence on HIV outcomes, particularly after Highly Active Antiretroviral Treatment (HAART). Discrepant findings may be related to confounding variables including gender, patterns of alcohol abuse and type of alcohol beverage beyond the amount consumed. Liquor was associated with thymus deterioration and thus with poorer viro-immune outcomes after HAART.[20] Sub-typing participants by alcohol consumption patterns seems to be clinically relevant and needs to be accounted for in future studies.[21]

Antiretroviral Therapy (ART) for treating HIV infection is now being turned towards HIV prevention. The Swiss Federal Commission for HIV/AIDS has declared that HIV-positive persons who are treated with ART have an undetectable viral load, and are free of co-occurring Sexually Transmitted Infections (STIs) should be considered non-infectious for sexual transmission of HIV. This study examined the implications of these assumptions in a sample of HIV-positive individuals who drink alcohol. Adherence was generally suboptimal. Less than half of people who drank alcohol and took ART met the Swiss criteria for no infectiousness. Poor adherence and prevalent STI threaten the long-term potential of using ART for prevention among alcohol drinkers.

Timely initiation of Antiretroviral Therapy (ART) is particularly important for HIV-discordant couples, because viral suppression greatly reduces the risk of transmission to the uninfected partner.[22] Antiretroviral have substantial promise for HIV-1 prevention, either as Antiretroviral Treatment (ART) for HIV-1 infected persons to reduce infectiousness or as pre-exposure prophylaxis (PrEP) for HIV-1 uninfected persons to reduce the possibility of infection with HIV-1, HIV-1 serodiscordant couples in long-term partnerships (one member is infected and the other is uninfected) are a priority for prevention interventions. Earlier ART and PrEP might both reduce HIV-1 transmission in this group, but the merits and synergies of these different approaches have not been analysed.

Methods and Findings: We constructed a mathematical model to examine the impact and cost-effectiveness of different strategies including earlier initiation of ART and/or PrEP for HIV-1 prevention for serodiscordant couple. Although, the cost or PrEP is high, the cost per infection averted is significantly offset by future savings in lifelong treatment, especially among couples with multiple partners, low condom use and a high risk of transmission. In some situations, highly effective PrEP could be cost-saving overall.

To keep couples alive and without a new infection, providing PrEP to the uninfected partner could be at least as cost-effective as initiating ART earlier in the infected partner if the annual cost of PrEP is < 40% of the annual cost of ART and PrEP is > 70% effective.[23]

In current study, the effect of ART on prevention of sexual transmission of HIV in serodiscordant couples was not evaluated. There was a higher incidence of LART in men than in women high alcohol consumption singlehood and level of education lower than secondary were associated to LART at vicariate analysis. Male sex was the only associated factor both in vicariate and multivariate analysis. Our data reinforce the need of expanding HIV testing and should assist programs to define actions promoting early entry in HIV care.[24] A significant proportion of those initiating Antiretroviral Treatment (ART) for HIV infection are lost to follow-up. Causes (Including HIV symptoms, quality of life, depression, herbal treatment and alcohol use) for discontinuing ART follow-up in predominantly rural resource - limited settings are not well understood.

The high early mortality rates indicate that patients are enrolling into ART programmes with far too advanced immunodeficiency; median CD_4 cell counts 119 (IQR = 59-163). Causes of late access to the ART programme, such as delays in health care access (Delayed health care seeking), health system delays or inappropriate treatment criteria need to be addressed. Differences in health status (Lower CD_4 cell counts and higher depression scores) should be taken into account when initiating patients on ART. Treating depression at ART initiation is recommended to improve treatment outcome.[25]

Quality of Life (QOL) among patients with HIV/AIDS has been shown to improve once treatment with Antiretroviral Therapy (ART) has been started, older age, rural dwelling, alcohol use, CD_4 count less than 200 and ART duration of less than one year were significantly associated with lower PHS scores.

Alcohol consumption has a direct association with depression in HIV infected patients on ART, extreme elevations of ALT were infrequent but minor elevations were common so that patient-linked variables such as use of alcohol intake must be taken into account for better clinical management of ART patients.

This study found a high symptom burden among HIV patients, which significantly decreased with progression on antiretroviral treatment. The utilisation of different symptom management strategies (Medical, spiritual, complementary and traditional) should be taken into consideration in HIV treatment.[26] In India, clinician should be taken into consideration all possible risk factors associated with the use of HAART in order to avoid and minimise ADRs. As initial CD_4 + T-cell count and age of patient decides the rise of CD_4 + T-cell counts with HAART. HAART should be initiated at the earliest age in order to attain maximum CD_4 + T-cell counts recovery.[27]

Little is known about the impact of combination of HIV prevention interventions for men who have sex with men (MSM) HPTN 052 randomised controlled trial, ART used in combination with condoms and counselling reduced HIV transmission by 96.4%. Evidence is growing that wider, earlier initiation of ART could reduce population-level incidence of HIV. However, the full benefits of this strategy will probably need universal access to a very early ART and excellent adherence to treatment. Challenges to this approach are substantial. First, not all HIV-infected individuals can be located, especially people with acute and early infection who are most contagious. Second, the ability of ART to prevent HIV transmission in men who have sex with men (MSM) and people who use intravenous drugs has not been shown. Indeed, the stable or increased incidence of HIV in MSM in some communities where widespread use of ART has been established emphasises the concern that not enough is known about treatment as prevention for this crucial population.[28]

There is interest in expanding ART to prevent HIV transmission, but in the group with the highest levels of ART use, men-who-have-sex-with-men (MSM), numbers of new infections diagnosed each year have not decreased as ART coverage has increased for reasons which remain unclear. ART has almost certainly exerted a limiting effect on incidence. Increased condom use should be promoted to avoid the erosion of the benefits of ART and to prevent other serious sexually transmitted infections.[29]

Compared with high-income countries, patients starting HAART in low-income settings had lower CD_4 cell counts (Median 108 cells per muL vs 234 cells per muL) were more likely to be female (51% vs 25%), and more likely to start treatment with a Non-Nucleoside Reverse Transcriptase Inhibitor (NNRTI). It remains unclear whether the natural course of Human Immunodeficiency Virus (HIV) differs in subjects infected through Injecting Drug Use (IDU). People with a history of IDU had a statistically significant faster decline in CD_4 cells.

Food incentives, medical incentives, streamlining services to minimise patient visits may decrease attrition, increased pre-ART retention, but the quality of the current evidence base is low. Few studies have investigated combined interventions or assessed the impact of interventions across the HIV cascade.

Anti-Retroviral Therapy (ART) in pregnancy is a crucial intervention in the Prevention of Mother-to-Child Transmission (PMTCT) of HIV. It is recognised that mother-to-child transmission is reduced with each week on ART.[30] All seropositive mothers should be assessed for ART eligibility, if not they require ARV prophylaxis without any intervention, risk of HIV transmission from pregnant women to her child is around 20 - 45%. Women conceiving on an effective HAART regimen should continue ART ante-partum, intra-partum and post-partum. The initial comparative immunological advantage possessed by fertile women before they become pregnant is subsequently lost as a result of their pregnancy with a decrease in immunoglobulin, complement and cell mediated immunity level during pregnancy. Women should be informed about the potential negative effect of pregnancy on their immunological status and should be offered contraception. In resource-limited settings, women

determined to become pregnant should be given priority for ART if eligible.

Rural women living with AIDS (WLA) on antiretroviral therapy self-reported a high prevalence of physical symptoms, high levels of depressive symptoms and major barriers to accessing health care. CD_4 levels, body weight and basal metabolic rate were also low. While the rural and urban WLA faced similar health care challenges, the demographic characteristics of the rural women may make them more vulnerable as they are less adherent to ART and slimmer than their urban counterparts.

Little is known about the variability of CD_4 counts in the general population. CD_4 counts are primarily determined by sex in HIV-uninfected adults and by sex, age and duration of antiretroviral treatment in HIV-infected adults. Lower CD_4 counts at ART initiation in men could be a consequence of lower CD_4 cells counts before HIV acquisition in multivariable regression analysis, women had 19.4% (95% Confidence Interval (CI) 16.1-22.9) higher CD_4 counts than men, controlling for age, HIV status, urban/rural residence, household wealth, education, BMI, self-reported tuberculosis, high blood pressure, other chronic illnesses and sample processing delay.

A baseline genotype HIV test for all patients of acute HIV infection may be necessary, though they may not be opting for therapy because anti-retroviral drugs are accessible since more than 25 years and 6 - 16% of individuals who are newly infected might have acquired the HIV strains, which are drug resistant.

CONCLUSION

1. In this study, there were 100 patients with CD_4 count of less than 350/uL who were started on highly active anti-retroviral therapy and followed up, whose followup CD_4 count was done after 6 months of HAART and analysed to evaluate the impact of HAART on CD_4 cell count.
2. CD_4 cell count is mandatory in all the patients who are confirmed as HIV/AIDS, irrespective of the clinical stage, since the clinical stage and the CD_4 count need not correlate.
3. Patients were classified into eight groups as per the initial CD_4 cell count.

CD_4 Count	Male	Female
< 50	9	5
51 - 100	15	5
101 - 150	10	5
151 - 200	10	4
201 - 250	6	7
251 - 300	5	7
301 - 350	3	7
> 350	1	1

4. In these 100 patients, 6 months followup CD_4 count was analysed and it showed an improvement by a mean of 180.28 cells/mm3, which was also statistically significant when analysed by using the paired 't' test that showed a 'p' value of < 0.001.
5. When the groups were analysed individually all the groups age wise 5, initial CD4 count group wise, gender wise showed statistically significant improvement in CD4 counts post 6-month therapy except in groups > 60 years and initial CD4 count > 350 group where improvement was not significant.
6. HAART has improved the BMI/weight reflecting improvement in general condition and well-being of the patients. This could also be attributed to the nutritional advice and intervention.
7. HAART decreases the incidence of opportunistic infections as evidenced by improved clinical stages.
8. Tuberculosis was the most common opportunistic infection.
9. CD4 cell count monitoring is very important and could be done every 3 months, but for resource constraints it is being done every 6 months.

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